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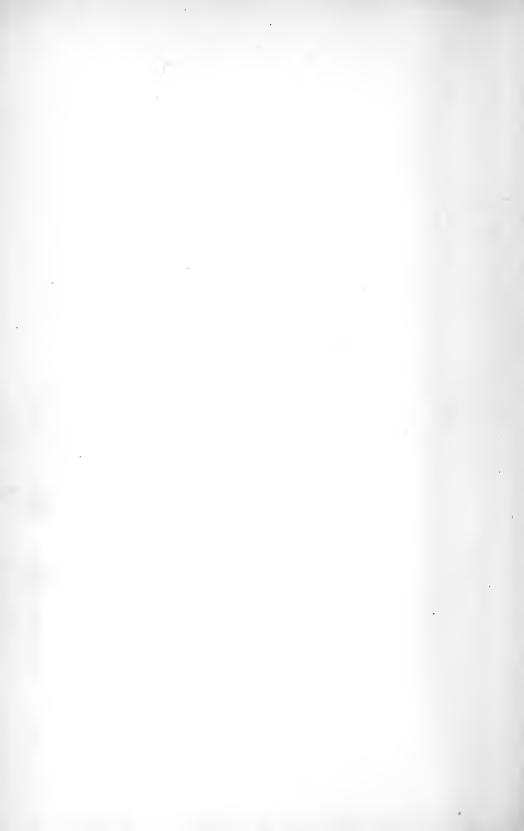
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#### A

## TEXT-BOOK OF HISTOLOGY

FREDERICK R. BAILEY, A. M., M. D.

THIRD REVISED EDITION
PROFUSELY ILLUSTRATED

NEW YORK
WILLIAM WOOD AND COMPANY
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#### PREFACE TO THE THIRD EDITION.

THE very gratifying approval which the first and second editions of the Text-book received has made it seem unwise to attempt any change in the general plan and scope of the work as outlined in the preface to the first edition. The text has been thoroughly revised. some parts of it practically rewritten. Some figures have been replaced by new ones and a considerable number of new figures, some original, others borrowed, have been added. For the latter the writer wishes to acknowledge his obligations. To Mr. A. M. Miller the writer is indebted for many valuable criticisms and suggestions. chapter on the nervous system has been rewritten by Dr. Oliver S. Strong. For Dr. Strong's careful and painstaking work on this chapter. for his thoroughly original treatment of his subject, and for the original drawings and photographs in this chapter, the author wishes to express his most grateful appreciation. Dr. Strong wishes to renew the acknowledgment, made in the preface to Bailey and Miller's Embryology, of indebtedness to Dr. Adolf Meyer for many ideas and terms found valuable in the preparation of the chapter on the nervous system. There may be mentioned here the terms segmental and suprasegmental to denote an important distinction between certain parts of the nervous system.

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#### PREFACE TO THE FIRST EDITION.

THE primary aim of the writer in the preparation of these pages has been to give to the student of medicine a text-book of histology for use in connection with practical laboratory instruction, and especially to furnish to the instructor of histology a satisfactory manual for classroom teaching. With these objects in view, the text has been made as concise as possible consistent with clearness, and the writer has attempted to make the more essential elements stand out somewhat from the necessarily accompanying details.

It has been impossible to accomplish this without some sacrifice of uniformity of treatment and of logical sequence. This is especially noticeable in the chapter on the nervous system, which has been made much fuller and more "practical" than is usual. The author's reason for the method of treatment there adopted and for the considerable amount of anatomy which this chapter contains being the apparent success the method has met with in the teaching of this always difficult subject to students.

The chapter on general technic is intended to furnish the student with only the more essential laboratory methods. For special and more elaborate methods the student is referred to the special works on technic mentioned at the close of the chapter. The special technic given in connection with the different tissues and organs is in most cases such as can be conveniently used for the preparation of class sections.

The original illustrations are from drawings by Mr. A. M. Miller, to whom the writer is greatly indebted for his careful and accurate work. The uselessness of redrawing perfectly satisfactory illustrations has led the writer to borrow freely from various sources, each cut being duly accredited to the work from which it has been taken. For

vi PREFACE.

all of these the author wishes to express his appreciation and obligation. He is also deeply indebted to Dr. O. S. Strong for his careful review and criticism of the chapter on the nervous system and for his supervision of the drawing of Figs. 263 and 264; to Dr. G. C. Freeborn, his predecessor as Instructor of Histology at the College of Physicians and Surgeons, for many valuable suggestions; and to Dr. T. Mitchell Prudden for his careful and critical review of the author's copy.

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### PART I. HISTOLOGICAL TECHNIC.



#### CHAPTER I.

#### GENERAL TECHNIC.

CERTAIN body fluids, e.g., blood, urine, etc., may be examined by simply placing them on a slide under a cover glass. A few tissues, e.g., thin membranes, such as the omentum and the mesentery, may be examined fresh in some such inert medium as blood serum or normal salt solution (0.75-per-cent. aqueous solution sodium chlorid). For such examination the tissue is immersed in the salt solution on a slide and covered with a cover-glass. Most tissues and organs, however, require much more elaborate preparation to render them suitable for microscopic examination. Tissues too dense and thick to be readily seen through with the microscope must be so treated as to make them transparent. This is accomplished either by pulling the tissue apart into fine shreds, teasing, or by cutting it into thin slices, section cutting. Some tissues admit of teasing in a fresh condition; others can be satisfactorily teased only after they have been subjected to the action of a chemical which breaks down the substance holding the tissue elements together, maceration. Fresh tissue can rarely be cut into sections sufficiently thin for microscopic examination. It must first be treated in such a manner as to preserve as nearly as possible the living tissue relations, fixation. If too soft for section cutting it must next be put through a process known as hardening. If, however, as in the case of bone, the tissue is too hard, it must be softened by dissolving out the mineral salts, decalcification. If very thin sections are to be cut, it is further necessary to impregnate the tissue with some fluid substance which will harden in the tissue and give to the mass a firm, even consistency. This is known as embedding.

Furthermore, most tissue elements have refractive indices which are so similar that their differentiation under the microscope is often extremely difficult. To overcome this difficulty, recourse is had to staining the tissue with dyes which have an affinity for certain only of the tissue elements, or which stain different elements with different degrees of intensity. This is known as *differential* or *selective staining*.

The final step in the process is the *mounting* of the specimen, after which it is ready for microscopic study.

Only the more common procedures used in the preparation of tissues for microscopic study are described in this section. At the end of each section are given the technical methods most satisfactory for the demonstration of the tissues described in that section. For other methods the student is referred to special works upon microscopic technic.

#### Dissociation of Tissue Elements.

This method of preparing tissues for microscopic study has only a limited application, most specimens being preferably fixed, and cut into thin sections. Certain of the structural features of such tissues as nerves, muscle, and epithelium, which have but little intercellular substance may be well demonstrated by dissociation.

This is accomplished by (1) teasing, or (2) maceration, or both.

- (1) Teasing.—This consists in pulling apart fresh or preserved tissues by means of teasing needles. Instructive specimens of such tissues as muscle and nerve may be obtained in this way.
- (2) MACERATION.—This is the subjecting of a tissue to the action of some chemical which breaks down the substance uniting the tissue elements, thus allowing them either to fall apart or to be more easily dissociated by teasing. The most commonly used macerating fluids are:
- (a) Ranvier's Alcohol (33-per-cent., made by adding 35 c.c. of 96-per-cent. alcohol to 65 c.c. of water).—Bits of fresh tissue are placed in this fluid for from twenty-four to forty-eight hours. The cells may then be easily separated by shaking or by teasing. Ranvier's alcohol is an especially satisfactory macerating fluid for epithelia.
- (b) Formaldehyde, in very dilute solutions (0.2- to 0.4-per-cent. commercial formalin¹).—Tissues should remain in the formaldehyde solution from twenty-four to forty-eight hours. This is also especially useful for dissociating epithelial cells.
- (c) Sodium or Potassium Hydrate (30- to 35-per-cent. aqueous solution).—From twenty minutes to an hour is usually sufficient to cause the tissue elements to fall apart or to be readily pulled apart with the teasing needles. If it is at any time desirable to stop the action of the caustic alkali, this may be accomplished by neutralizing

<sup>&</sup>lt;sup>1</sup>Commerical formalin is a 40-per-cent. solution of formaldehyde gas in water.

with glacial acetic acid or by replacing the alkali with a 6o-per-cent. aqueous solution of potassium acetate. The specimens may then be preserved in the potassium-acetate solution, in glycerin, or in 5o-per-cent. alcohol. This dissociating fluid is largely used for muscle cells and fibres.

(d) Nitric acid (10- to 20-per-cent. aqueous solution).—This is especially useful for dissociating involuntary and voluntary muscle.

After any of the above procedures, the macerating fluid containing the tissue elements should be placed in a long tube, allowed to stand for a time and the fluid decanted. Water is then poured into the tube, the tissues allowed to settle and the water poured off, this being repeated until all trace of macerating fluid is removed. The tissue elements may then be preserved or mounted in glycerin or in glycerin jelly. It is frequently advisable to stain the tissues. For this purpose alum-carmin (p. 17) is especially satisfactory. (For details see technic 1, p. 109 and technic 2, p. 109). After staining and washing, the tissues may be preserved or mounted in glycerin, eosin glycerin, or glycerin jelly. It frequently happens that on examining dissociated tissue elements after mounting, the bits of tissue are still too large. This may be remedied by gently tapping on the cover-glass with a lead pencil.

#### PREPARATION OF SECTIONS.

#### I. Fixation.

Fixation is the first step in the preparation of sections of tissues for microscopic study. Its object is to so preserve the tissues that they retain as nearly as possible the same structure and relation which they had during life. Fixation of such a thin film of tissue as a blood smear may be accomplished by heating. A blood smear or even small pieces of tissue may be fixed by exposure to certain chemical vapors as, e.g., the vapor of formalin or of osmic acid. Fixation is, however, usually accomplished by means of chemicals in solution, the solution being known as a fixing agent or fixative. Pieces of tissue are immersed in the fixative and allowed to remain there until fixation is complete. The length of time required depends upon the character of the tissue and upon the fixative used. The pieces of tissue should be small, and large quantities of the fixative should be used. It may be necessary to change the fluid a number of times, in order to keep it up to the proper strength.

Organs and even bodies may be fixed *in toto* by injecting the fixative through an artery and allowing it to escape through the veins. After the injection, the whole specimen should be placed in a large quantity of the same fixative. This method fills the entire vascular system including the capillaries with the fixative, thus bringing the latter into very prompt and close contact with the tissue elements. The result is a very rapid and accurate fixation which is especially valuable where it is necessary to preserve the topographic relations of various parts of an organ or a body.

A mercuric chlorid solution (p. 7) followed immediately by strong alcohol makes a very good injection fixative. Satisfactory fixation is largely dependent upon the freshness of the tissue when placed in the fixative. The following are the fixatives in most common use:

- (1) Strong Alcohol (96-per-cent.).—This is a rapid fixative and should be used on small pieces of tissue. The time required is from six to twenty-four hours, though tissues may remain longer without injury. The alcohol should be changed after two or three hours. This fixative should not be used where fine histological detail is desired, since it causes some shrinkage. One advantage in its use is the fact that tissues are hardened and ready for embedding at the end of fixation.
- (2) Dilute Alcohol (30-per-cent. to 80-per-cent.).—This, as a rule, gives unsatisfactory results, causing much shrinkage of the tissue elements.
- (3) Formaldehyde (2-per-cent. to 10-per-cent. aqueous solution).— Formalin is rapid in its action and probably has better penetrating qualities than any other fixative. For general purposes a 4-per-cent. solution (1 part commercial formalin to 9 parts water) should be used. This fixes in from six to twenty-four hours. The results after formal-dehyde are not always good, owing to the fact that it has little hardening power, and the subsequent action of alcohol is likely to cause some distortion of the tissues. It acts better when combined with other fixatives than when used alone. (See Orth's fluid.)

#### (4) Müller's Fluid.

Potassium bichromate, 2.5 gm.
Sodium sulphate, 1.0 gm.
Water, 100.0 c.c.

This fluid gives very good results, but is extremely slow in its action, requiring from a week to several months. Fairly large pieces of tis-

sue may be fixed, but in all cases large quantities of the fixative should be used and frequently renewed.

#### (5) Orth's Fluid.

Müller's fluid (double strength),
Formaldehyde, 8-per-cent.,

Equal parts.

This is one of the best general fixatives. Its action is similar to that of Müller's fluid but much more rapid, fixation being accomplished in from twenty-four to forty-eight hours, though specimens may remain in the fluid several days without disadvantage. Fairly large pieces of tissue may be fixed with good results. The fixative should be changed after a few hours. Fixation with Orth's fluid gives an excellent basis for a hæmatoxylin-eosin stain (see (1), p. 18.) The fixative should always be freshly prepared. It is convenient to keep the 8-per-cent. formaldehyde solution and the double-strength Müller's fluid in stock. Orth's fluid is then prepared by simply taking equal parts of each.

(6) Osmic Acid.—This, in a 1-per-cent. aqueous solution, is a quick and excellent fixative of poor penetrating power. Very small pieces of tissue must therefore be used. They should remain in the fluid from twelve to twenty-four hours. Osmic acid stains fat and myelin black and is consequently useful in demonstrating their presence in tissues. Fixation should take place in the dark.

#### (7) Flemming's Fluid.

Chromic acid, 1-per-cent. aqueous solution,	25	c.c.
Osmic acid, 1-per-cent. aqueous solution,	10	c.c.
Glacial acetic acid, 1-per-cent. aqueous solution,	10	c.c.
Water,	5.5	c.c.

Flemming's fluid is one of the best fixatives for nuclear structures, and is of especial value in demonstrating mitotic figures. Very small pieces of tissue should be placed in the fixative, where they remain for from twenty-four hours to three days. The solution should be freshly made as required, or a stock solution without the osmic acid may be kept, and the latter added at the time of using.

(8) Mercuric Chlorid.—This may be used either in saturated aqueous solution or in saturated solution in 0.75-per-cent. salt solution. Fixation is complete in from twelve to twenty-four hours, and is usually very satisfactory.

A saturated solution of mercuric chlorid in 5-per-cent. aqueous solution of glacial acetic acid also gives good results.

#### (9) Zenker's Fluid.

Potassium bichromate,	2.5 gm.
Sodium sulphate,	1.0 gm.
Mercuric chlorid,	5.0 gm.
Glacial acetic acid,	5.0 c.c.
Water,	100.0 C.C.

This fluid should be freshly made, or the salts may be kept in solution and the acetic acid added at time of using.

Zenker's fluid is a good general fixative, but usually causes some shrinkage of the tissue elements. Fixation requires from six to twenty-four hours. The most serious drawback to Zenker's fluid is the fact that the mercuric chlorid sometimes produces dark, irregular precipitates in the tissues. This may be remedied, however, by the use of iodine and iodid of potassium in the hardening process (see Hardening, p. 9).

(10) Picric acid is an excellent fixative for cytoplasm. It may be used in: (a) Saturated aqueous solution; (b) saturated solution of picric acid in 1-per-cent. aqueous solution of acetic acid; (c) saturated solution of picric acid in 2-per-cent. aqueous solution of sulphuric acid.

#### II. Hardening.

Most fixatives are also hardening agents if their action is prolonged. This is, however, often detrimental. It is, therefore, customary, after fixation is complete, to carry the specimens, with or without washing, through successively stronger grades of alcohol for the purpose of hardening the tissues. For general histological purposes the specimens may be transferred directly to 70-per-cent. or 80-per-cent. alcohol, which should be changed once or twice. In the case of delicate tissues the first grade of alcohol should be 40-per-cent. or 50-per-cent., the second 70-per-cent., and the third 80-per-cent. The specimens should remain in each grade from twelve to twenty-four hours.

Washing the tissues after fixation is not a matter of indifference. In some cases water should be used, while in other cases water is liable to undo the action of the fixative, in which cases alcohol must be used for washing.

After fixation in alcohol no washing, of course, is necessary. Specimens fixed in strong alcohol are embedded immediately (see Embedding, p. 10), or preserved (see Preserving, p. 9). After fixation in dilute

alcohol the specimens are passed through the graded alcohols up to 80-per-cent.

After fixation in formaldehyde solutions the specimens are passed directly through the graded alcohols without washing in water. Specimens fixed in any solution containing picric acid should not be washed in water, but passed directly through the alcohols; and it is usually necessary to change each grade in order to wash out the picric acid.

Specimens fixed in osmic acid or any solution containing osmic acid should be washed in running water before being passed through the graded alcohols. After solutions containing potassium bichromate the specimens should be washed in water sufficiently to remove the excess of bichromate, though too prolonged washing seems to be detrimental. A precipitate forms in the alcohols, but this apparently does no harm.

After mercuric chlorid or Zenker fixation the washing may be done either in water or in alcohol. To avoid precipitates in the tissues add a small quantity of an iodin solution (equal parts tincture iodin and 10-per-cent. aqueous solution potassium iodid) to any of the grades of alcohol. As the alcohol becomes clear more of the solution is added until the alcohol remains slightly tinged.

#### III. Preserving.

Hardened tissues are usually preserved in 80-per-cent. alcohol. Formalin in aqueous solutions of 1-per-cent. to 10-per-cent. is also used as a preservative. In either case, when it is necessary to preserve the specimens for a considerable length of time (several months or longer), the tissues are likely to lose their staining qualities to a certain extent. Preserving the specimens in equal parts of strong alcohol, glycerin, and distilled water is successful as a partial remedy for this.

#### IV. Decalcifying.

Tissues containing lime salts, like bones and teeth, must have the lime salts dissolved out before sections can be cut. This process is known as *decalcification*.

Tissues to be decalcified must be first fixed and hardened. Fixation in Orth's fluid and hardening in graded alcohols give good results. After hardening, the tissue is washed in water and placed in one of the

following decalcifying fluids. The quantity of fluid should always be large and the fluid frequently changed. The completion of decalcification can be determined by passing a needle through the specimen or by cutting it with a scalpel. The time required varies with the size and hardness of the specimen and the decalcifying fluid used.

(I) Hydrochloric Acid.—This may be used in aqueous solutions of from 0.5-per-cent. to 5-per-cent. A very satisfactory decalcifying mixture is that known as Ebner's hydrochloric-salt solution. It consists of:

Sodium chlorid, saturated aqueous solution, 1 part.
Water, 2 parts.
Hydrochloric acid, sufficient to make a from 2-per-cent. to 5-per-cent. solution.

The addition of the salt prevents swelling of the tissue. This fluid is slow in acting and should be changed every day. When decalcification is complete, the specimen is washed in sufficient changes of water to remove all trace of acid. This may be quickly accomplished by the addition of a little ammonium hydrate to the water. The specimen is then carried through graded alcohols.

- (2) Nitric Acid.—This is less used than the preceding. The strength should be from 1-per-cent. to 10-per-cent. aqueous solution. Weak solutions (1-per-cent. to 2-per-cent.) will decalcify small feetal bones in from three to twelve days. For larger bones stronger solutions and longer time are required.
- (3) Small bones may be satisfactorily decalcified in *Zenker's fluid* (see Fixatives, page 8), or in the following:

Picric acid, 1 part.
Chromic acid, 1 part.
Glacial acetic acid, 5 parts.

#### V. Embedding.

Most hardened tissues are still not firm enough to be cut into the thin sections suitable for microscopic study. In order to support the tissue elements and render them more firm for section cutting, recourse is had to embedding. This consists in impregnating the tissues with some substance which is liquid when the tissues are placed in it, but which can be made to solidify throughout the tissues. In this way the tissue elements are held firmly in place. The embedding substances most used are celloidin and paraffin.

#### CELLOIDIN EMBEDDING.

(1) Alcohol-Ether Celloidin.—Two solutions should be made. Solution No. 2. Thick celloidin—a 5-per-cent. solution of celloidin in equal parts 96-per-cent. alcohol and ether.

Solution No 1. Thin celloidin—made by diluting solution No. 2 with an equal volume of equal parts of alcohol and ether.

The hardened tissues are placed successively in:

Strong alcohol (96-per-cent.) twelve to twenty-four hours, to dehydrate.

Equal parts alcohol and ether, twelve to twenty-four hours.

Thin celloidin, twenty-four hours to several days.

Thick celloidin, twenty-four hours or longer.

The exact time tissues should remain in the different grades of celloidin depends upon the character of the tissue, the size of the specimen, and the thinness of section desired. Many tissues may be advantageously left for weeks in thin celloidin.

The specimen must now be "blocked" and the celloidin hardened. By blocking is meant fastening the specimen impregnated with celloidin to a block of wood or other suitable material which may be clamped in the microtome (see Section Cutting, p. 13). The specimen may be taken from the thick celloidin (considerable of the latter adhering to the specimen), quickly pressed upon a block of wood or vulcanized fibre, allowed to harden five to ten minutes in air, and then immersed in 80-per-cent. alcohol. The alcohol gives an even hardening of the celloidin, attaching the specimen firmly to the block. Another method, and one by which very even-shaped blocks may be obtained, is to place the specimen from the thick celloidin into a little paper box (made by folding paper over a wooden block), slightly larger than the specimen, and covering with thick celloidin. The celloidin should dry slowly under a bell-jar for from two to twelve hours, according to the amount of celloidin, after which it should be immersed in 80-per-cent. alcohol and the paper pulled off. Such a block may be cut into any desired shape. It is attached to the wooden or vulcanized block by dipping for a moment in thick celloidin, and then pressing firmly down upon the block. After five to ten minutes' drving in air it is transferred to 80-per-cent. alcohol.

Old, hard, celloidin-embedded specimens are sometimes difficult to attach to blocks. This usually may be accomplished by first thoroughly drying the specimen and then dipping it in equal parts alcohol and ether for a few minutes. This softens the surface of the celloidin, after which the specimen is dipped in thick celloidin and blocked. Embedded or blocked specimens can be kept in 80-per-cent. alcohol. After several months, however, the celloidin is likely to become too soft for good section cutting. In that case the specimens can be readily re-embedded by dissolving out the old celloidin with alcohol and ether and putting them again through the regular embedding process.

(2) CLOVE-OIL CELLOIDIN.—A more rapid impregnation of the tissue may be obtained by means of what is known as clove-oil celloidin.

Celloidin,	30	gm.
Clove oil,	100	c.c.
Ether,	400	c.c.
Alcohol, absolute,	20	c.c.

The celloidin is first placed in a jar and the clove oil and ether added. From two to four days are required for solution of the celloidin. During this time the jar should be shaken several times. After the celloidin is dissolved the absolute alcohol is added and the solution is ready for use.

The specimen must be thoroughly dehydrated, placed in alcohol and ether or pure ether for a few hours, and then transferred to the clove-oil celloidin. From six to twelve hours is sufficient to impregnate small pieces of tissue. The tissue is now taken from the celloidin, placed directly upon a wooden or vulcanized block, and immersed in chloroform. The celloidin hardens in about an hour, and is then ready for sectioning. The specimen is very firm, and very thin sections can be cut.

A disadvantage in clove-oil celloidin is that neither the blocks nor the sections can be kept permanently in alcohol, as can those embedded in alcohol-ether celloidin. They may, however, be kept for several weeks in pure chloroform.

#### PARAFFIN EMBEDDING.

For paraffin embedding a thermostat or paraffin oven is necessary in order that a constant temperature may be maintained. The temperature should be about 56° C. Pure paraffin, the melting-point of which is from 50° to 55° C., is used. In very warm weather it may be necessary to add to this a little paraffin, the melting-point of which is 62° C.

The hardened tissue is first put in 96-per-cent. alcohol for from twelve to twenty-four hours, and then completely dehydrated by putting in absolute alcohol for the same length of time, or less for small specimens. It is then transferred to some solvent of paraffin. Some of the solvents used are xylol, oil of cedarwood, chloroform, and toluol. Of these the best are perhaps xylol and oil of cedarwood. The tissue should remain in either of these for several hours, or until the tissue becomes more or less transparent. It is then placed in melted paraffin, in the paraffin oven, for from one to three hours, according to the size and density of the specimen. This allows the tissues to become impregnated with the melted paraffin. The paraffin should be changed twice.

In case of very delicate tissues it is well to transfer them from the absolute alcohol to a mixture of equal parts absolute alcohol and xylol for a short time before putting them into the pure xylol. In the same way a mixture of equal parts xylol and paraffin may be used before putting the tissues into pure paraffin.

For hardening the paraffin in and around the tissue a very convenient apparatus consists of a plate of glass and several L-shaped pieces of iron or lead. Two of these are placed on the glass plate in such a manner as to enclose a space of the desired size. Into this are placed the specimen and sufficient melted paraffin to cover it. Both glass and irons should be smeared with glycerin to prevent the paraffin from adhering, and should be as cold as possible, so that the paraffin may harden quickly. The same paper boxes described under celloidin embedding may also be used for paraffin. Another good method for small pieces of tissue is to place the specimen in paraffin in an ordinary watch-glass which has been coated with glycerin. Both paper-box and watch-glass specimens are immersed in cold water as soon as the surface of the paraffin has become hard. After the paraffin has hardened any excess may be cut away with a knife.

Paraffin-embedded specimens may be kept indefinitely in air. For section cutting, the block of paraffin is attached to a block of wood or of vulcanite or to the metallic block-holder of the microtome. This is done by heating the block-holder, pressing the paraffin block firmly upon it, and then dipping the whole into cold water.

# VI. Section Cutting.

The older method of making free-hand sections with a razor has been almost completely superseded by the use of a cutting instrument known as the *microtome*. This consists essentially of a clamp for holding the specimen and a microtome knife or razor. The two are so arranged that when knife and specimen meet, a section of any desired thickness may be cut.

The technic of section cutting differs according to whether the specimen is embedded in celloidin or in paraffin.

In cutting celloidin sections the knife is so adjusted that it passes obliquely through the specimen, as much as possible of the cutting edge being used. The knife is kept flooded with 80-per-cent. alcohol and the specimens are removed by means of a camel's-hair brush to a dish of 80-per-cent. alcohol where they may be kept for some time if desired. When celloidin sections tear or when very thin sections are desired, it is often of advantage to paint the surface of the block, after cutting each section, with a coat of very thin celloidin.

Celloidin sections are usually not thinner than  $10\mu$ , although under favorable conditions sections  $5\mu^1$  or even  $3\mu$  in thickness may be obtained.

In cutting paraffin sections the knife is kept dry and is passed not obliquely but straight through the specimen, only a small part of the cutting edge being used. An exception is made in the case of very large paraffin sections, where an oblique knife is used. Sections are removed from the knife by a dry or slightly moistened brush. If not desired for immediate use the sections may be conveniently kept for a short time on a piece of smooth paper. If sections curl they may be flattened by floating on warm 30-per-cent. alcohol or on warm water.

Paraffin sections may be so cut that the edges of the sections adhere. Long series or "ribbons" of sections may thus be secured. This is of decided advantage when serial sections are desired. Failure of the sections to cut evenly or to adhere in ribbons, is usually due to the paraffin being too hard and brittle, which of course is due to its low temperature. If much section cutting is to be done, the operator will find himself amply repaid by having the room-temperature fairly high. In case paraffin of a melting-point of 50° to 55° C. is used, a room temperature of 73° to 75° F. will greatly facilitate the work. Where it is not possible to have a high room temperature, recourse may be had to coating the surface of the block with a paraffin of lower melting-point than that used for the embedding. A similar effect

 $<sup>^1\</sup>mu=$  micromillimeter or micron =  $_{1\,\theta\,\overline{\theta}\,\overline{\theta}}$  of a millimeter = microscopic unit of measure = about  $_{2\,\overline{5}\,\overline{\theta}\,\overline{\theta}}$  of an inch.

may be obtained by holding a heated metal plate or bar near the block until the paraffin is slightly softened. This process may be repeated as often as necessary.

In addition to the fact that ribbon series can be cut in paraffin, this embedding substance also has the advantage over celloidin that thinner sections can be obtained. On the other hand, celloidin embedding produces less shrinkage of the tissues than paraffin embedding with the accompanying heat.

## VII. Staining.

This is for the purpose of more readily distinguishing the different tissue elements from one another by their reactions to certain dyes.

Based upon their action upon the different tissue elements, stains may be classified as (1) nuclear dyes, which stain nuclear structures; and (2) plasma dyes, which stain the cell body or cytoplasm. Plasma dyes, also, as a rule, stain the intercellular tissue elements, and are therefore known as diffuse stains.

The dyes most frequently used for staining tissues are:

- I. Nuclear dyes: (a) Hæmatoxylin and its active principle, hæmatein; (b) carmine and its active principle, carminic acid; (c) basic aniline dyes.
- II. Plasma dyes: (a) Eosin; (b) neutral carmine, (c) picric acid; (d) acid aniline dyes.
  - I. Nuclear Dyes.—(a) H.EMATOXYLIN.
  - 1. Gage's Hæmatoxylin.

Ammonia or potash alum,

7 · 5 gm.

Ammonia or potash a Distilled water,

200.0 C.C.

Boil for 10 minutes to sterilize; cool and add the following solution:

Hæmatoxylin crystals,

o.1 gm.

Alcohol 95-per-cent.,

10.0 C.C.

Four grams chloral hydrate are then added to the mixture to prevent growth of germs.

This dye may be used in full strength or diluted with alum water. It stains in from two to five minutes.

2. Delafield's Hæmatoxylin.

Hæmatoxylin crystals, Alcohol,

ı gm.

6 c.c.

Ammonia alum, saturated aqueous solution,

100 C.C.

The hæmatoxylin should be first dissolved in the alcohol and then added to the alum solution. The mixture should next be allowed to stand in the light for from seven to ten days to ripen. It is then filtered, and to the filtrate are added:

Glycerin, 25 c.c. Wood naphtha, 25 c.c.

The mixture is again allowed to stand for from two to four days and filtered. It may be used full strength or diluted with equal parts of water. It stains in from two to five minutes.

# 3. Heidenhain's Hæmatoxylin.

Hæmatoxylin crystals, 1 gm. Water, 100 c.c.

Sections are first placed for from four to eight hours in a 2.5-per-cent. aqueous solution of ammonium sulphate of iron. They are then washed in water and transferred to the hæmatoxylin solution until they are intensely blue or black (usually several hours). The sections are now washed in water and differentiated by again placing in the iron solution till they have a light grayish color. After this they are thoroughly washed in water.

## 4. Mayer's Hæmalum.

Hæmatein, 1 gm.
Alcohol, 50 c.c.
Ammonia alum, 5-per-cent. aqueous solution, 1,000 c.c.

The hæmatein is first dissolved in the alcohol, after which the alum is added. This dye does not require any ripening, and is thus available for immediate use. It is a rapid nuclear dye usually requiring not more than from three to five minutes.

5. A combination of Gage's and Mayer's formulæ makes a very satisfactory nuclear dye.

Hæmatein, 5 gm.
Alcohol, 50 c.c.
Chloral hydrate,
Ammonia alum, 5-per-cent. aqueous solution (sterilized), 1,000 c.c.

The hæmatein is first dissolved in the alcohol and then added with the chloral hydrate to the alum solution. This solution is used in full strength and stains in from three to five minutes.

## 6. Weigert's Hæmatoxylin.

Two stock solutions should be made up as follows:

A. 1-per-cent. hæmatoxylin, in 96-per-cent. alcohol.

B. Hydrochloric acid (sp. gr. 1.126),	10	C.C.
Ferric chloride, 30-per-cent.,	40	c.c.
Distilled water,	950	c.c.

For use, mix equal parts of A and B. The mixture will keep two or three days. This is a rapid stain usually requiring not more than a minute. A more brilliant nuclear stain may be obtained by overstaining and then decolorizing. After the stain wash the sections in water and then decolorize to the proper degree in weakly acidulated water. To stop the action of the acid the sections should be dipped in water made slightly alkaline with ammonia. This is an excellent stain and gives brilliant results. It is especially good in cases where the material has become old and lost its affinity for ordinary hæmatoxylin stains.

## (b) Alum-Carmine.

Carmine,	2	gm.
Alum,	5	gm.
Carbolic acid,	2	gm.
Water,	100	c.c.

The alum is first dissolved in the 100 c.c. of warm distilled water, after which the carmine is added. This mixture is then boiled for twenty minutes, allowed to cool, and filtered. The carbolic acid is then added. This is a slow-acting pure nuclear dye.

(c) Basic Aniline Dyes—gentian violet, methyl violet, methyl green, methyl blue, toluidin blue, fuchsin, thionin, safranin, etc.

These are best kept in stock in saturated alcoholic solutions. When desired to use, a few drops of the alcoholic solution are added to distilled water. No rule as to exact proportions can be given, as these depend upon the material, the fixation, and the intensity of stain desired.

# II. Plasma Dyes.—(a) Eosin.

This is prepared as follows: Water-soluble cosin is dissolved in water to saturation. It is then precipitated by hydrochloric acid and the precipitate washed with water upon a filter until the filtrate is tinged with cosin. After drying, the precipitate is dissolved in strong alcohol, 1 gm. of eosin to 1,500 c.c. of alcohol. This is a rapid plasma stain.

## (b) NEUTRAL CARMINE.

Carmine,	I	gm.
Liquor ammonii caustici,	5	c.c.
Distilled water,	50	c.c.

The last two ingredients are first mixed, and the carmine then added. This solution is allowed to remain in an open vessel for about three days, or until the odor of ammonia has disappeared, after which it is filtered.

- (c) Picric Acid—used mainly as the plasma-staining element of such a staining mixture as picro-acid-fuchsin.
- (d) ACID ANILINE DYES.—Of these, acid fuchsin, erythrosin, and orange G are most used. They may be prepared and kept in stock in the same manner as the basic aniline dyes (see above). Erythrosin is of especial value for sections which take the eosin stain poorly.

#### STAINING SECTIONS.

It is often of advantage to stain the different tissue elements different colors. This may be accomplished either by staining successively with several dyes, or by a single staining with a mixture of dyes. The following are the methods in most common use:

(1) STAINING DOUBLE WITH HÆMATOXYLIN AND EOSIN.—Sections are first washed in water. They are then stained with hæmatoxylin (solutions 1, 2, 4, 5, or 6, pp. 15–17) from one to five minutes. After being thoroughly washed in water, they are dehydrated in strong alcohol and transferred to the alcoholic eosin solution (page 17). Most sections stain in from two to five minutes. By this method nuclei are stained blue or purple, cell bodies and intercellular substances red.

Very often a more brilliant staining may be accomplished as follows: Overstain in hæmatoxylin and wash thoroughly in water; decolorize in water slightly acidulated (8 or 10 drops of hydrochloric acid to 100 c.c. of water) until only the nuclei retain the stain; wash in water which has been made slightly alkaline with ammonium hydrate; then stain with eosin as usual.

# (2) STAINING WITH PICRO-ACID-FUCHSIN.

Acid-fuchsin, 1-per-cent. aqueous solution,	5	c.c.
Picric acid, saturated aqueous solution,	100	c.c.

This solution usually stains in from one to three minutes. Occasionally a longer staining is required. Cell bodies including muscle

cells and fibres are stained yellow by the picric acid, connectivetissue fibres red by the fuchsin. After staining, the sections are washed in distilled water.

(3) Triple Staining with Hæmatoxylin and Picro-acid-fuchsin.—This is the same as the preceding except that before staining with picro-acid-fuchsin, the sections are overstained in hæmatoxylin (solutions 1, 2, 4, 5, or 6, pp. 15–17). The usual purple of hæmatoxylin-stained nuclei is changed to brown by the action of the picric acid. Care should be taken that the sections do not remain too long in the picro-acid-fuchsin, or the hæmatoxylin may be completely removed. After staining, sections are washed in distilled water and transferred to 96-per-cent. alcohol.

If sections overstain with fuchsin, the staining solution may be diluted with water; if sections are understained with fuchsin, more fuchsin may be added. If the picric-acid stain is not sufficiently intense, the 96-per-cent. alcohol should be tinged with picric acid.

## (4) STAINING WITH PICRO-CARMINE.

Ammonium carminate,	I	gm.
Distilled water,	35	c.c.
Picric acid, saturated aqueous solution,	15	c.c.

The ammonium carminate is first dissolved in the water, after which the saturated aqueous solution of picric acid is added with constant stirring. The mixture is then allowed to stand in an open vessel for two days, when it is filtered. This fluid stains nuclei and connective tissue red, cell protoplasm yellow.

#### STAINING IN BULK.

By this is meant the staining of blocks of tissue before cutting into sections. The method is much less used than formerly. It is slower than section staining and more difficult to control. Blocks of the hardened tissue are transferred to the stain from water or alcohol according to the solvent of the stain. Alum-carmine and borax-carmine are the most used general bulk stains.

## (1) Alum-Carmine.

Carmine, 0.5 to 1 gm. Ammonia alum, 4-per-cent. aqueous solution, 100 c.c.

After mixing the ingredients, the solution should be boiled fifteen minutes, and after cooling, enough sterile water added to replace that lost by evaporation. The time required for staining depends upon the size of the specimen. There is, however, little danger of overstaining. After washing out the excess of stain with water the specimen is dehydrated and embedded in the usual way.

(2) Borax-Carmine, Alcoholic Solution.

Carmine, 3 gm.
Borax, 4 gm.
Water, 93 c.c.
After mixing the above, add 100 c.c. 70-per-cent. alcohol,

After mixing the above, add 100 c.c. 70-per-cent. alcohol, allow the mixture to settle, then filter.

About twenty-four hours is required to stain blocks 0.5 cm. in diameter. Larger blocks require longer staining.

# VIII. Mounting.

It is usually desirable to make permanent preparations or "mounts" of the stained specimens.

The most satisfactory media for mounting specimens are glycerin and Canada balsam.

(1) GLYCERIN.—Sections may be transferred to glycerin from either water or alcohol. In the case of double-stained specimens—hæmatoxylin-eosin—the glycerin should be tinged with eosin, as the pure glycerin abstracts the eosin from the tissues. In many cases satisfactory eosin staining may be obtained by simply placing the hæmatoxylin-stained specimens in glycerin strongly tinged with eosin (eosin-glycerin). The specimen in a drop of glycerin is transferred to the glass mounting slide, the excess of glycerin removed with filter paper or with a pipette, and a cover-glass put on.

Glycerin mounts, as a general rule, are unsatisfactory. Furthermore, they must be cemented to exclude the air. This can be done by painting a ring of gold-size, or a thick solution of gum shellac in alcohol to which a little castor oil has been added, around and over the edge of the cover-glass. Both cover-glass and slide must be cleaned free from glycerin before the cement is applied. A camel's-hair brush moistened with alcohol is the best means of removing the excess of glycerin.

Glycerin jelly is a more satisfactory mounting medium than pure glycerin. It can be purchased from firms dealing in microscopical supplies and needs merely the application of heat to make it fluid. Specimens can then be mounted in it in the usual manner, and after being allowed to cool, do not require cementing.

(2) Balsam.—This is the most satisfactory general mounting medium. It has an advantage over glycerin in drying down perfectly hard and thus needing no cement, and in preserving colors more permanently. Its disadvantage is that its refractive index is so high that it sometimes obscures the finer details of structure, especially of unstained or slightly stained specimens.

Specially prepared Canada balsam is dissolved either in xylol or in oil of cedar, the solution being made of any desired consistence. Xylol-balsam dries much more quickly than does the oil-of-cedar balsam.

Preparatory to mounting in balsam, stained sections must be thoroughly dehydrated and then passed through some medium which is miscible with both alcohol and balsam. This medium, which at the same time renders the section transparent, is known as a *clearing medium*. For *celloidin specimens* the most satisfactory are:

- (1) Oil of origanum Cretici.
- (2) Carbol-xylol (xylol, 100 c.c., carbolic-acid crystals, 22 gm.), followed by pure xylol.
  - (3) Xylol and cajeput oil, equal parts, followed by pure xylol.

After clearing, the section is transferred by means of a section-lifter to a glass mounting slide. In case oil of origanum is used, it is then blotted firmly with filter paper to remove the excess of oil. Care must be taken to have the filter paper several layers thick in order that the oil may be completely removed. The specimen should also be blotted firmly, giving the oil time to soak into the paper. These two precautions are necessary to prevent the section adhering to the paper instead of to the slide. After blotting, a drop of balsam is placed upon the centre of the specimen and a cover-glass put on.

When xylol is used, blotting is not necessary. Drain off the excess of oil, put a drop of balsam on the specimen and put on a cover-glass.

Paraffin Sections.—The technic of staining and mounting paraffin sections differs from that of celloidin sections. This is due mainly to the fact that while celloidin is transparent and may remain permanently in the specimen, paraffin is opaque and must be dissolved out before the section is fit for microscopic study.

Bulk staining with carmine (page 19) is frequently used for specimens which are to be embedded in paraffin. Sections may be counterstained if desired.

The following are the steps to be followed in staining and mounting paraffin sections:

#### 1. To attach sections to slide:

Place a drop of egg albumen (equal parts white of egg and glycerin to which a little carbolic acid may be added for preserving) on a slide, and spread it out thin with the finger.

Place a few drops of distilled water on the slide.

Float sections on the water.

Warm gently to allow sections to flatten—must not melt paraffin.

Pour off excess of water, holding the ends of the ribbons to prevent them floating off.

Stand slides on end a few hours to allow water to evaporate.

2. To remove paraffin:

Place slide in xylol three to five minutes.

3. To stain sections:

Place slide in fresh xylol three minutes.

Transfer to absolute alcohol.

Transfer to 90-per-cent. alcohol.

Transfer to 80-per-cent. alcohol.

Transfer to 50-per-cent. alcohol. (May be omitted.)

Transfer to water.

Stain with an aqueous stain.

Wash in water.

Transfer to 50-per-cent. alcohol. (May be omitted.)

Transfer to 80-per-cent. alcohol.

Transfer to 90-per-cent. alcohol.

Transfer to absolute alcohol.

Transfer to xylol.

Transfer to fresh xylol.

Mount in xylol-balsam.

If an alcohol stain is used instead of an aqueous one, the carrying down and up through the graded alcohols is omitted.

If it is desired to stain double with cosin-hæmatoxylin (page 18) use the above technic in staining with hæmatoxylin; then the alcoholic cosin stain before final transfer to absolute alcohol.

# IX. Injection.

For the study of the distribution of the blood-vessels in tissues and organs, it is often necessary to make use of sections in which the blood-vessels have been injected with some transparent coloring matter. The injecting fluid most commonly used is a solution of colored gelatin.

The gelatin solution is prepared by soaking 1 part gelatin in from 5 to 10 parts water—the proportion depending upon the consistence desired—and when soft, melting on a water-bath.

Various dyes are used for coloring the gelatin, the most common being Prussian blue and carmine.

PRUSSIAN BLUE GELATIN is prepared by adding saturated aqueous solution Prussian blue to the gelatin solution, the proportions depending upon the depth of color desired. Both solutions should be at a temperature of 60° C. After thoroughly mixing, the blue gelatin is filtered through cloth.

CARMINE GELATIN is prepared by first dissolving I gm. carmine in 30 c.c. distilled water. To this is added ammonia until the mixture becomes a dark cherry red. A 10-per-cent. aqueous solution of acetic acid is next added, drop by drop, with constant stirring until the mixture becomes neutral. The carmine and gelatin solutions both being at about 60° C., are now mixed in the desired proportions. If the carmine injection mass is alkaline, it diffuses through the walls of the vessels; if acid, there is a precipitation of the carmine which may interfere with its free passage through the capillaries. If, however, the alkaline carmine and gelatin be first mixed, and the 10per-cent, acetic acid solution be then added as directed above, the precipitated granules are so fine, even with an acid reaction, that they readily pass through the capillaries. The precipitation of the carmine in the shape of coarser granules is of advantage when it is desired to have an injection mass which will fill the arteries or veins only, without passing over into the capillaries.

The *injecting apparatus* consists of a vessel which contains the injection mass, and some means of keeping the latter under a constant but easily varied pressure. With the vessel is connected a tube ending in a cannula, through which the injection is made.

A very simple apparatus consists of a shelf which can be raised and lowered, and upon which the vessel stands. The tube connecting with the cannula may be attached to a faucet in the vessel or to a bent glass tube which passes into the top of the vessel and acts on the principle of a siphon.

In a somewhat more elaborate apparatus the injection mass is placed in a closed vessel, and this is connected with a second vessel containing air compressed by means of an air pump.

Accurate regulation of the pressure may be obtained by connecting the injection vessel with a manometer.

If the injection is to occupy considerable time, a hot-water bath in which the gelatin may be kept at an even temperature is also necessary.

Whole animals or separate organs may be injected. For injecting a whole animal, the animal, which is usually a small one such as a guinea-pig, rat, mouse, or frog, is chloroformed, the tip of the heart is cut away and a cannula is inserted through the heart into the aorta. This is first connected with a tube leading to a bottle containing warm normal saline solution. Pressure is obtained in the same manner as above described for the injection mass. By this means the entire arterial and venous systems are thoroughly washed out until the return flow from the vena cava is perfectly clear. The cannula is next connected with the tube from the vessel containing the injection mass, the pressure being only sufficient to keep the liquid flowing. When the injection mass flows easily and freely from the vena cava, the vessel is tied and the pressure is increased slightly and continued until the color of the injection mass shows clearly in the superficial capillaries. The aorta is now tied and the animal immersed in cold water to solidify the gelatin. After the gelatin becomes hard, the desired organs are removed and fixed and hardened in the usual way. Sections of injected material are usually cut rather thick, that the vessels may be traced the greater distance.

Better results are frequently obtained by injecting separate organs. This is accomplished by injecting through the main artery of the organ (e.g., the lungs through the pulmonary, the kidney through the renal). The injection is best done with the organ in situ, although it may be accomplished after the organ has been removed. The method is the same as given above for injecting an animal in toto.

The so-called *double injection* by means of which an attempt is made to fill the arteries with an injection mass of one color (red), while the veins are filled with an injection mass of another color (blue), often gives pretty, but usually inaccurate pictures, it being, as a rule, impossible to confine each injection mass to one system. Double injection is accomplished by first washing out the vessels with normal saline and then connecting the artery with the red gelatin, the vein with the blue gelatin, and injecting both at the same time, the pressure driving the saline out of the vessels into the tissues. The difficulty is that either the arterial injection carries over into the veins, or the venous injection carries over into the arteries. A somewhat more accurate method is first to inject the veins with an

injection mass in which the coloring matter is in the form of granules too large to pass through the capillaries, and then to inject the arteries and capillaries in the usual manner. This method is especially useful in demonstrating the vessels of the kidney, liver, and gastro-intestinal canal.

#### CHAPTER II.

#### SPECIAL STAINING METHODS.

Of these only the more common will be described.

- (1) SILVER-NITRATE METHOD OF STAINING INTERCELLUIAR SUBSTANCE.—After first washing, the tissue, *e.g.*, omentum or cornea, is placed in a from 0.2- to 1-per-cent. solution of silver nitrate, or better, protargol, where it is kept in the dark for a half-hour or more according to the thickness and density of the tissue. The specimen is then washed in water, transferred to 40-per-cent. alcohol and placed in the direct sunlight until it assumes a light brown color. It is then placed in fresh 80-per-cent. alcohol for preservation.
- (2) CHLORID OF GOLD in 1-per-cent. aqueous solution is used in the same manner for demonstrating connective-tissue cells and their finer processes.
- (3) Weigert's Elastic-tissue Stain.—This is prepared as follows:

Fuchsin, 2 gm.
Resorcin, 4 gm.
Water, 200 c.c.

These are boiled for five minutes, during which 25 c.c. of liquor ferri sesquichlorati are stirred in. The result is a precipitate which should be filtered out after the liquid has become cool. After drying, 200 c.c. of 95-per-cent. alcohol are added to the filtrate and boiled until the latter dissolves. Lastly, 4 c.c. of hydric chlorid are added to the solution. Sections should remain in the stain thirty minutes, after which they are washed in alcohol until the stain ceases to be given off.

(4) Golgi's Chrome-silver Method for Demonstrating Secretory Tubules.—Small pieces of perfectly fresh tissue, e.g., liver, are placed in the following:

Potassium bichromate, 4-per-cent. aqueous solution, 4 vols. Osmic acid, 1-per-cent. aqueous solution, 1 vol.

After three days they are transferred without washing to a 0.75-percent. aqueous solution of silver nitrate, which should be changed as

soon as a precipitate forms. The specimens remain in the second silver solution from two to three days, after which they are rapidly dehydrated, embedded in celloidin, and cut into rather thick sections.

(5) MALLORY'S PHOSPHOMOLYBDIC ACID HEMATOXYIIN STAIN FOR CONNECTIVE TISSUE.—Thin sections are placed for from two to ten minutes in a 10-per-cent. aqueous solution of phosphomolybdic acid. They are then washed in distilled water and transferred to:

Phosphomolybdic acid, 10-per-cent. aqueous solution,
Distilled water,

Hæmatoxylin crystals,
Carbolic-acid crystals,

5.00 gm.

The phosphomolybdic acid and water are first mixed, after which the hæmatoxylin and carbolic acid are added.

After staining from ten to twenty minutes the sections are washed in distilled water, placed for five minutes in 50-per-cent. alcohol, then in strong alcohol, cleared in xylol and mounted in xylol-balsam. This stain works best after Zenker's fluid fixation.

(6) Mallory's Phosphotungstic Acid Hæmatoxyiin Stain for Connective Tissue.

Hæmatoxylin (or hæmatein ammonium), o. 1 gm.
Water, 80. c.c.
Phosphotungstic acid (Merck), 10-per-cent. aqueous
solution. 20. c.c.

The hæmatoxylin should be dissolved in a little water with the aid of heat and, when cool, added to the rest of the solution. Allow to ripen for several weeks or months. Or, if it is desired to use immediately, the solution can be ripened by the addition of 10 c.c. of a 1/4-per-cent. solution of potassium permanganate.

Tissues should be fixed in Zenker's fluid (p. 8).

- 1. Treat sections with iodin solution to remove mercury precipitate, 5 to 10 minutes (p. 9.)
  - 2. Several changes 95-per-cent. alcohol.
  - 3. Water.
- 4. One-fourth-per-cent. aqueous solution potassium permanganate, 5 to 10 minutes.
  - 5. Wash in water.
  - 6. Five-per-cent. aqueous solution oxalic acid, 5 to 10 minutes.
  - 7. Wash thoroughly in water.
- 8. Phosphotungstic acid hæmatoxylin solution, twelve to twenty-four hours.

- 9. Dip for a few seconds in 95-per-cent. alcohol.
- 10. Clear in carbol-xylol and xylol and mount in xylol-damar.
- (7) MALLORY'S ANILINE BLUE STAIN FOR CONNECTIVE TISSUE.— Tissues should be fixed in Zenker's fluid (p. 8.)
- 1. Stain thin sections in a 0.2-per-cent. aqueous solution of acid fuchsin for five to ten minutes. (This step may be omitted.)
  - 2. Stain in the following solution for twenty minutes:

Aniline blue (soluble in water), 0.5 gm.
Orange G., 2.0 gm.
Phosphomolybdic acid, 1-per-cent. aqueous solution, 100.0 cc..

- 3. Decolorize in several changes of 95-per-cent. alcohol.
- 4. Clear in carbol-xylol and xylol and mount in xylol-damar.
- (8) OSMIC-ACID STAIN FOR FAT.—For this purpose osmic acid is used in a 1-per-cent. aqueous solution. The method is especially useful for demonstrating developing fat, fatty secretions (mammary gland), and fat absorption (small intestine). Very small bits of the tissue are placed in the osmic-acid solution for from twelve to twenty-four hours. They are then hardened in graded alcohols, embedded in celloidin, and the sections mounted in glycerin.
  - (9) JENNER'S BLOOD STAIN.

Water-soluble eosin (Grübler), 1-per-cent. aqueous solution, 100 c.c.

Methylene blue—pure (Grübler), 1-per-cent. aqueous solution, 100 c.c.

Mix, and after standing 24 hours, filter. The filtrate is dried at 65° C., washed, again dried and powdered.

To make the staining solution, 0.5 gm. of the powder is dissolved in 100 c.c. pure methyl alcohol. Blood smears stain in from two to five minutes. They are then washed in water, dried, and mounted in balsam.

This solution acts as a fixative as well as a stain.

## CHAPTER III.

## SPECIAL NEUROLOGICAL STAINING METHODS.

Weigert's Method of Staining Medullated Nerve Fibres.

In preparing material for the Weigert method, two points are to be kept in mind: 1st, proper fixation and preservation of the myelin sheaths; 2d, treatment (mordanting) with a reagent which enters into combination with the myelin, the result being that the myelin sheaths stain specifically with hæmatoxylin. Formalin fulfils the first requirement, the bichromates the first and second. Consequently the material may be fixed and hardened in bichromate, and, if not to be used immediately, is best kept in formalin to avoid overhardening. Or the material may be fixed and kept in formalin and impregnated with the bichromate before using, the latter being done before dehydrating in alcohol. Further mordanting, which is usually done, especially when the material has been kept for some time in formalin or alcohol, is for the purpose of intensifying the stain.

Material is fixed in one of the following fluids:

- (a) Müller's fluid (page 6).
- (b) Potassium bichromate, 5-per-cent. aqueous solution.
- (c) Formalin, 10-per-cent. aqueous solution.
- (d) Formalin, 1 volume; potassium bichromate, 5-per-cent. aqueous solution, 9 volumes.

In Müller's fluid or in plain potassium-bichromate solution a hardening of two days to four weeks is required; in formalin or formalin-bichromate from a week to ten days is sufficient. All material is better kept until used in 5-per-cent. to 10-per-cent. formalin solution than in alcohol. The specimens are then hardened in graded alcohols, embedded in celloidin, and sections cut in the usual way. Material fixed in formalin should be placed for several days in the following:

Chrome alum, 1 gm.
Potassium bichromate, 3 gm.
Water, 100 c.c.

before hardening in alcohol.

Sections from material fixed in any of the chrome-salt solutions are placed for from twelve to twenty-four hours in a saturated aqueous

solution of neutral cupric acetate diluted with an equal volume of water. The cupric acetate forms some combination with the tissues which intensifies their staining qualities, thus acting like the chrome salts as a mordant.

After mordanting, the sections are washed in water and transferred to the following staining fluid:

Hæmatoxylin crystals,	ı gn	n.
Alcohol, 95-per-cent.,	10 C.	c.
Lithium carbonate—saturated aqueous solution,	I C.	c.
Water,	90 c.	c.

This solution must either be freshly made before using, the hæmatoxylin being dissolved first in the alcohol, or the hæmatoxylin may be kept in ro-per-cent. alcoholic solution, the lithium carbonate in saturated aqueous solution, and the staining fluid made from these as needed.

Sections remain in the hæmatoxylin solution from two to twentyfour hours, the longer time being required for staining the finer fibres of the cerebral and cerebellar cortices. They are then washed in water and decolorized in the following:

Potassium ferricyanid,	2.5 gm.
Sodium biborate,	2.0 gm.
Water,	300.0 c.c.

While in the decolorizer, sections should be gently shaken or moved about with a glass rod to insure equal decolorization. In the decolorizer the sections lose the uniform black which they had on removal from the hæmatoxylin. They remain in the decolorizing fluid until the gray matter becomes a light gray or yellow color, in sharp contrast with the white matter which remains dark. Sections are then washed in several waters to remove all traces of decolorizer, and dehydrated in alcohol.

Weigert-Pal Method.—In this modification of the Weigert method, material hardened in formalin should be further hardened in potassium bichromate 5-per-cent. for two weeks, or in copper bichromate 3-per-cent. for about a week, after which it may be cut and stained without further mordanting. Sections from material hardened in the other above-mentioned ways are mordanted in a 3- to 5-per-cent. aqueous solution of potassium bichromate instead of in the copper-acetate solution. After rinsing in water the sections are stained in hæmatoxylin as in the ordinary Weigert method. The

lithium carbonate may, however, be omitted. They are then washed and transferred to a 0.25-per-cent. solution of potassium permanganate, where they remain from one-half to two minutes, after which they are again washed and placed in the following:

Oxalic acid,	I	gm.
Potassium sulphite,	I	gm.
Water,	200	c.c.

In this solution differentiation takes place, the medullary sheaths remaining dark, while the color is entirely removed from the rest of the tissue. If the section is still too dark, it may again be carried through the permanganate and oxalic-acid solutions, rinsing in water between changes, until sufficiently decolorized.

All formalin-fixed material is best stained by the Weigert-Pal method. An intensification of the stain, especially of the very fine fibres, may sometimes be obtained by placing the sections for a minute in a 0.5-per-cent. aqueous solution of osmic acid before decolorizing.

## MARCHI'S METHOD FOR STAINING DEGENERATING NERVES.

Small pieces of tissue are fixed and hardened for from seven to ten days in Müller's fluid. Thin slices of the tissue are then transferred to a solution of one part 1-per-cent. osmic acid and two parts Müller's fluid, in which they remain from two to seven days. After embedding and sectioning in the usual manner, sections are mounted, usually without further staining, in xylol-balsam. The treatment with Müller's fluid so affects the normal medullary sheaths that they will not take the osmic-acid stain, but appear vellowish-brown, while the degenerating sheaths (probably fatty) stain black. The result is a positive picture of stained degenerating fibres in contrast with the stained normal and unstained degenerated fibres as seen after Weigert staining. Another advantage of the Marchi method is that, as the picture is a positive one, an early or slight degeneration may be recognized which would escape notice in material stained by Weigert's method; on the other hand, in a long-standing degeneration when the medullary sheaths have completely disappeared and their places have been taken by connective tissue, there being no degenerated myelin remaining, the Marchi method is inapplicable.

Busch's modification of the Marchi method gives sharp pictures and has the advantage of allowing formaldehyd fixation and harden-

ing. Tissues thus treated are placed for from five to seven days in a solution of one part osmic acid, three parts iodate of sodium, and 300 parts water. They are then embedded, cut, and mounted as usual.

## Golgi Methods of Staining Nerve Tissue.

The Golgi methods in most common use at present are the following:

- (1) Golgi Silver Methods.—(a) Slow Method.—Blocks of tissue are placed for several months in a 3-per-cent. aqueous solution of potassium bichromate. Small pieces of the tissue are then transferred immediately to a 0.75-per-cent. aqueous solution of silver nitrate. This is changed several times or until no more precipitate is formed. In the last silver solution they remain for from one to three days. The only method of determining whether the tissue has been sufficiently long in the bichromate is to try at intervals small bits of the tissue in the silver solution until a satisfactory result is secured. Sections should usually be from 50 to 80μ thick and are mounted in balsam without a cover-glass.
- (b) Rapid Method.—Small pieces of tissue, 2 to 4 mm. thick, are placed in the following solution for from two to six days, the time depending upon the age and character of the tissue, the temperature at which fixation is carried on, and the elements which it is desired to impregnate:

Osmic acid, 1-per-cent. aqueous solution, 1 part. Potassium bichromate, 3.5-per-cent. aqueous solution, 4 parts.

As a rule, the longer the hardening the fewer are the elements stained, but these few are clearer. The tissue is next transferred to silver nitrate as in the slow method. Pieces of tissue should be tried each day until a satisfactory result is obtained. The pieces may be kept in silver nitrate some time, but not in alcohol, and are better cut without embedding, the pieces being simply washed in 95-per-cent. alcohol several hours, then gummed to the block with celloidin, cut in 95-per-cent. alcohol, and mounted as in the slow method.

(c) Mixed Method.—Specimens are placed in the bichromate solution for about four days, then from one to three days in the osmium-bichromate mixture (see Rapid Method), after which they are transferred to the silver solution (see Slow Method).

(d) Formalin-bichromate Method.—Tissues are placed for from two to six days in the following solution:

Formalin, 10 to 20 parts.

Potassium bichromate, 3-per-cent. aqueous solution, 90 to 80 parts.

Subsequent treatment with silver is the same as in the previously described method. The results resemble those of the slow method. The specimens may be kept in strong alcohol. The method is satisfactory only for the adult cerebrum and cerebellum.

(2) Golgi Bichlorid Method.—Material, which need not be cut into small pieces, remains for several months in the potassium-bichromate solution (see Slow Silver Method), after which it is transferred to a 0.25-per-cent. to 1-per-cent. aqueous solution of mercuric chlorid for from four to twelve months or longer, the solution being changed as often as discolored. The degree of impregnation must be determined by frequently testing the material, but is usually indicated by the appearance of small white spots on the surface of the tissue.

A modification of the bichlorid method, known as the *Cox-Golgi Method*, often gives good results. The following fixing solution is used:

Potassium bichromate, 5-per-cent. aqueous solution, 20 parts.

Mercuric chlorid, 5-per-cent. aqueous solution, 20 parts.

Distilled water, 40 parts.

After mixing the above, add

Potassium chromate, 5-per-cent. aqueous solution, 16 parts.

Tissues remain in this fluid for from two to five months.

In the Golgi silver methods the result of the treatment, first with bichromate and then with silver nitrate, is that a precipitate is formed in the tissue, a chromate or some other silver salt, which in favorable cases is largely confined to certain of the nerve cells and their processes. It must be remembered that only a few of the cells and processes are stained, these often only partially, and that other irregular precipitations are usually present. In the mercury methods, the bichromate of potassium and the bichlorid of mercury may be used combined in the same solution. There are other modifications of the Golgi methods, in which similar precipitates of other metallic salts are secured.

Golgi specimens should be dehydrated and embedded as rapidly as possible. This is especially true of specimens treated by the rapid and the mixed methods. Those treated by the slow silver method and by the bichlorid method are more permanent, and more time may be taken with their dehydration. Sections should be cut thick (75 to 100µ) and mounted in xylol-balsam. After the rapid method, it is safer to mount without a cover-glass; after the slow method, specimens may be mounted with or without a cover. The balsam should be hard, and melted at the time of using. (See Mounting, page 21.)

# Cajal's Methods for Staining the Neurofibrils in the Nerve-cells.

In these methods, besides the neurofibrils, the cell processes and especially the axis cylinders are often beautifully displayed, the stain giving a picture in this respect much more general than that of the Golgi methods, but much more specific, and sharper than that of the ordinary stains.

The methods consist mainly of two steps: (1) The staining of the tissue in a solution of silver nitrate; (2) the further reduction of the silver stain with a weak photographic developer. Three methods, or variations, are here given:

- (1) Pieces about 0.5 cm. thick are placed in a liberal quantity of from 1-per-cent. or 1.5-per-cent. (new-born or embryonic mammalian material) to 5-per-cent. (adult material) solution of silver nitrate and kept at a temperature of 32° to 40° C. for two to five days. When properly stained (shown by a yellowish or light brown coloration of freshly cut surfaces) the pieces are very briefly rinsed in distilled water and placed in: pyrogallol (or hydroquinone) I gram, distilled water 100 c.c., formalin 5 to 10 c.c., for twenty-four hours or more. They are then washed a few minutes in water and transferred to 95-per-cent. alcohol, which is changed when discolored, and where they may often be kept for some time without injury. They may then be embedded in celloidin or paraffin and sections cut, usually  $15-25\mu$  in thickness. Different depths of the blocks of tissue usually vary in stain, the most favorable being intermediate between the surface and centre of the block. Celloidin sections usually keep well in 95-per-cent. alcohol. They may be cleared in carbol-xylol, rinsed in xylol, and mounted in xylol-balsam or xylol-damar in the usual way. In delicate objects (study of pathological changes in neurofibrils) it may be best to abbreviate the dehydration, and block and cut without infiltration with celloidin.
- (2) Pieces are first placed in 95-per-cent. alcohol or in absolute alcohol (32° to 40° C.) for twenty-four hours. For neurofibrils it is

better to add from 0.25 c.c. to 1 c.c. of ammonium hydrate to each 10 c.c. of the alcohol. They are then treated with silver nitrate 1-percent. or 1.5-per-cent., as in (1). This method gives better pictures of the cell processes and axis cylinders and a better fixation of the cells.

(3) Pieces are first placed in distilled water 100 c.c., formalin 20 c.c., ammonia 1 c.c., for twenty-four hours at 32°-40° C., washed in water twelve to twenty-four hours, and then treated with silver nitrate 1-per-cent. or 1.5-per-cent., as in (1). This method gives pictures of the terminations of nerve fibres on the periphery of nervecells and their dendrites (end-feet or end-buttons of Auerbach).

In general it is best to avoid, in the above methods, any excessive exposure to the light while the pieces are in the silver bath (especially when the pieces are very small), though they may be brought into the light for examination and while being transferred to the reducing fluid.

#### NISSL'S METHOD.

This method is useful for studying the internal structure of the nerve cell. It depends upon a rapid fixation of the tissue, its subsequent staining with an aniline dye, and final decolorization in alcohol.

The aniline dye most commonly used is *methylene blue*. There are many variations and modifications of Nissl's method. The following is simple and gives uniformly good results:

Specimens are first fixed in mercuric-chlorid solution (page 7), in formalin (10-per-cent. aqueous solution), or in absolute alcohol, and embedded in celloidin.

Thin sections are stained in a 1-per-cent. aqueous solution of pure methylene blue (Grübler). The sections are gently warmed in the solution until steam begins to be given off. They are then washed in water and differentiated in strong alcohol. The degree of decolorization which gives the best results can be learned only by practice. Several alcohols must be used, and the last alcohol must be perfectly free from methylene blue. The sections are cleared in equal parts xylol and cajeput oil and mounted in xylol-balsam. A contrast stain may be obtained by having a little eosin or erythrosin in the last alcohol.

# General References for Further Study of Technic.

Freeborn: Histological Technic. Reference Handbook of Medical Sciences, vol. iv.

Lee: The Microtomist's Vade-mecum.
Mallory and Wright: Pathological Technic.



PART II.
THE CELL.



### CHAPTER I.

#### THE CELL.

In the simplest forms of animal life the entire body consists of a little albuminous structure, the essential peculiarity of which is that it possesses properties which we recognize as characteristic of living organisms. This albuminous material basis of life is known as *protoplasm*, while the structure itself is known as a *cell*. Within the cell is usually found a specially formed part, the *nucleus*. Peripherally some cells are limited by a distinct *cell wall* or *cell membrane*.

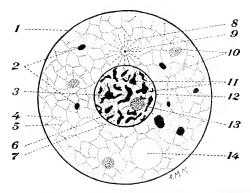


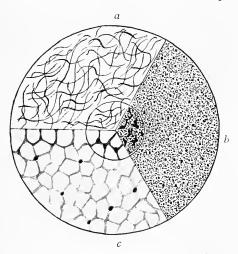
FIG. 1.—Diagram of a typical cell. 1, Cell membrane. 2, Metaplasm granules.
3, Karyosome or net-knob. 4, Hyaloplasm. 5, Spongioplasm. 6, Linin network.
7, Nucleoplasm. 8, Attraction-sphere. 9, Centrosome. 10, Plastids. 11, Chromatin network. 12, Nuclear membrane. 13, Nucleolus. 14, Vacuole.

An actively multiplying cell contains a minute structure associated with the reproductive function and known as the *centrosome*.

A typical cell thus consists of the following structures (Fig. 1): (1) The cell body; (2) the cell membrane; (3) the nucleus; (4) the centrosome. Of these the cell body is the only one present in all cells. Most animal cells have no cell membrane. A few cells contain, in their fully developed condition, no nuclei. In many mature cells it is impossible to distinguish a centrosome.

All plants and animals consist of cells and their derivatives, and if an attempt be made to resolve any of the more complex living structures into its component elements, it is found that the smallest possible subdivision still compatible with life is the cell. The cell may therefore be considered as the *histological element* or *unit of structure*.

1. **The Cell Body.**—This consists of a viscid semi-fluid substance, belonging to the general class of albumens. It is of complex chemical composition containing the elements carbon, hydrogen, oxygen and nitrogen in quite constant proportions, and smaller variable 'quantities of phosphorus, sulphur, iron and other substances. It contains a peculiar nitrogenous proteid, *plastin*. Structurally it can be differentiated into a formed element, *spongioplasm*, and a homogeneous



F16. 2.—Diagram Illustrating Theories of Protoplasmic Structure. a, Fibrillar theory; b, granule theory; e, "foam" theory. (The general structure of cell body and nucleus corresponds.)

element, hyaloplasm. tributed along the spongioplastic network are minute granules, microsomes. The exact relations which these elements bear to one another and to the cell as a whole have been the subject of much investigation and speculation. The earlier cytologists concerned themselves with the question as to whether protoplasm was homogeneous (i.e., a mere solution or at most a mixture of various substances) or had a definite structure. The theory of a structureless protoplasm having been long

since abandoned, the question as to the character of the protoplasmic structure still remains unanswered.

Altmann's granule theory considers protoplasm as composed of fine granules embedded in a gelatinous intergranular substance. Altmann believed these granules the ultimate vital elements, and for this reason gave them the name of bioblasts (Fig. 2, b).

According to Bütschli, protoplasm is a foam or emulsion, the microscopic appearance of which can be simulated by artificial emulsions. He ascribes the appearance of a reticulum to the fact that each little foam space forms a complete cavity filled with fluid, the cut walls of these spaces giving a reticular appearance on section (Fig. 2,  $\epsilon$  and Fig. 3).

Other investigators consider protoplasm as made up of  $(\tau)$  a fibrillar element, either in the form of a network of anastomosing fibrils (cytoreticulum) or of a feltwork of independent fibrils (filar mass or miton), and (2) a fluid or semi-fluid sub-

stance which fills in the meshes of the reticulum or separates the fibrils (interfilar mass or paramiton) (Fig. 2, a).

That the question as to the ultimate structure of protoplasm still remains

unanswered is dependent mainly upon the extreme technical difficulties which have confronted the cytologist. Living protoplasm has a homogeneous glossy appearance, showing even under the highest magnification rarely more than a granular structure. It is usually only after death of the cell and the use of chemical fixatives and stains, that the so-called "structure" of protoplasm becomes visible. How closely the picture presented by such chemically treated protoplasm corresponds to the structure of living protoplasm is as yet undetermined. It is quite possible that the structure of protoplasm is not entirely uniform. It certainly differs somewhat both as to structure and chemical composition in different cells. It also differs in the same cell under different functional conditions. These variations may account, in part at least, for the lack of uniformity of results of different observers.

Protoplasm is thus probably best considered as the material basis of cell activity, i.e., of life, rather than as a substance having fixed and definite chemical or morphological characteristics.

It is convenient to use the term proto blasm to mean the entire substance of the cell, karyoplasm to designate the protoplasm of the nucleus, and cvtoplasm the protoplasm of the cell body exclusive of the nucleus.

Peculiar bodies known as plastids (Fig. 1) are of frequent occurrence in vegetable cells, and are also found in some animal cells. They are apparently to be regarded as a differentiation of the cytoplasm, but possess a remarkable degree of independence, being capable of subdivision and in some

cases of existence outside of the cell.

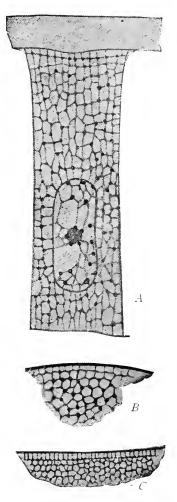


Fig. 3.—Foam or emulsion structure of protoplasm according to Bütschli (Bütschli). A, Epidermal cell of the earthworm. B. Peripheral cytoplasm of sea urchin's egg. C, Artificial emulsion of olive oil, sodium chloride and water.

In addition to the granules which are apparently an integral part of the protoplasmic structure, other granules and various cell "inclusions" occur, to which the term *metaplasm* (*paraplasm*, *deutoplasm*) granules, has been applied (Fig. 1). Some of these are intimately associated with the cell activities and represent either food substances in process of being built up into the protoplasm of the cell or waste products of cell metabolism. Others, such e.g., as the glycogen granules of the liver cell or the mucous granules of the mucous cell, are specific secretion products. Still others are fat droplets, pigment granules, and various excrementitious substances.

When the protoplasm of a cell can be differentiated into a central granular area and a peripheral clear area, the former is known as



Fig. 4—Intracellular canals (trophospongium) of a ganglion cell (E. Holmgren).

endoplasm, the latter as exoplasm. When the exoplasm forms a distinct limiting layer, but blends imperceptibly with the rest of the protoplasm, it is known as the *crusta*.

In some cells minute channels or canals are present in the cytoplasm (Fig. 4). These channels may contain branching processes from other cells, forming what is known as a *trophospongium*. Some intracellular canals are apparently secretory in character and may communicate with fine intracellular secretory channels. In

this way the secretion of such cells as the serous cells forming the demilunes of mucous tubules (p. 195), or of the parietal cells of the stomach glands (Fig. 136), is carried to the lumen.

- 2. The Cell Membrane (Fig. 1).—This is present in but few animal cells, and is a modification of the peripheral part of the protoplasm. In most vegetable cells the membrane is the most conspicuous part of the cell and was responsible for the name "cell" which the seventeenth-century botanists, overlooking the importance of the enclosed protoplasm, gave to the little spaces or cavities of which they thought plants composed. When a membrane surrounds the cell, it is known as the *pellicula*; when cells lie upon the surface, and only the free surface of the cells is covered by a membrane, it is known as the *cuticula*.
- 3. The Nucleus (Fig. 1).—This is a vesicular body embedded in the cytoplasm. The typical nucleus, like the typical cell, is spheroidal, but the shape of the nucleus varies for different cells and corresponds

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somewhat to the shape of the cell body, *e.g.*, the rod-shaped nucleus of the elongated smooth muscle cell. It may also be modified by intracellular pressure as, *e.g.*, in the mucous cell and in the fat cell.

The position of the nucleus is usually near the center of the cell. It may, however, be eccentric. Such eccentricity may be due to pressure of cell contents as, e.g., in the mucous cell and in the fat cell. Considered by earlier cytogists an unessential part of the cell, the nucleus is now known to be most intimately associated with cellular activities. It is not only essential to the carrying on of the ordinary metabolic processes of the cell, but is an active agent in the phenomena of mitosis, which in most cases determine cell reproduction.

As a rule, each cell contains a single nucleus. Some cells contain two nuclei (quite common in the liver cell, rare in the ovum and in the nerve cell). A few cells contain many nuclei, e.g., the multinuclear "giant" cells of the spleen, bone-marrow, and certain tumors. Some cells, such as the human red blood cell and the respiratory epithelium, are, in their mature condition, non-nucleated. All non-nucleated cells, however, contained nuclei in the earlier stages of their development. Non-nucleated cells, while capable of performing certain functions, are wholly incapable of proliferation. The non-nucleated condition must, therefore, be regarded as not only a condition of maturity, but of actual senility, at least so far as reproductive powers are concerned.

In some of the lowest forms of animal life, the nuclear material instead of being grouped to form a definite body or nucleus, is more or less evenly distributed as granules through the cytoplasm.

Chemically the nucleus is extremely complex, being composed of the proteids nuclein, paranuclein, linin, paralinin, and amphipyrenin.

Morphologically also the nucleus is complex, much of the apparent structural differentiation being determined by the staining reactions of the different elements when treated with certain aniline dyes. The nuclear structures and their relations to the chemical constituents of the nucleus are as follows:

(a) The nuclear membrane (amphipyrenin). This forms a limiting membrane separating the nucleus from the cell protoplasm. It is doubtful whether the nuclear membrane is different either chemically or morphologically from the nucleoreticulum. It is wanting in some nuclei. When present it appears from its staining reactions to be structurally continuous with, and chemically identical with, in some cases, the linin, in others, the chromatin of the intranuclear network.

It may be complete, or fenestrated allowing free communication between the cytoplasm and the nuclear contents.

- (b) The intranuclear network, or nucleoreticulum, consists of a chromatic element (nuclein or chromatin) and of an achromatic element (linin). The linin constitutes the groundwork of the reticulum along which the chromatin granules are distributed. At nodal points of the network there are often considerable accumulations of chromatin. These nodal points, at first thought to be nucleoli, are now known as false nucleoli, or karyosomes. Instead of a distinct network there may be disconnected threads or simply granules of chromatin. Chromatin is the most characteristic of the chemical constituents of the nucleus, the only one which contains phosphoric acid, and also, apparently, the only nuclear substance which is always transmitted from parent to daughter cell in cell-division. Fine granules have been described as occurring in the linin, differentiated from chromatin by the fact that they are most susceptible to acid dyes, while chromatin takes basic dyes.
- (c) The nucleolus or plasmosome (paranuclein, pyrenin) is a small spherical body within the nucleus. Not infrequently there are several nucleoli. Similar cells vary as to the number of nucleoli they contain. The same cell may vary as to the number of its nucleoli under varying functional conditions. The nucleolus stains intensely with basic dyes. Its function is unknown.
- (d) Karyoplasm (nucleoplasm, nuclear fluid, nuclear sap). This is the fluid or semi-fluid material which fills in the meshes of the nucleoreticulum.

While the nucleus is a perfectly distinct structure capable in some animal and in some vegetable cells of moving about more or less actively in the cytoplasm, and is usually separated by a membrane from the rest of the cell, a marked similarity exists between the structure of nucleoplasm and cytoplasm. This similarity is emphasized by the absence in some resting cells of any nuclear membrane, by the apparent direct continuity in some cases of nucleoreticulum and cytoreticulum, and by the continuity of karyoplasm and cytoplasm in all cells during cell-division.

4. The centrosome (Fig. 5) is a small spheroidal body found sometimes in the nucleus, or more commonly in the cytoplasm near the nucleus. In actively dividing cells the centrosome is frequently double, this being apparently in preparation for the succeeding cell-division. In some cases the centrosome is triple or even multiple. It was first

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found in the ovum and described as peculiar to that cell. It is now believed to occur in most, if not in all, animal cells. It usually consists of (1) a minute central granule or granules—the *centriole*, which stains

intensely with iron-hæmatoxylin, and outside of which is (2) a clear zone, the attraction sphere. From this centre, radiations extend outward into the cytoplasm. There is much confusion of terms in connection with the centrosome, the term centrosome being by some applied to the entire structure including the radiating fibrils, by others to the central granule only, by still others to the central granule plus the surrounding clear area. By some the radiations are believed to be composed of a different substance than the general cytoplasm, which is designated archoplasm. The main signifi-

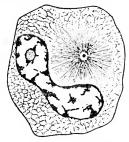


Fig. 5.—Spermatogonium from frog (Hermann). Single centrosome at center of attraction sphere or aster. Nucleus contains a plasmosome.

cance of the centrosome is in connection with cell-division, under which head it will be further considered (page 48).

# Vital Properties of Cells.

It has already been noted that the essential peculiarity of the cell is that it possesses certain properties which are characteristic of life. By this is meant that a cell is able: 1. To nourish itself and to grow—metabolism. 2. To do work—function. 3. To respond to stimulation—irritability. 4. To move—motion. 5. To produce other cells—reproduction.

In the simplest forms of animal life, where a single cell constitutes the entire individual, all of these functions are performed by the one cell. In all higher, that is, multicellular animals, there are not only many cells but many *kinds* of cells, and this morphological differentiation corresponds to a physiological differentiation, each group of cells developing along certain well-defined lines for the performance of its own special function.

1. **Metabolism.**—This term is used to designate those cellular activities which have to do with the nutrition of the cell. A cell is able (1) to take up from without substances suitable for its nutrition and to transform these into its own peculiar structure, and (2) to dispose of the waste products of intracellular activities. The former is known as *constructive metabolism* or *anabolism*, the latter as *destructive metabolism* or *katabolism*.

- 2. **Function.**—This is the special work which it is the part of the cell to perform. It varies greatly for different cells. Some cells, as, *e.g.*, the surface cells of the skin, appear to act mainly as protection for more delicate underlying structures. Other cells—gland cells—in addition to maintaining their own nutrition, produce specific substances (secretions), which are of great importance to the body as a whole. Still other cells, *e.g.*, nerve cells and muscle cells, have the power to store up their food substances in such a way as to make them available in the form of energy. This appears to be accomplished by the building up within the cell of highly complex and, consequently, unstable molecular combinations. By reduction of these unstable combinations, molecules of greater stability and less complexity are formed. This results in the transformation of potential into kinetic energy, and the expenditure of this energy is expressed in function.
- 3. Irritability is that property which enables a cell to respond to external stimuli. Cells vary in respect to their irritability, the most



Fig. 6.—Amœboid Movement. Successive changes in shape and position of freshwater amœba.

markedly irritable cells in higher animals being those of the neuromuscular mechanism. Stimulation may be mechanical, electrical, thermal, chemical, etc. The response of the cell to certain forms of chemical stimulation is known as *chemotaxis*. Some substances attract cells (positive chemotaxis); others repel cells (negative chemotaxis). Stimuli other than chemical possess similar properties, as indicated by the terms thermotaxis, galvanotaxis, etc. Some cells are so specialized as to react only to certain kinds of stimulation, *e.g.*, the retinal cells only to light stimuli.

- 4. **Motion.**—This is dependent wholly upon the protoplasm of the cell, and is exhibited in several somewhat different forms.
- (a) Amæboid Movement. This consists in the pushing outward by the cell of processes (pseudopodia). These may be retracted or may draw the cell after them. In this way the cell may change both its shape and position (Fig. 6).

- (b) Protoplasmic Movement. This occurs wholly within the limits of the cell, changing neither its shape nor position. It occurs in both plant and animal cells, and consists of a sort of circulation or "streaming" of the protoplasm. It is evidenced by the movement of minute granules present in the protoplasm, by changes in the position of the nucleus, etc.
- (c) Ciliary Movement. This is the whipping motion possessed by little hair-like processes called cilia, which project from the surfaces of some cells.

Certain cells which are specialized for the particular purpose of motion as, e.g., muscle cells, possess such powers of contraction that they are able to move not only themselves but other parts with which they are connected. This power of contractility is dependent upon the spongioplasm, the hyaloplasm playing a more passive rôle. In muscle cells the highly developed contractile powers appear to be due to the excessive development and peculiar arrangement of the spongioplasm.

5. **Reproduction.**—The overthrow of the long-held biological fallacy of spontaneous generation was soon followed by the downfall of

a similar theory regarding the origin of cells. We now know that all cells are derived from cells, and that the vast number and complex of cells which together form the adult human body are all derived from a single primitive cell, the ovum.

Reproduction of cells takes place in two ways, by direct cell division or amitosis, and by indirect cell division or mitosis. In both amitosis and mitosis the division of the cell

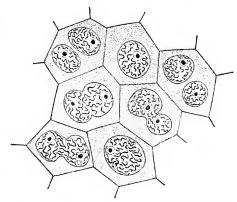


Fig. 7.—Epithelial Cells from Ovary of Cockroach, Showing Nuclei Dividing Amitotically. (Wheeler.)

body is preceded by division of the nucleus.

DIRECT CELL-DIVISION—AMITOSIS (Figs. 7 and 8).—In this form of cell-division the nucleus divides into two daughter nuclei without any apparent preliminary changes in its structure. The division of the nucleus may or may not be followed by division of the cell body, in the latter case resulting in the formation of polynuclear cells. This form of cell-division is uncommon in higher animals where Flemming consid-

ers it a degenerative phenomenon rather than a normal method of cell-increase. It is a common method of cell-division in the protozoa.

INDIRECT CELL-DIVISION—MITOSIS (Figs. 9, 10).—In this form of cell-division also, the nucleus divides into two daughter nuclei, and the cell into two daughter cells, but only after they have passed through certain characteristic and complicated changes. These changes occur

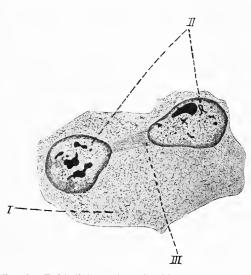


Fig. 8.—Epithelial cell from bladder showing amitotic division of its nucleus. (Nemileff.) *I*, Cytoplasm; *II*, two daughter nuclei; *III*, fibrils uniting daughter nuclei.

as a continuous process, but it is convenient for clearness of description to arbitrarily divide them into stages or phases. Thus we recognize in mitosis: (a) the prophase; (b) the metaphase; (c) the anaphase; (d) the telophase. The prophase is the stage of preparation on the part of the nucleus for division; the metaphase, the actual separation of the nuclear elements; the anaphase, the formation of the two daughter nuclei; the telophase, the reconstruction of the two daughter resting nuclei and the divi-

sion of the cytoplasm.

- (a) The Prophase (Fig. 9, B, C, D) is marked by the following changes:
- 1. The centrosome, if single, divides into two daughter centrosomes. In most actively dividing cells, however, the centrosome is at this stage already double (Fig. 9, A) having divided as early, frequently, as the anaphase of the preceding mitosis.

The two daughter centrosomes, each surrounded by its attraction sphere, now move apart but remain connected by fibrils, probably derived from the linin (Fig. 9, B). These fibrils form the central or achromatic spindle. Two other sets of fibrils radiate from each centrosome—one, known as the polar rays, passes out toward the periphery of the cell; the other, known as the mantle fibres, extends from the centrosome to the chromosomes (Fig. 9, C). The two centrosomes with their fibres constitute the amphiaster.

2. During or immediately following the formation of the amphiaster, important changes take place in the nucleus. It increases in size and loses the reticular appearance of the resting nucleus, its chromatic elements becoming arranged in a long spireme-thread or in several shorter threads, the *closed skein* or *closed spireme*. This next becomes thicker and more loosely arranged, thus forming the *open spireme*. That some

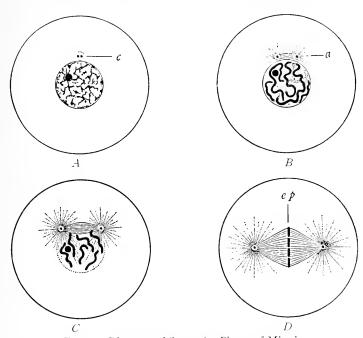


Fig. 9.—Diagrams of Successive Phases of Mitosis.

A, Resting cell, with reticular nucleus and true nucleolus; c, attraction sphere with two centrosomes.

B, Early prophase. Chromatin forming continuous thread—the spireme; nucleolus still present; a, amphiaster; the two centrosomes connected by fibrils of achromatic spindle. C, Later prophase. Segmentation of spireme to form the chromosomes; achromatic

spindle connecting centrosomes; polar rays; mantle fibres; fading of nuclear membrane. D, End of prophase. Monaster—mitotic figure complete: ep, chromosomes arranged around equator of nucleus; fibrils of achromatic spindle connecting centrosomes; mantle fibres passing from centrosomes to chromosomes. (E. B. Wilson, "The Cell," The Macmillan Co)

chemical as well as morphological change has taken place in the transformation of the reticulum of the resting nucleus into the spireme is shown by the marked increase in staining intensity, the spireme taking a much darker stain than the reticulum. Late in the prophase the nucleolus and nuclear membrane disappear. The cytoplasm and karyoplasm then become continuous and both spireme and amphiaster lie free in the general cell protoplasm (Fig. 9, C).

3. The spireme next breaks up into a number of segments—chromosomes (Fig. 9, C). These are usually rod-shaped at first, later they may become U's or V's or may even become spheroidal. chromosomes now arrange themselves regularly around the equator of the nucleus, their closed ends being directed centrally.

The details of the transformation of the reticulum into chromosomes varv. In some cases a single spireme-thread is formed. In others

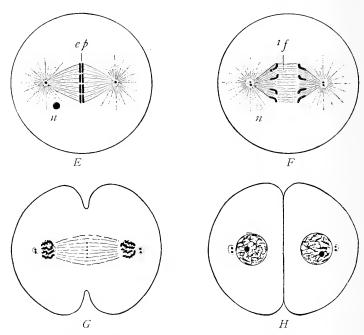


Fig. 10.—Diagrams of Successive Phases of Mitosis.

 $E,\ Metaphase.$  Longitudinal cleavage; splitting of chromosomes to form daughter chromosomes,  $ep;\ n,\ cast-off\ nucleolus.$ 

F, Anaphase. Daughter chromosomes passing along fibrils of achromatic spindle toward centrosomes; division of centrosomes; if, interzonal fibres or central spindle.

G, Late anaphase. Formation of diaster; beginning division of cell body.

H, Telophase. Reappearance of nuclear membrane and nucleolus; two complete daughter cells, each containing a resting nucleus. (E. B. Wilson, "The Cell," The Macmillan Co.)

the spireme-thread first splits longitudinally into two threads before segmenting into chromosomes. Again the spireme-thread may show segmentation into chromosomes from the beginning. In still other cases the chromosomes apparently form directly from the reticulum without the intervention of the spireme stage. It is most important to note that while the number of chromosomes varies for different species of plants and animals, it is fixed and characteristic for a given species.

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Thus in Ascaris megalocephala (much used for study on account of its small number of chromosomes) the number is 4, in the mouse 24, in man, estimated by some as 16, by others 24. This means that whenever mitosis occurs in Ascaris, the spireme-thread invariably segments into 4 chromosomes. Chromosomes and amphiaster now constitute the *mitotic figure* which at this stage is known as the *monaster*, its formation marking the end of the prophase.

- (b) Metaphase (Fig. 10, E). This marks the beginning of actual division of the nucleus. Each chromosome splits longitudinally (longitudinal cleavage) into two daughter chromosomes, each containing exactly one-half the chromatin of the parent chromosome. U- and V-shaped chromosomes always begin to split at the apex, from which point the separation extends to the open ends.
- (c) Anaphase (Fig. 10, F, G).—An equal number of daughter chromosomes now travels along the fibrils of the achromatic spindle—apparently under the influence of the mantle fibres—toward each daughter centrosome around which they become grouped. In this way are formed two daughter stars, the mitotic figure being known at this stage as the diaster (Fig. 10, G). These daughter stars are at first connected by the fibrils of the achromatic spindle. In this stage may also occur beginning division of the cell body. In actively dividing cells each centrosome frequently undergoes division at this stage, resulting in four centrosomes to the cell.
- (d) Telophase (Fig. 10, H).—This is marked by division of the cell protoplasm and consists of a cycle of changes, by means of which each group of daughter chromosomes is transformed into the chromatin network of a resting nucleus. These changes are the same as those described in the prophase, but occur in the reverse order, the chromosomes uniting to form the spireme, and the spireme becoming transformed into the nuclear network. The result is the formation of two daughter cells. The nuclear membrane reappears, as does also the nucleolus. Each daughter cell is thus provided with a resting nucleus. The fact that the number of chromosomes which enter into the formation of the chromatic reticulum of the nucleus of each daughter cell is the same as the number into which the spireme of the parent cell divided, has suggested the hypothesis that the chromosomes maintain their identity even during the resting stage.

The time required for the mitotic process is usually from one-half to three-quarters of an hour. Exceptionally it is prolonged to several hours. The parts which the several cell structures play in mitosis have been the subjects of much study and are as yet not fully determined.

As to the behavior of the chromatic portion of the mitotic figure little doubt exists. It originates in the chromatic portion of the nuclear reticulum of the parent cell and its destination is the chromatic portion of the reticulum of the daughter cells.

The rôle of the centrosome in mitosis is not so clear. It has been called the "dynamic centre" of the cell because in most cases it appears to be the active agent in initiating and probably further directing the mitotic process. The origin of the astral fibres is not always the same. In Infusoria the centrosome is found within the nucleus and both amphiaster and chromosomes are of nuclear origin. In some of the higher plants the amphiaster is derived wholly from the spongioplasm. In the egg cells of Echinoderm, part of the amphiaster (central spindle) is of nuclear, the remainder (asters) of cytoplasmic origin. That the centrosome is not always the active factor in mitosis is shown by the fact that in the higher plants no centrosome can be demonstrated during any stage of mitosis, and also that in some cases the chromosomes divide without previous division of the centrosome. mitotic periods the centrosome with or without its aster may remain as an integral part of the resting cell. It may, on the other hand, entirely disappear during the resting stage.

It is through the above-described process of cell-division that new cells are produced to replace those worn out as a result of their labors or destroyed by injury. It is through the same process that the vast number of cells which make up the adult body are developed from one original cell—the ovum. Such powers of evolution are not, however, inherent in the ovum itself, but, in sexual reproduction, are acquired only after its union with germinal elements from the male. This union of male and female germinal elements is known as *fertilization* of the ovum.

#### FERTILIZATION OF THE OVUM.

Prior to and in preparation for fertilization, both male and female cells must pass through certain changes. These are known as *maturation of the spermatozoön* on the male side (p. 315) and of the *ovum* on the female (p. 328).

The *spermatozoön* (Fig. 11) is developed from a cell of the seminiferous tubule of the testis. The nucleus of this cell so divides its chromosomes that *each spermatozoön contains just one-half the number of* 

chromosomes characteristic of cells of the species. These are contained in the head of the spermatozoon, which thus represents the nucleus of the male sexual cell, the middle piece probably containing the centrosome, the tail piece the remains of the protoplasm.

The nucleus of the ovum or germinal vesicle also passes through a series of changes by which it loses one-half its chromosomes.

germinal vesicle or nucleus of the ovum first undergoes mitotic division with the usual longitudinal cleavage of its chromosomes and the formation of two daughter nuclei. One of these and its centrosome are extruded from the cell as the first polar body. The remaining nucleus and centrosome again divide mitotically, only in this second division, instead of the usual longitudinal cleavage of chromosomes, by which each daughter nucleus is provided with the same number of chromosomes as the mother nucleus. the chromosomes simply separate, one-half going to each daughter nucleus. One of the daughter nuclei and its centrosome are now extruded as the second polar body. The polar bodies ultimately disappear, as does also the centrosome remaining within the egg. This leaves in the now matured ovum a single nucleus, which is known as the female pronucleus, and which Fig. 11.—Human contains one-half the number of chromosomes characteristic of cells of the species.

During this process in some animals—in others after its completion—the spermatozoön enters the ovum. The head of the spermatozoon becomes the



Spermatozoa. (After Retzius.) Head seen on flat; 2, head seen on edge; k, head; m, body; f, tail; e, end piece.

male pronucleus, the middle piece becomes a centrosome, while the tail is, in some instances at least, left behind as the spermatozoön enters the egg. The chromatin of the male next becomes arranged as chromosomes. Male and female pronuclei now lose their limiting membranes and approach each other, their chromosomes intermingling. As each pronucleus contained one-half the number, the monaster thus formed contains the full number of chromosomes characteristic of the species. Meanwhile the male centrosome, formed from the body of the spermatozoön, divides into two daughter centrosomes. These with their radiating fibrils have the same arrangement relative to the monaster of mingled male and female chromosomes, already described under mitosis. By longitudinal cleavage of these chromosomes, as in ordinary mitosis, two sets of daughter chromosomes are formed. Each set passes along the filaments of the achromatic spindle to its centrosome. Thus is formed the *diaster*. By continuation of the mitotic process two new nuclei are formed, each nucleus contain-

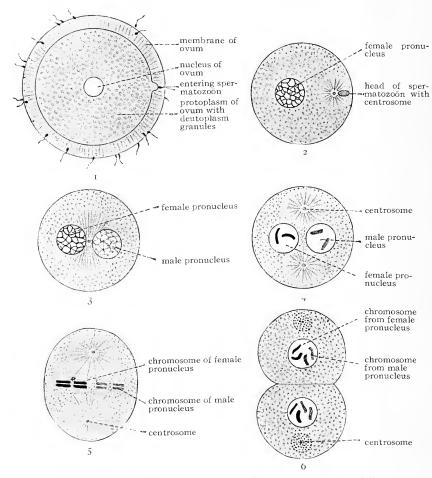


Fig. 12.—Diagram of Fertilization of the Ovum. (The somatic number of chromosomes being four.) (From Bohm and von Davidoff, after Boveri.)

r, Ovum surrounded by spermatozoa, only one of which is in the act of penetration. Toward the latter the protoplasm of the ovum sends out a process; 2, Head of spermatozoön has entered ovum, its body becoming the male centrosome, its tail having disappeared; 3, The head of spermatozoön has become the male pronucleus. Male and female pronuclei approach each other. Between them is the (male) centrosome; 4, The spiremes of male and female pronuclei have each formed two chromosomes. The centrosome has divided; 5, Male and female chromosomes have mingled and by longitudinal cleavage (see Mitosis, p. 51) have become eight. These become arranged in the equatorial plane of the ovum. Mantle fibres extend from centrosomes to chromosomes; 6, Division of the ovum; two daughter cells, each containing a daughter nucleus. Each daughter nucleus contains four chromosomes, two derived from each pronucleus.

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ing the number of chromosomes characteristic of the species, and each being made up *equally of male and female chromosome elements*. Thus occurs the first division of the fertilized ovum into two daughter cells.

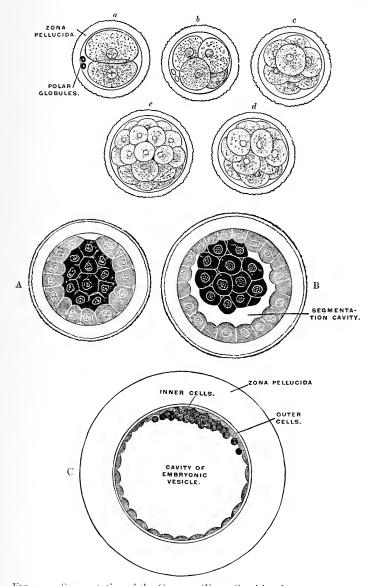


FIG. 13.—Segmentation of the Ovum. (From Gerrish, after van Beneden.) a, Two-cell stage resulting from first division of fertilized ovum: b, four-cell stage; c, d, e, later stages. A, Differentiation into inner and outer cells; B, Formation of segmentation cavity; C, Embryonic vesicle, showing two primary germ layers. Outer cells, ectoderm; inner cells, entoderm.

By similar mitotic processes these two cells become four, the four cells become eight, etc. This is known as *segmentation of the ovum*.

The earlier generations of these cells are morphologically alike and are known as *blastomeres*. Soon, however, these cells become spread out and at the same time differentiated into *two primary germ layers*. The outer of these is known as the *ectoderm* or *epiblast*, the inner as the *entoderm* or *hypoblast*. Between these two layers and derived from them a third layer is formed, the *mesoderm* or *mesoblast*. These three layers constitute the *blastoderm*.

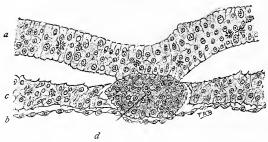


Fig. 14.—The Two Primary Germ Layers; from transverse section through primitive groove of a chick of 27 hours' incubation. a, Ectoderm (outer germ layer); b, entoderm (inner germ layer); c, mesoderm (middle germ layer); d, anlage of notochord.

As to what determines and controls fertilization, comparatively little is known. As in ordinary mitosis, the origin of the centrosome is obscure. In some forms, at least, the centrosome of the spermatid enters into the formation of the middle piece of the spermatozoön. The male centrosome thus enters the ovum. It is also known that in some eggs the egg-centrosome disappears soon after the extrusion of the second polar body, and that the centrosome of the fertilized egg develops in close relation to the middle piece of the spermatozoön. These facts point to the male centrosome as the centrosome of fertilization.

The ovum and spermatozoön are apparently brought together by a definite attraction on the part of the ovum toward the spermatozoön. The nature of this attraction is unknown. It is possibly chemical, and is exerted only between ova and spermatozoa of the same species. This has been proved for lower forms by mixing ova of one species and spermatozoa from several species in an inert medium when only spermatozoa of the same species will attach themselves to the ova. That the attractive force lies in the cytoplasm is shown by the fact that small pieces of the egg protoplasm free from nuclear elements will exert sufficient attractive powers to cause spermatozoa to enter them.

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As to the point of entrance of the spermatozoön, some eggs may be entered at any point, others are permeable at but one point.

One spermatozoön only is required for fertilization, and when this spermatozoön has entered, the egg apparently loses its power of attracting spermatozoa, or else develops some actual defense against further entrance of spermatozoa.

#### TECHNIC.

- 1. Fresh cells may be studied by gently scraping the surface of the tongue, transferring the mucus thus obtained to a glass slide and covering with a cover-glass.
- 2. Red blood cells from the frog are prepared as follows: After killing the frog the heart is opened and the blood allowed to drop into a tube containing Hayem's fluid (sodium chlorid 1 gm., sodium sulphate 5 gm., mercuric chlorid 0.5 gm., distilled water 100 c.c.). After shaking, the cells are allowed to settle for from twelve to twenty-four hours. The fixative is then replaced by water, the tube again shaken, the cells allowed to settle, and the water is replaced with 80-per-cent. alcohol tinged with iodin. After from twelve to twenty-four hours the alcohol is decanted and the tube partly filled with alum-carmine solution (page 17). About twenty-four hours usually suffices for staining the nuclei. The alum-carmine is then poured off and the cells well shaken in water. After settling, the water is replaced by glycerin, to which a small amount of picric acid has been added. In this the cells may be permanently preserved. The nuclei are stained red by the carmine, the cytoplasm yellow by the picric acid.
- 3. Surface cells from the mucous membrane of the bladder. The bladder is removed from a recently killed animal, pinned out mucous membrane side up on a piece of cork and floated, specimen side down, on equal parts Müller's fluid and Ranvier's alcohol (technic 4, p. 6, and a, p. 4) for from twenty-four to forty-eight hours. The specimen is then washed in water and the cells removed by gently scraping the surface. These may then be stained and preserved in the same manner as the preceding. Cells from the different layers should be studied; also the appearance of the large surface cells seen on flat and on edge, showing pitting of under surface by cells beneath.
- 4. Amœboid movement may be studied by watching fresh-water amœbæ or white blood cells. A drop of water containing amœbæ is placed on a slide, covered, and a brush moistened with oil is passed around the cover to prevent evaporation. The activity of the amœbæ may be increased by slightly raising the temperature. An apparatus known as the warm stage is convenient for demonstrating amœboid movement. A drop of blood, human, or better from one of the cold-blooded animals, may be used for the study of amæboid movement in the white blood cells. It should be placed on a slide, covered, and immediately examined on the warm stage.
- 5. Ciliary movement is conveniently studied by removing a small piece of the gill of an oyster or mussel, teasing it gently in a drop of normal salt solution and covering. The cilia being very long, their motion may be easily studied, especially after it has become slow from loss of vitality.

6. Mitosis. The salamander tadpole and the newt are classical subjects for the study of cell-division. The female salamander is usually full of embryo tadpoles in January and February. The embryos are removed and fixed in Flemming's fluid (technic 7, p. 7), after which they may be preserved in equal parts of alcohol, glycerin, and water. Mitotic figures may be found in almost any of the tissues. Pieces of epidermis from the end of the tail, the parietal peritoneum, and bits of the gills are especially satisfactory. If the newt's tail is used, it should be fixed in the same manner, embedded in paraffin and cut into thin sections. These are stained with Heidenhain's hæmatoxylin, technic 3, p. 16.

Certain vegetable tissues, such as the end roots of a young, rapidly growing onion or magnolia buds, are excellent for the study of mitosis. The technic is the same as for animal tissues.

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PART III.
THE TISSUES.



## CHAPTER I.

# HISTOGENESIS—CLASSIFICATION.

ECTODERM, mesoderm, and entoderm (see page 56) are known as the primary layers of the blastoderm. They differ from one another not only in position, but also in the structural characteristics of their cells. The separation of the blastomeres into these three layers represents the first morphological differentiation of the cells of the developing embryo. By further and constantly increasing differentiation are developed from these three primary layers all tissues and organs, each layer giving rise to its own special group of tissues. The tissue derivations from the primary layers of the blastoderm are as follows:

**Ectoderm.**—(1) Epithelium of skin and its appendages—hair, nails, sweat, sebaceous and mammary glands, including smooth muscle of sweat glands.

- (2) Epithelium of mouth and anus, of glands opening into mouth, and enamel of teeth.
- (3) Epithelium of nose and of glands and cavities connected with nose.
- (4) Epithelium of external auditory canal and of membranous labyrinth.
- (5) Epithelium of anterior surface of cornea, of conjunctiva, and of crystalline lens.
  - (6) Epithelium of male urethra, except prostatic portion.
  - (7) Epithelium of pineal bodies and of pituitary body.
  - (8) Entire nervous system, including retina.

**Entoderm.**—(1) Epithelium of digestive tract excepting mouth and anus, and of glands connected with digestive tract.

- (2) Epithelium of respiratory tract and of its glands.
- (3) Epithelium of bladder except the trigonum, of female urethra, and of prostatic portion of male urethra.
  - (4) Epithelium of tympanum and of Eustachian tube.
  - (5) Epithelium of thyreoid and of Hassall's corpuscles of thymus.

Mesoderm.—(1) All the connective or supporting tissues except neuroglia.

(2) Lymphatic organs with the exception of Hassall's corpuscles and reticulum of the thymus.

- (3) Blood cells and bone-marrow.
- (4) Striated, cardiac and smooth muscle (with the possible exception of smooth muscle of sweat glands).
- (5) Endothelium lining blood-vessels and lymphatics.
- (6) Mesothelium lining serous membranes—pleura, pericardium, and peritoneum.
- (7) Epithelium of genito-urinary system with the exception of the urethra and a large part of the bladder.

In all but the lowest forms of animal life the body consists of an orderly arrangement of many kinds of cells. From the cells is developed a substance which lies outside the cells and is known as intercellular substance. This may be small in amount, just sufficient to unite the cells, as in epithelium, or it may so predominate as to determine the character of the tissue, as in some forms of connective tissue. It does not always completely separate the cells which may be connected across the intercellular substance by extensions of their protoplasm, as in the "intercellular bridges" of epithelium or the anastomosing processes of connective-tissue cells. Less commonly cells are united in such a multinuclear continuum that their boundaries are almost or wholly lost. Such a structure is known as a syncytium. The association of a particular type of cell with a particular type of intercellular substance is known as a tissue. The character of a tissue depends upon the character of its cells, of its intercellular substance, and their relations to each other. Further differentiation of cells and intercellular substance within a particular tissue gives rise to various sub-groups of the tissue. The association of tissues to form a definite structure for the performance of a particular function is known as an organ. The physiological association of organs constitutes a system.

A scientific classification of the tissues is at present impossible.

The foregoing list of tissue derivations shows how unsatisfactory is any attempt at classification on the basis of histogenesis, many tissues which are morphologically similar being derived from two or even all three of the blastodermic layers.

The following is the usual classification of adult tissues: (1) Epithelial tissues; (2) connective tissues; (3) blood; (4) muscle tissue; (5) nerve tissue.

Of these, epithelium and connective tissue may be regarded as the more elementary tissues, being common to both plants and animals. Blood is sometimes classified among the connective tissues. Muscle and nerve are the most highly specialized tissues and are peculiar to animals.

## CHAPTER II.

# EPITHELIUM (INCLUDING MESOTHELIUM AND ENDOTHELIUM).

General Characteristics.—Epithelium is derived from all three germ layers. It consists almost wholly of cells. The intercellular substance is merely sufficient to attach the cells to one another and is, consequently, known as cement substance. In some instances the protoplasm of adjacent epithelial cells is seen to be even more closely associated, the intervening cement substance being bridged over by delicate processes of protoplasm which pass from one cell to another and are known as "intercellular bridges" (see Fig. 19, p. 66). It seems probable that the minute spaces between the processes serve as channels for the passage of food (lymph) to the cells. The surface cells of epithelium are united by continuous cement substance in which there are apparently no spaces. In this way escape of lymph is prevented.

Epithelial cells vary in size and shape, the element of pressure being a frequent determining factor as regards shape. Their protoplasm may be clear, finely or coarsely granular, or pigmented. Each cell usually contains a single well-defined nucleus. Two or more nuclei are sometimes present. Some epithelial cells are, when fully matured, non-nucleated, e.g., respiratory epithelium of lung.

When epithelium rests upon connective tissue, it is usually separated from the latter by a thin, apparently homogeneous membrane known as the *basal membrane* or *membrana propria*. Authorities differ as to whether this membrane is of connective-tissue or of epithelial origin.

Surface epithelial cells frequently have thickened free borders or cuticulæ, which unite to form a continuous membrane, the cuticular membrane. Striations extend from the cytoplasm into the cuticulæ. A still greater specialization of the surface of the cell is seen in the ciliated cell. In this cell fine hair-like projections—cilia—extend from the surface of the cell.

Some epithelial cells show important changes dependent upon their functional activities. An example of this is seen in the mucous cell in which there is a transformation of the greater part of the cytoplasm into, or its replacement by, mucus.

Epithelia are devoid, as a rule, of both blood- and lymph-vessels. An exception to this is the stria vascularis of the cochlea. Nerves, on the other hand, are abundant.

Classification.—Epithelia may be classified according to shape and arrangement of cells as follows:

- (1) Simple Epithelium.—(a) Squamous; (b) columnar.
- (2) Stratified Epithelium.—(a) Squamous; (b) columnar.
- (3) Mesothelium and Endothelium.

Specializations of the above-mentioned types are known as: (a) Ciliated epithelium; (b) pigmented epithelium: (c) glandular epithelium; (d) neuro-epithelium.

Pigment may occur in any type of epithelium. Cilia are found only in the simple columnar and stratified columnar forms.

# 1. Simple Epithelium.

In simple epithelium the cells are arranged in a single layer.

(a) Simple squamous epithelium consists of flat scale-like cells which are united by an extremely small amount of intercellular sub-

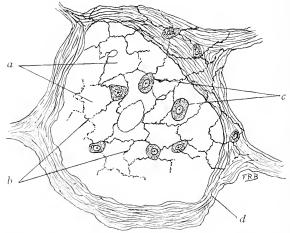


Fig. 15.—From Section of Cat's Lung, stained with silver nitrate, showing outlines of the Simple Squamous Epithelium Lining the Air Vesicle. a, Two epithelial cells; b, the wavy stained intercellular substance; c, fœtal cells; d, connective tissue.

stance. The edges of the cells are smooth or serrated. Seen on flat, they present the appearance of a mosaic. Seen on edge, the cells appear fusiform, being thickest at the centre, where the nucleus

is situated, and thinning out toward the periphery. Simple squamous epithelium has but a limited distribution in man. It occurs in the lungs as non-nucleated respiratory epithelium, in Bowman's capsule of the renal corpuscle, in the descending arm of Henle's loop of the uriniferous tubule, in the retina in the form of pigmented cells, and on the posterior surface of the anterior lens capsule.

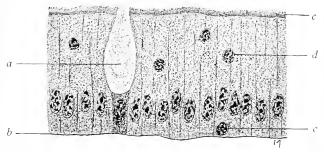


Fig. 16.—Simple Columnar Epithelium from the Human Small Intestine, a, Mucous (goblet) cell; b, basement membrane; c, thickened free border (cuticula); d, leucocyte among the epithelial cells; e, replacing cell.

(b) Simple columnar epithelium consists of a single layer of elongated cells. The bases of the cells are usually separated from the underlying connective tissue by a basement membrane. The nucleus is, as a rule, in the deeper part of the cell, near the basement membrane. Many of these cells have prominent thickened free borders or cuticulæ. This form of epithelium is often ciliated. The height of the cell varies greatly, there being all gradations from high columnar to law subsidal. Simple

height of the cell varies greatly, there columnar to low cuboidal. Simple columnar epithelium lines the gastro-intestinal canal, the uriniferous tubule (excepting the descending arm of Henle's loop), simple tubular glands, the ducts of some compound tubular glands, the smaller bronchi, the membranous and penile portions of the male uretha, and the gall-bladder.

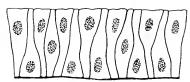


Fig. 17.—Diagram of Pseudostratified Epithelium, showing Nuclei situated at Different Levels.

In simple columnar epithelium, in addition to the single row of epithelial cells, there are found lying near the basement membrane, between the bases of the epithelial cells, small, spherical, or irregular cells, which frequently show mitosis and which are known as *replacing cells*. They appear to develop into columnar epithelial cells as they are needed to replace older cells. The so-called *pseudo-stratified* 

epithelium is a form of simple columnar epithelium, in which, from crowding of the cells, the nuclei have come to lie at different levels, thus giving the appearance of stratification (Fig. 17).

# 2. Stratified Epithelium.

In stratified epithelium the cells are arranged in more than one layer.

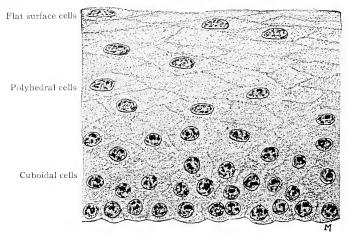


Fig. 18.—Stratified Squamous Epithelium from Cat's Œsophagus.

(a) Stratified squamous epithelium is developed from simple epithelium by the growth of new cells between the old cells and the under-

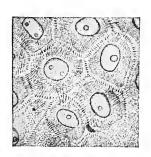


Fig. 19.—Epithelial Cells from the Stratum Spinosum of the Human Epidermis showing "Intercellular Bridges." × 700. (Szymonowicz.)

lying connective tissue. It consists of several layers of cells which vary greatly in size and shape. The surface cells are large and flat. Beneath these are several layers of polyhedral cells, with often very distinct protoplasmic intercellular connections ("intercellular bridges," see also page 63). The deepest cells are columnar or cuboidal. It is thus seen that in stratified squamous epithelium only the surface cells are squamous. This form of epithelium rests upon a more or less distinct basement membrane, which is frequently thrown up into folds by papille of the underlying connective tissue. Stratified forms the surface of the skin and of

squamous epithelium forms the surface of the skin and of mucous membranes of cavities opening upon it, mouth and œsophagus, conjunctiva, external ear, vagina, and external sheath of hair follicle.

(b) Stratified Columnar Epithelium.—Only the surface cells are columnar, the deeper cells being irregular in shape. The surface cells frequently send long processes down among the underlying cells. The free surface is often marked by a well-developed cuticula.

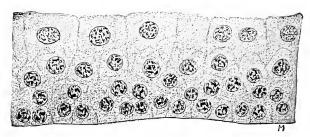


Fig. 20.—Transitional Epithelium from the Human Bladder.

Some epithelia of this type are ciliated. Stratified columnar epithelium is found in the larynx, nose, palpebral conjunctiva, largest of the gland ducts, the vas deferens, and part of the male urethra.

Stratified epithelium composed of only from three to six layers of cells is sometimes designated "transitional epithelium." This type of epithelium usually rests upon a basement membrane free from



Fig. 21.—Stratified Columnar Epithelium from the Human Male Urethra. ×400.

papillæ. The surface cells are large and frequently contain two or three nuclei. Their free surfaces are flat, while their under surfaces show depressions due to pressure from underlying cells. The deeper cells are polygonal or irregularly cuboidal. This form of epithelium lines the bladder, ureter, pelvis of the kidney, and prostatic portion of male urethra.

#### Modified Forms of Epithelium.

(a) Ciliated Epithelium.—In this form of epithelium, fine hair-like processes—cilia—extend from the surface of the cell. These cilia vary from twelve to twenty-five for each cell and may be short as in the

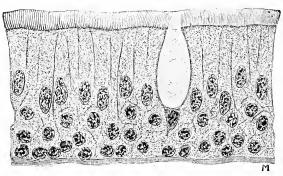


Fig. 22.—Stratified Columnar Ciliated Epithelium from the Human Trachea. A mucous (goblet) cell also is present.

trachea or long as in the epididymis. There is usually a well-defined cuticula from which the cilia appear to spring. According to Apáthy, the cilia extend through the cuticula, giving to the latter a striated

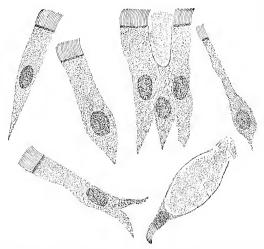


Fig. 23.—Isolated Ciliated Cells and Goblet Cells from Dog's Trachea. ×700.

appearance (Fig. 24). Just beneath the cuticula each cilium shows a swelling—the *basal granule*. Lenhossék considers these granules centrosomes. The intracellular extensions of the cilia converge

toward the nucleus, and are continuous with the reticular or fibrillar structure of the cell body. The motion of cilia is wave-like, the wave always passing in the same direction. Various explanations of ciliary motion have been given. The most plausible is that it is due to the contractile powers of the spongioplasm.



Cilia are confined to the surface cells of simple columnar and stratified columnar epithelium.

Simple columnar ciliated epithelium occurs in the smaller bronchi, uterus, Fallopian tubes and central canal of the spinal cord.

Stratified clumnar ciliated epithelium occurs in large bronchi, trachea, larynx, nose, Eustachian tube, vas deferens and epididymis.

(b) Pigmented epithelium consists of cells the cytoplasm of which contains brown or black pig-

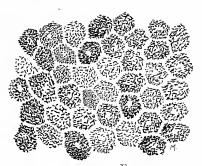


FIG. 25.

Fig. 24.—Ciliated Epithelial Cell from Intestine of Mollusk (Engelmann), showing, a, cuticula, b, basal granules, and c, intracellular extensions of cilia.

Fig. 25.—Pigmented Epithelial Cells from the Human Retina (×350), showing different degrees of pigmentation. The clear spots in the centres of the cells represent the unstained nuclei.

ment. It is usually present in the form of spherical or rod-like granules. Examples of it are seen in the pigmented epithelium of the retina and in the pigmented cells of the deeper layers of the epidermis in colored races (Fig. 25).

- (c) Glandular Epithelium.—This forms the essential or secreting element of glands and is mostly of the simple cylindrical variety. The different kinds of glands and their epithelia will be described among the organs.
- (d) Neuro-epithelium.—This is a highly specialized form of epithelium which occurs in connection with the end organs of nerves. under which heading it will be described.

# 3. Mesothelium and Endothelium.

While recognizing the present tendency toward considering those tissues formerly classified as endothelium, as simple squamous epithelium, the correctness of the newer classification still remains *sub judice* 

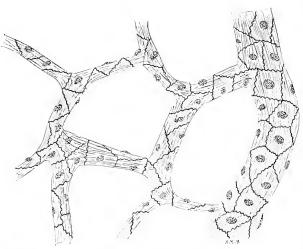


Fig. 26.—Mesothelium from Omentum of Dog Treated according to Technic 7, p. 77.  $\times$  350. Black wavy lines indicate the intercellular cement substance. The mesothelial cells cover the strands of connective tissue, the fibres of the latter being visible through the transparent cell bodies.

and, so long as this is the case, we prefer to retain the certainly much more convenient classification of Minot, which coincides with his subdivision of the mesoblast. According to this classification, for those tissues which resemble epithelium in structure and which are derived from the sublayer of the mesoderm which he designates the

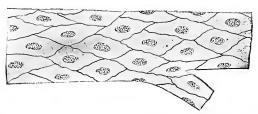


Fig. 27.—The Endothelium of a Small Blood-vessel. Silver nitrate stain. ×350.

mesenchyme, the term *endothelium* is retained. The term *mesothelium* is used for those tissues which resemble epithelium but are derived from a subdivision of the mesoderm which he designates the mesothelial layer.

Mesothelium and endothelium are similar in structure. Each consists of thin flattened cells with clear or slightly granular protoplasm and bulging oval or spherical nuclei. The edges of the cells are usually wavy or serrated. The cells are united by an extremely small amount of intercellular "cement" substance, which is usually indistinguishable except by the use of a special technic.

Endothelium forms the walls of the blood and lymph capillaries and lines the entire blood-vessel and lymph-vessel systems.

Mesothelium lines the body cavities—the pleura, the pericardium, and the peritoneum.

#### TECHNIC.

- 1. Simple Squamous Epithelium.—That of the lung may be demonstrated by injecting with silver solution (technic 1, p. 26) through a bronchus and then immersing the tissue in the same solution. The lungs of young kittens furnish especially satisfactory material.
- 2. Simple Columnar Epithelium.—A piece of small intestine, human or animal, is pinned out flat on cork and fixed in formalin-Müller's fluid (technic 5, p. 7). Sections are cut perpendicular to the surface, stained with hæmatoxylin and eosin (technic 1, p. 18) and mounted in glycerin tinged with eosin (page 20). Little processes known as villi project from the inner surface of the intestine. These are covered by a single layer of columnar epithelial cells. The cuticulæ and cuticular membrane are usually well shown. Among the simple cylindrical cells are seen large clear or slightly blue-stained cells. These are known from their secretion as mucous cells, from their shape as goblet cells, and are classed as modified epithelium of the glandular type. These should be studied in their various stages of secretion, from the cell in which only a small amount of mucus is present near the outer margin, to the cell whose protoplasm is almost wholly replaced by mucus. Some cells will be found in which the surface has ruptured and the mucus can be seen pouring out of the cell.
- 3. Stratified Squamous Epithelium.—The cornea furnishes good material for the study of stratified squamous epithelium. An eye is removed from a freshly killed animal and the cornea cut out and fixed in formalin-Müller's fluid. Sections are cut perpendicular to the surface, and treated as in the preceding. The cells are laid down in from six to eight layers. The æsophagus may be used instead of the cornea, its mucous membrane being lined by a somewhat thicker epithelium.
- 4. Transitional Epithelium.—This is conveniently studied in the mucous membrane of the bladder. Technic same as 2, above.
- 5. Stratified Columnar Epithelium.—A portion of trachea from a recently killed animal is treated according to the same technic. The surface cells are ciliated so that this specimen also serves to demonstrate that type of modified epithelium. Isolated cells or clumps of cells may be obtained from the trachea in the manner described in technic 3, p. 57.
- 6. Pigmented Epithelium.—Fix a freshly removed eye in formalin-Müller's fluid (page 7). After hardening, cut transversely and remove the vitreous and

retina. The pigmented cells remain attached to the inner surface of the chorioid, and may be removed by gently scraping. They may be preserved and mounted in glycerin.

- 7. Mesothelium.—Part of the omentum of a recently killed animal is removed and washed in water, care being taken not to injure the tissue in handling. The water is then replaced by a 1 to 500 aqueous solution of silver nitrate. After half an hour the specimen is removed from the silver, washed in water, transferred to 80-per-cent. alcohol and placed in the sunlight until it becomes light brown in color. It is then preserved in fresh 80-per-cent. alcohol. The nuclei may be stained with hæmatoxylin (stain 5, p. 16). The specimen should be mounted in glycerin. Wavy black lines indicate the intercellular cement substance. The nuclei of the mesothelial cells are stained blue, those of the underlying connective-tissue cells a paler blue. It must be borne in mind in studying this specimen that the strands or trabeculæ of the omentum are not composed of mesothelium, but of fibrous connective tissue, and that the flat mesothelial cells merely lie upon the surface of the connective-tissue strands.
- 8. Endothelium may be demonstrated by removing the bladder from a recently killed frog, distending it with air and subjecting it to the same technic. By this means the intercellular substance of the endothelium of the blood-vessels of the bladder wall is stained and the outlines of the cells are thus shown.

## CHAPTER III.

## THE CONNECTIVE TISSUES.

General Characteristics.—All of the connective tissues, with the single exception of the connective tissue peculiar to the nervous system (neuroglia), are developed from the mesoderm. This consists at first wholly of round or polygonal cells united by a small amount of intercellular cement substance. As development proceeds the cells gradually become more and more separated from one another by an increased amount of intercellular substance. This intercellular substance is a product of the cells and is at first homogeneous or granular. The appearance presented at this stage is that of irregular, branching, anastomosing cells, lying in a semi-fluid ground substance. This is embryonic connective tissue. With further changes in both cells and intercellular substance, but mainly in the latter, embryonic connective tissue differentiates to form the adult types of connective tissue.

The most prominent characteristic of the connective tissues, with the exception of adenoid tissue and fat, is the predominance of the intercellular substance. In this respect the connective tissues differ markedly from epithelial tissues and this difference in structure corresponds to difference in function. The rôle which the connective tissues play is mainly passive, and the cells instead of taking, as in epithelium, muscle and nerve tissues, the most active part, serve mainly for the maintenance of the nutrition of the more important intercellular substance. Moreover, with the exceptions mentioned above, it is the intercellular substance and not the cells which determines the physical character of the tissue. The denser forms of connective tissue. such as bone and cartilage, are supportive in function; somewhat less dense tissues, such as tendons, serve to attach muscles to bones; while more loosely arranged connective tissue forms the frame-work of the various organs. Connective tissue differs also from epithelium as regards its blood supply, being usually though not always very vascular. A further characteristic of the connective tissues is the apparent ease with which one type may become transformed into another.

The division of connective tissue into its various sub-groups is also based upon structural differences in the intercellular substances.

Classification.—The connective tissues may be classified as follows, although embryonal tissue and mucous tissue are essentially developmental forms.

- I. Fibrillar connective tissue, including arcolar tissue.
- Elastic tissue.
- 3. Embryonal tissue and mucous tissue.
- 4. Reticular tissue.
- 5. Lymphatic or adenoid tissue.
- 6. Fat tissue.
- 7. Cartilage.  $\begin{cases} (a) & \text{Hyaline.} \\ (b) & \text{Elastic.} \\ (c) & \text{Fibrous.} \end{cases}$
- 8. Bone tissue.
- o. Neuroglia.

# I. Fibrillar Connective Tissue.

Fibrillar connective tissue, also known as white fibrous tissue or connective tissue proper, consists of cells and fibres lying in a basement or ground substance. The elements of fibrillar tissue may be classified as follows:

Cells  $\begin{cases} \text{ (a) The ordinary connective-tissues cells.} \\ \text{ (b) Plasma cells.} \\ \text{ (c) Mast cells.} \\ \text{ 2. Wandering.} \end{cases}$ Intercellular substance.  $\begin{cases} \text{ (a) Fibres } \\ \text{ (b) Constraints} \end{cases}$   $\begin{cases} \text{ (b) Constraints} \end{cases}$ 

(b) Ground or basement substance.

Connective-tissue Cells.—(a) The ordinary fixed connective-tissue cell is often the only connective-tissue cell seen in ordinary sections. It is a flat, irregularly stellate cell with many branches (Fig. 30). The nucleus lies in the thickest part of the cell. The cytoplasm is usually clear or slightly granular. Each cell lies in a cell space or lacuna. From the cell spaces minute channels (canaliculi) extend in all directions to unite with canaliculi from adjoining spaces (Fig. 29). Delicate cell processes extend into the canaliculi and there anastomose with processes from other cells (Fig. 30). Owing to the extreme sensitiveness of the protoplasm of the connective-tissue cell to most fixatives, its usual appearance is that of a minute amount of cytoplasm shrunken down around a nucleus.

- (b) Plasma Cells.—These cells occur mainly near the smaller blood-vessels. Their protoplasm is finely granular and stains with basic aniline dyes. They frequently contain vacuoles. Small plasma cells are about the size of leucocytes, which they closely resemble. Large plasma cells are larger than leucocytes and richer in protoplasm. Some consider them as derived from leucocytes, others as a modified form of the ordinary fixed connective-tissue cell.
- (c) Mast cells are spherical or irregular-shaped cells, found like the preceding in the neighborhood of the blood-vessels. Their proto-

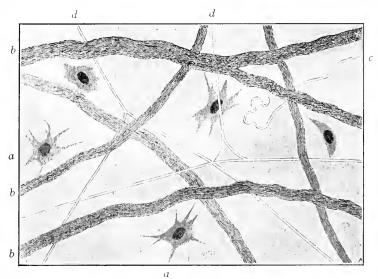


Fig. 28.—Fibrillar Connective Tissue (Areolar Type) from Subcutaneous Tissue of Rabbit (technic 2, p. 80).  $\times$ 500. a, Fixed connective-tissue cell; b, fibrillated fibres;  $\epsilon$  elastic fibre with curled broken end; d, elastic fibres showing Y-shaped branching.

plasm contains coarse granules which stain intensely with basic aniline dyes. They are believed by some investigators to be connected with the formation of fat; by others to represent a stage in the development of the fixed connective-tissue cell.

Connective-tissue cells may be pigmented (Fig. 31). In such cells the cytoplasm is more or less filled with brown or black pigment granules. In man pigmented connective-tissue cells occur in the skin, chorioid and iris.

The so-called *wandering cells* are not properly a part of connective tissue, being merely amæboid white blood cells (see page 98) which have passed out from the vessel into the tissues. They are not peculiar to connective tissue, being found in other tissues, *e.g.*, in epithelium.

The Intercellular Substance.—(a) Fibres. White or fibrillated fibres are bundles of extremely fine fibrillæ (o.  $5\mu$  in diameter) (Fig. 28). The fibrillæ lie parallel to one another and are united by a small amount of cement substance. The fibrillæ do not branch. The fibre bundles,

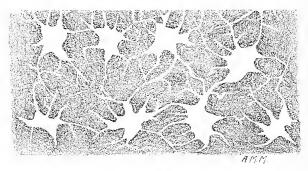


Fig. 29.—Section of Human Cornea cut Tangential to Surface. X 350. (Technic 9, p. 81.) Connective-tissue Cell Spaces (Lacunæ) and Anastomosing Canaliculi, white; whole Intercellular Substance (Ground Substance and Fibres), dark.

on the other hand, branch dichotomously and anastomose. White fibres, on boiling, yield *gelatin*.

Yellow or elastic fibres are apparently homogeneous, highly refractive fibres, varying in diameter from 1 to  $10\mu$  (Fig. 28). They

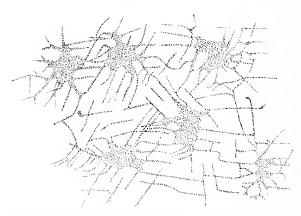


Fig. 30.—Section of Human Cornea cut Tangential to Surface. X 350. (Technic 8, p. 81.) Connective-tissue Cells with Anastomosing Processes, stained; Intercellular Substance (Ground Substance and Fibres), unstained.

branch and anastomose, forming networks. The smaller fibres are round on cross section, the larger flattened or hexagonal (Figs. 33 and 34). Their elasticity is easily demonstrated in teased specimens by curling of the broken ends of the fibres (Fig. 28). On boiling

they yield *elastin*. Although, when subjected to the usual technic, elastic fibres appear homogeneous, they are probably composed of a thin sheath or membrane, enclosing the more granular elastin. The latter stains intensely with magenta, the sheath remaining unstained.

In addition to the white fibres and elastic fibres above described, so-called "reticular" fibres are frequently present in fibrillated connective tissue. (See p. 83.)

(b) Basement or ground substance occurs in extremely minute amounts between the individual



Fig. 31.—Pigmented Connective-tissue Cells from Chorioid Coat of Human Eye. × 350. (Technic 7, p. 81.)

fibrillæ of the white fibres, where it acts as a cement substance. The same material also forms the basement or ground substance in which the connective-tissue cells and fibres lie (Fig. 29). Difficulty in seeing this ground substance is due to its transparency. It may be demonstrated by staining with silver nitrate. (See technic 9, p. 81.)

Much variation exists in regard to the proportions of the different elements. This gives rise to variations in the physical characteristics of the tissue. When fibres predominate over cells and ground sub-

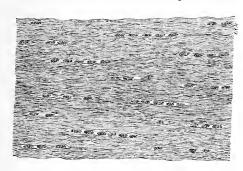


Fig. 32.—Longitudinal Section of Tendon from Frog's Gastrocnemius. ×250. The nuclei of the flattened cells are seen lying in rows between the connective-tissue fibres.

stance, the tissue is dense and hard and is known as *dense fibrous tissue*. The terms *fine* connective tissue and *coarse* connective tissue designate the character of the fibres. When many cells are present, the tissue is softer and is known as *cellular* connective tissue.

According to the arrangement of the white fibres, fibrous connective tissue is

#### subdivided as follows:

(1) AREOLAR OR LOOSE CONNECTIVE TISSUE.—In this the fibres are irregular, running in all directions and interlacing, leaving between them meshes or *areolæ* (Fig. 28).

Subcutaneous connective tissue is a typical example of areolar tissue. Both white and elastic fibres are present, although the former predominate. Areolar tissue varies greatly as regards the relative number of cells and fibres and the closeness with which the different elements are packed. It thus varies greatly in density.

(2) Formed Connective Tissue.—In this the fibres all run in approximately the same direction, and are united by a small amount of ground substance (Fig. 32). There are but few cells and these are flattened out by pressure and lie between the fibres, their long axes corresponding to the direction of the fibres. This arrangement of tissue elements forms a firm, dense tissue, such as is found in tendons and ligaments. Formed connective tissue also occurs as anastomosing networks of fibres, as, e.g., in the omentum (page 235). It should be noted that between dense "formed" connective tissue on the one hand and loose "areolar" tissue on the other, all gradations exist.

Regarding the development of the connective-tissue fibrils, there are two theories: (1) According to one, they are developed directly from the protoplasm of the connective-tissue cells. The cells increase in length, and fine granules appear, which arrange themselves in rows in the cytoplasm; these granules unite to form fibrils. Such cells are known as fibroblasts, and their fibrils are the forerunners of the intercellular fibrils of connective tissue. A modification of this theory derives the fibrils from the peripheral portion of the cell—the exoplasm. (2) According to the other theory the fibrils are developed from the matrix, minute granules first becoming arranged in rows and later uniting to form fibrils.

Regarded as opposing theories, there is in reality but little antagonism between them. There is no doubt as to the intercellular matrix being a product of the cell. Whichever theory, therefore, is accepted, the entire intercellular substance, fibres and ground substance are ultimate derivatives of the cell. Recent studies, especially those of Mall, are confirmatory of the second of the theories given above. He maintains that the connective-tissue fibrils, both white and elastic, are derivatives of an active intercellular matrix, which latter is a direct product of the cell.

Two similar theories exist as to the development of elastic fibres, a cellular theory and an extracellular theory. According to some advocates of the cellular theory, the elastic fibres are derived from the exoplasm; according to others, from the cytoplasm immediately surrounding the nucleus. Recent researches favor the extracellular theory. Mall describes extremely minute fibrils in the ground substance, which later develop into elastic fibres.

#### 2. Elastic Tissue.

Elastic fibres occurring in fibrous connective tissue have been described. When the elastic fibres predominate the tissue is known as *elastic tissue*. Almost pure elastic tissue is found in the ligamentum

nuchæ of quadrupeds. Here the fibres are coarse and held together by a small amount of cement substance. A few white fibres and connective-tissue cells are also present (Figs. 33 and 34).

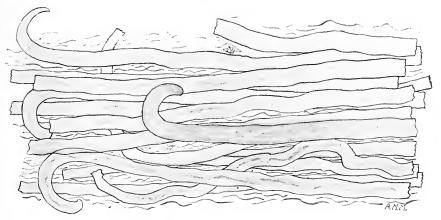


Fig. 33.—Coarse Elastic Fibres from Ligamentum Nuchæ. ×500. Teased specimen. (Technic 10, p. 81).

Elastic tissue may be arranged as thin *membranes*, as, *e.g.*, in the walls of blood-vessels. These membranes are usually described as composed of a dense mass of flat, ribbon-like elastic fibres, which inter-

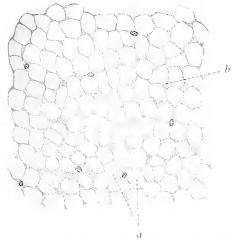


FIG. 34.—Cross Section of Coarse Elastic Fibres from Ligamentum Nuchæ.  $\times$ 500 (Technic 10, p. 81.) a, Elastic fibres; b, white fibrous tissue and cement substance. The nuclei are the nuclei of fixed connective-tissue cells.

lace in such a manner as to leave openings in the membrane. Hence the term "fenestrated membrane." They have been recently described as consisting of a central layer composed of elastin, staining with magenta, and on either side a thin, transparent sheath unstained by magenta. This is seen to correspond to Mall's description of the structure of the elastic fibre. Only the middle of these layers is fenestrated.

#### TECHNIC.

1. Areolar Tissue, to show White and Elastic Fibres.—Remove a bit of the subcutaneous tissue, as free from fat as possible, from a recently killed animal. Place it upon a mounting slide and with teasing needles quickly spread it out in a thin layer. During this manipulation the specimen should be kept moist by breathing on it. Put a drop of sodium chlorid solution upon the specimen and cover.

As the specimen is unstained, a small diaphragm should be used for the microscopic examination.

The white fibres are straight or wavy, are crossed in all directions, and are longitudinally striated. The elastic fibres have been stretched and show as sharp lines with curled ends where the fibres are broken.

Place a drop of hydric acetate, 1-per-cent. aqueous solution, at one side of the cover and a bit of filter paper at the other side. The filter paper absorbs the salt solution, which is replaced by the hydric acetate. The latter causes the white fibres to swell and become indistinct while the elastic fibres show more plainly.

2. Areolar Tissue, to show Cells and Elastic Fibres.—Prepare second specimen of areolar tissue in the same manner as the preceding. Instead of mounting in salt solution, allow it to become perfectly dry, then stain in the following solution:

Gentian violet, saturated aqueous solution, 40 c.c. Water, 60 c.c.

Wash thoroughly, dry, and mount in balsam.

The nuclei of the fixed connective-tissue cells are stained violet. Their delicate cell bodies show as an irregular haze around the nuclei. Both nuclei and cell bodies appear cut in all directions by the stretched elastic fibres. Wandering cells (leucocytes) may usually be seen. Plasma cells are frequently not demonstrable, and mast cells are only occasionally present. The elastic fibres are stained violet. The white fibres are almost unstained.

While these methods are most satisfactory for bringing out the different connective-tissue elements, they are misleading to the student in that they show a picture of connective tissue after special preparation, rather than as it usually appears in sections. For contrast the student should study carefully the connective tissue as it appears in sections through the skin, the mucous membranes and other organs.

- 3. Formed Connective Tissue.—Fibrous tissue arranged in the form of a network may be seen in the specimen of omentum (technic 7, p. 72).
- 4. Densely formed connective tissue may be studied in tendon. Cut through the skin of the tail of a recently killed mouse about half an inch from the tip and break the tail at this point. By pulling on the end of the tail this portion may now be separated from the rest of the tail, carrying with it long delicate tendon fibrils, which have been pulled out of their sheaths. These should be immediately ex-

amined in salt solution, using the high power and a small diaphragm. The fibrils are seen arranged in parallel bundles.

- 5. Place a drop of hydric acetate (2-per-cent. aqueous solution) at one side of the cover-glass, absorbing the salt solution from the opposite side by means of filter paper. The fibres swell and become almost invisible, while rows of connective-tissue cells (tendon cells) can now be seen. The cells may be stained by allowing a drop of hæmatoxylin or of carmine solution to run under the cover. After the cells are sufficiently stained, the excess of stain is removed by washing, and the specimen mounted in glycerin.
- 6. Fix a small piece of any good-sized tendon in formalin-Müller's fluid (page 7. After a week, harden in alcohol, embed in celloidin, and make longitudinal and transverse sections. Stain strongly with hæmatoxylin, followed by picro-acid fuchsin (page 19). Mount in balsam.
- 7. Pigmented connective-tissue cells are most conveniently obtained from the chorioid coat of the eye. Fix an eye in formalin-Müller's fluid (see page 7), cut in half, remove chorioid and retina and pick off the dark shreds which cling to the outer surface of the chorioid and inner surface of the sclera. These may be transferred directly to glycerin, in which they are mounted, or the bits of tissue may be first stained with hæmatoxylin (page 15). In addition to the pigmented cells should be noted the ordinary fixed connective-tissue cells which lie among them. Only the nuclei of these cells can be seen.
- 8. Connective-tissue cells to show anastomosing processes.—Stain a cornea with gold chlorid (see page 26). Sections are made tangential to the convex surface and are mounted in glycerin.
- 9. Connective-tissue cell spaces (lacunæ) and their anastomosing canaliculi may be demonstrated by staining a cornea with silver nitrate (see page 26). The silver stains the ground substance of the cornea, leaving the lacunæ and canaliculi unstained. The relation which this picture bears to the preceding should be borne in mind (see Figs. 29 and 39).
- 10. Coarse elastic fibres may be obtained from the ligamentum nuche, which consists almost wholly of elastic tissue. A piece of the ligament is fixed in saturated aqueous solution of picric acid and hardened in alcohol. A bit of this tissue is teased apart on a glass slide in a drop of pure glycerin, in which it is also mounted. Before putting into glycerin, the specimen may be stained with picro-acid-fuchsin. This intensifies the yellow of the elastic fibers and brings out in red the fibrillar connective tissue. Pieces of the ligament fixed and hardened in the same manner may be embedded in celloidin and cut into longitudinal and transverse sections. These stained with picro-acid-fuchsin show well the relation of the coarse elastic fibres (yellow) to the more delicate fibrous tissues (red).

# 3. Embryonal and Mucous Tissue.

Embryonal and mucous tissue are essentially developmental forms and represent early differentiations from the general parent type. They consist, according to their age, of oval, fusiform, or irregular branching and anastomosing cells, lying in a matrix, which is just beginning to show evidences of a fibrillar structure. By some his-

tologists the term "embryonic" connective tissue is limited to the stage of fusiform cells with slightly fibrillar matrix (Fig. 35), the term "mucous" tissue being applied to an embryonic form of connective

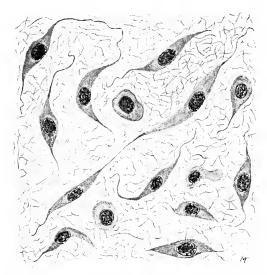


Fig. 35.—Embryonal Connective Tissue from Axilla of Five-inch Fætal Pig.  $\times 600$ . (Technic 1, p. 83.) Various shaped connective-tissue cells are seen lying in a slightly fibrillated matrix.

tissue in which irregular branching and anastomosing cells lie in a slightly fibrillated matrix which gives the chemical reaction for mucin (Fig. 36).

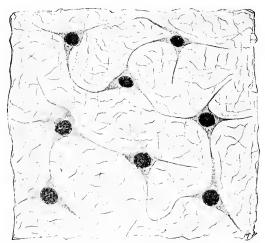


Fig. 36.—Mucous Connective Tissue from Umbilical Cord of Eight-inch Fætal Pig. ×600. (Technic 2, p. 83.)

Embryonal tissue is not found in the adult, while mucous tissue has only a very restricted distribution. It constitutes the vitreous humor of the eye and Wharton's jelly of the umbilical cord.

Much variation exists as to the shape and size of the cells in embryonal and mucous tissue. This is due to the fact that these cells represent transition stages in the development of the adult connective-tissue cell. Thus in embryonic connective tissue, while most of the cells are fusiform, one finds spherical and oval cells and some few cells which are triangular or stellate. The same holds true of mucous tissue, where, while most of the cells are of the triangular or stellate variety, round, oval, and fusiform cells are also present.

#### TECHNIC.

- 1. Embryonal Tissue.—Bits of the subcutaneous tissue from the axilla or groin of a five-inch fœtal pig are fixed in Zenker's fluid (technic, 9, p. 8), hardened in alcohol and stained for twelve hours in alum-carmine (technic b, p. 17). They are then transferred to eosin-glycerin, in which they are teased and mounted. Note the intercellular substance, that it is composed of delicate single fibrils interlacing in all directions with no arrangement into bundles, as in adult tissue, and that there is as yet no differentiation into two kinds of fibres.
- . 2. Mucous Tissue.—The umbilical cord of a four- or five-month human fœtus, or of a nine-inch fœtal pig is fixed in formalin-Müller's fluid (page 7), hardened in alcohol, and transverse sections stained with hæmatoxylin-eosin (technic 1, p. 18) and mounted in eosin-glycerin. Note the central blood-vessels with their thick walls and the surface epithelium. The mucous tissue is best studied near the surface just beneath the epithelium.

## 4. Reticular Tissue.

Reticular connective tissue is a form of fibrillar connective tissue. It consists of extremely delicately fibrillated connective-tissue cells which anastomose to form a reticulum (Fig. 37). According to latest researches there are apparently no extracellular fibres. Chemically it resembles white fibrous tissue in not being digested by pancreatin. It does not, however, like ordinary fibrous tissue, yield gelatin upon boiling in water, but *elastin* or a mixture of gelatin and elastin, perhaps due to the impossibility of wholly separating the two forms of tissue. Structurally white fibrous tissue and reticular tissue are apparently continuous as seen in the lymph node where the larger masses of fibrous tissue which constitute the trabeculæ pass over without demarcation into the reticulum of the lymphoid tissue.

Reticular connective tissue forms the framework of adenoid tissue

and of bone-marrow. It is also present in large amounts in the spleen and in the mucous membrane of the gastro-intestinal tract. Fibrils giving the chemical reaction of reticular tissue are associated with the fibrous and elastic-tissue framework of the lung, liver, kidney, and

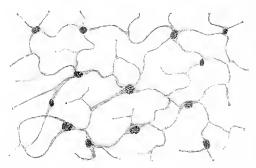


Fig. 37.—Reticular Connective Tissue from Human Lymph Node. ×600. (Technic, p. 85.)

other organs. The scope of the term "reticular tissue" is constantly broadening, many of the finer connective tissues formerly classed as white fibrous being now considered reticular.

# 5. Lymphatic Tissue.

Lymphatic tissue consists of reticular connective tissue and a special type of connective-tissue cells, lymphoid cells, filling the meshes of the reticulum. Lymphoid cells are small spherical cells. Each cell has a single nucleus which almost fills the cell. In lymphatic tissue the cell is a much more important factor in determining the character of the tissue than in most forms of connective tissue.

Lymphatic tissue may be diffuse or circumscribed. In diffuse lymphatic tissue (Fig. 38) the cells are not closely packed and there is no distinct demarcation between the lymphatic and the surrounding tissues. An example of diffuse lymphatic tissue is seen in the stroma of the mucous membrane of the gastro-intestinal canal. In circumscribed lymphatic tissue (Fig. 38) the cells are very closely packed, often completely obscuring the reticulum. There is also a quite distinct demarcation between the lymphatic and the surrounding tissues. Such a circumscribed mass of lymphatic tissue is known as a lymph nodule.

On account of both structure and function lymphatic tissue might more logically be considered an organ than a tissue, for it consists of a connective-tissue framework supporting a special type of cell which has a definite function. On account, however, of its wide distribution and of its close relations with connective tissue it is most conveniently described here.

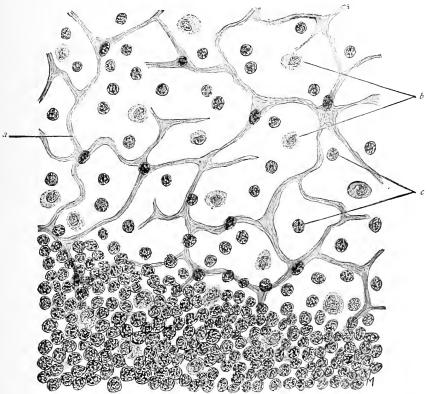


Fig. 38.—Lymphatic Tissue from a Human Lymph Node. (Technic, below.) a, Reticular connective tissue, in the meshes of which are suspended b, leucocytes, and c, lymphocytes. The reticular connective tissue is present also in the more dense lymphatic tissue seen in the lower part of the figure, but is not visible on account of the closely packed cells.

### TECHNIC.

Fix a lymph node in formalin-Müller's fluid (technic 5, p. 7), and stain very thin sections with hæmatoxylin and picro-acid fuchsin (technic 3, p. 19). In the lymph sinuses of the medulla the reticulum can usually be plainly seen.

#### 6. Fat Tissue.

Adipose tissue or fut tissue is a form of connective tissue in which some of the cells have become changed into fat cells. Fat tissue is peculiar among the connective tissues in that the cells and not the intercellular substance make up the bulk and determine the char-

acter of the tissue. The adult fat cell is surrounded by a distinct cell membrane, and almost the entire cell is occupied by a single spherical droplet of fat (Figs. 40 and 41). The nucleus, flattened and surrounded by a small amount of cytoplasm, is usually found pressed against the cell wall (Fig. 41). This appearance of a distinct cell membrane enclosing the spherical fat droplet, with the nucleus and cytoplasm pressed into a crescent-shaped mass at one side, has given rise to the term "signet-ring cell." Fat cells which occur singly, or in small groups, or in the developing fat of young animals, are spherical

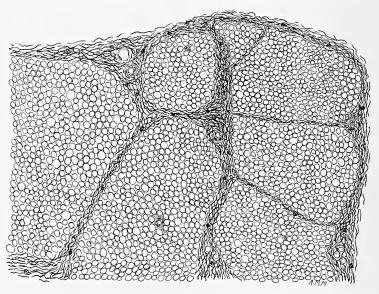


Fig. 39.—Fat Tissue from Human Subcutaneous Tissue (Child) to show Lobulation. ×25. (Technic 1, p. 89.)

(Fig. 40). In large masses of adult fat, the closely packed cells are subjected to pressure and are polyhedral (Fig. 41). Fat cells are usually arranged in groups or lobules, each lobule being separated from its neighbors by fibrillar connective tissue (Fig. 39). Adipose tissue is usually associated with loose fibrous tissue.

The appearance which adult fat presents can be understood only by reference to its histogenesis. Fat cells are developed directly from embryonic connective-tissue cells. In the human embryo they are first distinguishable as fat cells about the thirteenth week. The connective-tissue cells which are to become fat cells gather in groups in the meshes of the capillary network which marks the ending of a small artery. Each group is destined to become an adult fat lobule (Fig. 42)

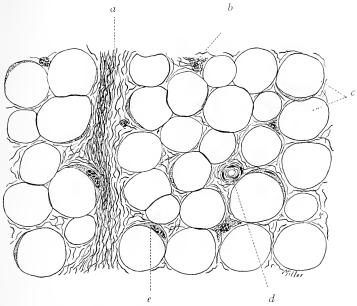


Fig. 40.—Young Fat from Human Subcutaneous Tissue (Child).  $\times$  175. (Technic I, p. 80.) a, Interlobular connective tissue; b, fixed connective-tissue cell; c, fat cells; d, artery; c, nucleus of fat cell and remains of cytoplasm ("signet ring").

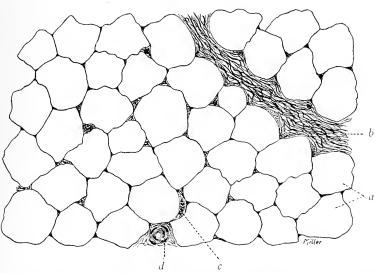


Fig. 41.—Adult Fat Tissue from Human Subcutaneous Tissue.  $\times$  175. (Technic 1 p. 89.) a, Fat cells; b, interlobular connective tissue; c, nucleus of fat cell and remains o' cytoplasm ("signet ring"); d, artery.

Fat first appears as minute droplets in the cytoplasm of the embryonic connective-tissue cell (Fig. 43). These small droplets in-

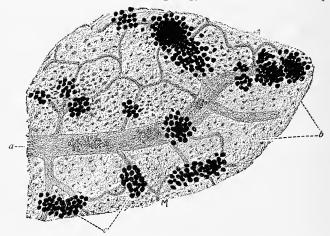


Fig. 42.—Developing Fat Tissue from Subcutaneous Tissue of Five-inch Fœtal Pig.  $\times$ 75. (Technic 2, p. 89.) a, Arteriole breaking up into capillary network; b, embryonal connective tissue; c, embryonal fat lobules developing around blood-vessels.

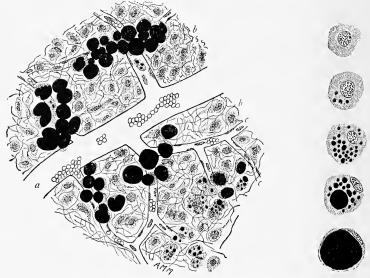


Fig. 43.—Developing Fat Tissue from Subcutaneous Tissue of Five-inch Fœtal Pig. (Technic 2, p. 89.) a, Arteriole breaking up into capillary network; b, embryonal connective tissue, embryonal cells from which fat cells are developing; c, capillaries. Fat droplets stained black. At the right are five individual cells showing stages of development from an embryonal cell to an adult fat cell.

crease in number and finally coalesce to form a single larger droplet. This increases in size and ultimately almost wholly replaces the cytoplasm. In this way the nucleus and remaining cytoplasm are pressed to one side and come to occupy the inconspicuous position which they have in adult fat.

The blood supply of fat is rich and the adult lobule maintains its embryonic vascular relations, in that the vascular supply of each lobule is complete and independent. One artery runs to each lobule, where it breaks up into an intralobular capillary network, which in turn gives rise to the intralobular veins, usually two in number.

Fat is thus seen to be a connective tissue in which some of the cells have undergone specialization. There still remain, however, embryonal connective-tissue cells which are not destined to become fat cells, but which develop into cells and fibres of ordinary fibrous connective tissue. A few of these remain among the fat cells to become the delicate intralobular connective tissue seen in adult fat. The majority are, however, pushed to one side by the developing lobules, where they form the interlobular septa.

#### TECHNIC.

- 1. Fat Tissue.—Human subcutaneous fat as fresh as possible is fixed in formalin-Müller's fluid (technic 5, p. 7), hardened in alcohol and embedded in celloidin. Sections are stained with hæmatoxylin and picro-acid-fuchsin (technic 3, p. 19). The alcohol and ether of the celloidin remove the fat from the fat cells, leaving only the cell membranes. The fat gives the celloidin a milky appearance. Such celloidin does not cut well. The celloidin should, therefore, be changed until it ceases to turn white. The sections are cleared in oil of origanum or carbol-xylol, and mounted in balsam. The fibrillar tissue is stained red by the fuchsin, and the protoplasm of the fat cell yellow by the picric acid.
- 2. Developing Fat Tissue.—Remove bits of tissue from the axilla or groin of a five-inch fœtal pig, or other fœtus of about the same development. Fix twenty-four hours in a 1-per-cent, aqueous solution of osmic acid (technic 8, p. 28), wash thoroughly and mount in glycerin. A part of the tissue mounted should be thoroughly teased, the rest gently pulled apart. The teased portion will show the fat cells in various stages of development. The unteased part will usually show brownish blood-vessels and the grouping of fat cells around them, to form embryonic fat lobules. Note the developing connective tissue between the groups of fat cells. It is from this that the arcolar tissue, which envelops and separates the lobules of adult fat, is developed.

# 7. Cartilage.

Cartilage is a form of connective tissue in which the ground substance is firm and dense and determines the physical character of the tissue. On boiling it yields *chondrin*. *Cartilage cells* are differen-

tiated connective-tissue cells. While varying greatly in shape they are most frequently spherical or oval. Each cell lies in a cell space or *lacuna*, which it completely fills. The intercellular substance immediately surrounding a lacuna is frequently arranged concentrically, forming a sort of *capsule*. Fine canaliculi connecting the lacunæ are present in some of the lower animals and have been described in human cartilage. They can be demonstrated, however, in human cartilage, only by special methods, and probably represent artefacts.

Cartilage contains no blood-vessels, and in human cartilage no lymph channels have been positively demonstrated.



Fig. 44.—Hyaline Cartilage from Head of Frog's Femur. ×350. (Technic 1, p. 62.) Groups of cartilage cells in apparently homogeneous matrix.

Cartilage is subdivided according to the character of its intercellular substance into three varieties: (1) Hyaline, (2) elastic, (3) fibrous.

1. Hyaline Cartilage (Fig. 44).—The cells occur singly or in groups of two or multiples of two. An entire group of cells frequently lies in one lucuna surrounded by a single capsule. Such a group of cells has developed within its capsule from a single parent cell. In other cases delicate hyaline partitions separate the cells of a group. The cells are spherical or oval, with flattening of adjacent sides. The nucleus is centrally placed, and has a distinct intranuclear network and membrane. The cytoplasm is finely granular, and may contain droplets of fat, of glycogen, or of both. Toward the perichondrium the arrangement of the cells in groups is less distinct. Here the cells are fusiform and parallel to the surface.

The intercellular matrix, when subjected to the usual technic, appears homogeneous. By the use of special methods, such, *e.g.*, as artificial digestion, this apparently structureless matrix has been shown

to be made up of bundles of fibres, quite similar to those found in fibrous connective tissue.

Hyaline cartilage forms the articular cartilages of joints, the costal cartilages, and the cartilages of the nose, trachea, and bronchi. In the embryo a young type of hyaline cartilage, known as embryonal cartilage, forms the matrix in which most of the bones are developed.

2. Elastic cartilage (Fig. 45) resembles hyaline, but differs

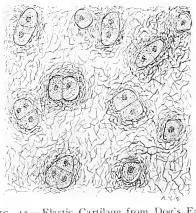


Fig. 45.—Elastic Cartilage from Dog's Ear. X350. (Technic 2, p. 92.) Groups of cartilage cells in fibro-elastic matrix.

from the latter in that its hyaline matrix contains a large number of elastic fibres. These vary in size, many being extremely fine. The elastic fibres branch and run in all directions, forming a dense network of interlacing and anastomosing fibres.

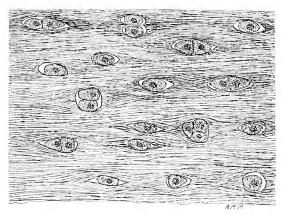


Fig. 46.—Fibrous Cartilage from Dog's Intervertebral Disc. ×350. (Technic 3, p. 92.) Groups of cartilage cells in matrix of fibrillar connective tissue.

Elastic cartilage occurs in the external ear, the Eustachian tube, the epiglottis, and in some of the laryngeal cartilages.

3. Fibrous cartilage (Fig. 46) is composed mainly of fibrillar

connective tissue. The fibres may have a parallel arrangement, or may run in all directions. Cells are few, and are usually arranged in rows of from two to six, lying in elongated cell spaces between the fibre bundles.

Fibrous cartilage occurs in the inferior maxillary and sternoclavicular articulations, in the symphysis pubis, and in the intervertebral discs.

Cartilage, except where it forms articular surfaces, is covered by a membrane, the *perichondrium*. This is composed of fibrillar connective tissue, and blends without distinct demarcation with the superficial layers of the cartilage.

Like the other connective tissues, cartilage develops from mesoderm. It is at first wholly cellular. Each cell forms a capsule around itself, and by blending of these capsules are formed the first elements of the intercellular matrix. This increases in quantity and assumes the structural characteristics of one of the forms of cartilage. The white fibres of fibro-cartilage and the yellow fibres of elastic cartilage develop in the same manner as in fibrillar and elastic tissue.

### TECHNIC.

- (1) Hyaline Cartilage.—Remove a frog's femur and immediately immerse the head in saturated aqueous solution of picric acid. Cut sections tangential to the rounded head, keeping knife and bone wet with the picric acid solution. As bone must be cut, a special razor kept for the purpose should be used. Cut sections as thin as possible. The first sections consist wholly of cartilage. As bone is reached, the cartilage is confined to a ring around the bone. Mount in the picric-acid solution, cementing the cover-glass immediately.
- (2) Elastic Cartilage.—Remove a piece of cartilage from the ear and fix in formalin-Müller's fluid (technic 5, p. 7). Stain sections strongly with hæmatoxylin, followed by picro-acid-fuchsin (technic 3, p. 19). Clear in carbol-xylol and mount in balsam. The capsules around the cartilage cells are thick and, as they usually retain some hæmatoxylin, can be readily seen. Note also the flattened cartilage cells near the surface, and the perichondrium.
- (3) Fibro-cartilage.—Fix pieces of an intervertebral disc in formalin-Müller's fluid. Sections are stained either with hæmatoxylin-eosin or with hæmatoxylin-picro-acid-fuchsin and mounted in balsam.

### 8. Bone Tissue.

Bone is a form of connective tissue in which the matrix is rendered hard by the deposition in it of inorganic matter, chiefly the phosphate and the carbonate of calcium. These salts are not merely

deposited in the matrix, but are intimately associated and combined with its histological structure. The intimacy of this association of the organic and inorganic constituents of bone is shown by the fact that, though the salts compose two-thirds of bone by weight, it is

impossible to distinguish them by the highest magnification. Furthermore, if either the lime salts are dissolved out by means of acids (decalcification) or the organic matter removed by heating (calcination), the histological structure of the bone still remains.

Like the other connective tissues, bone consists morphologically of *cells* and *intercellular substance*.

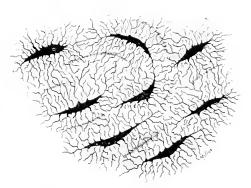


Fig. 47.—Bone Tissue showing Lacunæ and Canaliculi. ×700. (Technic 1, p. 94.)

Bone cells or bone corpuscles lie in distinct cell spaces or lacunæ. From the lacunæ pass off in all directions minute canals—canaliculi—which anastomose with canaliculi of neighboring lacunæ (Fig. 47). At the surface of bone these canaliculi open into the periosteal lymphatics. A complete system of canals is thus formed, which traverse



Fig. 48.—Bone Cell and Lacuna. (After Joseph.) At a the cell body has shrunken, allowing the outline of the lacuna to be

the bone and serve for the passage of nutritive fluids. The bone cells themselves (Fig. 48) are flat, ovoid, nucleated cells, with numerous fine processes, which extend in all directions into the canaliculi. In young developing bones the processes of adjacent cells anastomose. In adult bone the processes extend but a short distance into the canaliculi, and probably do not anastomose.

The basement substance or matrix has a fibrous structure, closely resembling that of fibrillar connective tissue, and it is in this

fibrillar matrix that the lime salts are deposited. The fibrils are held together by cement substance into bundles. In most bone the bundles are fine and arranged in layers or *lamella*. Less commonly the fibre bundles are coarser and have an irregular arrangement.

#### TECHNIC.

- (1) For the study of the minute structure of bone a section of undecalcified or hard bone is required. Part of the shaft of one of the long bones is soaked for several days in water and all the soft parts are removed. It is then placed in equal parts alcohol and ether to remove all traces of fat and thoroughly dried (the handle of a tooth or nail brush frequently furnishes good material and is already dried). Thin longitudinal and transverse sections are now cut out with a bone saw. surface is next ground smooth, first on a glass plate, using emery and water, then on a hone. The specimen is now fastened polished side down on a block of wood or glass by means of sealing wax, and the other side polished smooth in the same manner as the first, the bone being ground as thin as possible. The sealing wax is removed by soaking in alcohol and the specimen looked at with the low power. If not thin enough, it is gently rubbed on a fine hone. It is then soaked in equal parts alcohol and ether, dried thoroughly, and mounted in hard balsam. This is accomplished by placing a small bit of hard balsam on a slide, melting, pushing a bit of the bone into the hot balsam, covering and cooling as quickly as possible. The object of the hard balsam and quick cooling is to prevent the balsam running into the lacunæ and canaliculi and obscuring them by its transparency. The air imprisoned in the lacunæ and canaliculi causes them to appear black when viewed by reflected light.
- (2) The structure of the bone cell is best studied in sections of decalcified bone which has first been carefully fixed. (See technic 1, p. 171.)

# 9. Neuroglia.

This peculiar form of connective tissue is confined entirely to the central nervous system and is most conveniently studied in connection with nervous tissue (see page 125).

# CHAPTER IV.

# THE BLOOD.

BLOOD is best considered as a tissue, the intercellular substance of which is fluid. This fluidity of the intercellular substance allows the formed elements or cells to move about freely, so that there is not the same definite and fixed relation between cells and intercellular substance as in other tissues.

The fluid intercellular substance or *plasma* is slightly alkaline in reaction. It consists of serum albumen, globulin, fibrinogen and

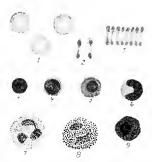
inorganic salts, chiefly the chlorid, carbonate, and bicarbonate of soda. Its specific gravity is about 1.030, while that of the whole blood is about 1.060. The bulk of the plasma is about equal to that of the red and the white cells.

The formed elements of the blood are:

(1) Red blood cells (red blood corpuscles, erythrocytes); (2) white blood cells (colorless corpuscles—leucocytes); (3) blood platelets (thrombocytes); (4) blood dust (hæmatokonia).

\*\*Fig. 49.—Cells from Human Blood. \*\*X 600. (Technic 2. p. 100.) 1, Red blood cell seen on flat; 2, red blood cell seen on flat;

1. **Red blood cells** (erythrocytes) (Fig. 49, 1, 2, 3) are in man non-nucleated circular discs. Their average diameter is about 7.5μ, their thickness 2μ at the thin centre. They are biconcave, with rounded edges. Seen on the flat, the difference in thickness between centre and periphery is evidenced by the difference in refraction (Fig. 49, 1).



tig. 49.—Cells from Human Blood. ×600. (Technic 2, p. 100.) 1, Red blood cell seen on flat; 2, red blood cell seen on edge; 3, red blood cells forming rouleaux; 4, 4, small and large lymphocytes; 5, mononuclear leucocyte; 6, ransitional leucocyte; 7, polymorphonuclear leucocyte, containing neutrophile granules; 8, polynuclear leucocyte, containing eosinophile granules; 9, mononuclear leucocyte, containing basophile granules.

Seen on edge, the shape resembles that of a dumb-bell (Fig. 49, 2). Singly or in small numbers, red blood cells have a pale straw color. Redness of the cells is apparent only when they are seen in large numbers. If fresh blood be allowed to stand for a moment, the red

<sup>&</sup>lt;sup>1</sup>Some observers describe the red blood cell as bell- or cup-shaped. (Lewis: Jour. Med. Research, N. S., vol. v, 1904.)

cells are seen to adhere to one another by their flat surfaces, forming rows or rouleaux (Fig. 49, 3).

Subjected to the usual technic, the red blood cell appears homogeneous. By the use of special methods, this apparently homogeneous substance can be separated into (a) a color-bearing proteid—hæmoglobin, and (b) a stroma, the latter representing the protoplasm of the cell. It is the hæmoglobin which gives color to the corpuscles. Hæmoglobin is a complex proteid, and is held in solution or in suspension in the stroma, which can be resolved into a globulin and a pigment, hæmatin.

The red blood cells are soft and elastic, and are easily twisted to accommodate themselves to the smallest capillaries.

The red blood cell is extremely susceptible to changes in the plasma. Thus even slight evaporation of the plasma results in osmosis between the now denser surrounding fluid and the contents of the cell. This causes fluid to leave the cell, with the result that the latter becomes spheroidal and irregularly shrunken, with minute knob-like projections from its surface. This is known as *crenation* of the red cell. The addition of water to blood, thus decreasing the specific gravity of the plasma, has the opposite effect, resulting in swelling of the cell. It also causes solution of the hæmoglobin, which leaves the cell, the latter then appearing colorless. This separation of the hæmoglobin from the corpuscle is also caused by freezing and thawing, by heat (60° C.), by the addition of dilute acids, ether, or chloroform.

Dilute alkaline solutions and bile first cause the red corpuscles to swell and become spherical, and then to dissolve. This is known as *hæmolysis*, and may also be effected by mixing the blood of one species with that of another. Dilute acetic acid causes swelling and fading of the red cells, with the formation of prismatic crystals of hæmoglobin.

The red blood cells number from 4,500,000 to 5,000,000 per cubic millimetre of blood.

2. White blood cells (leucocytes) (Fig. 49, 4 to 9 inclusive) are colorless nucleated structures which have a generally spherical shape, but which are able to change their shape on account of their powers of amœboid movement. They have a diameter of from 5 to  $10\mu$ , and are much less numerous than the red cells, the proportion being about one white cell to from three hundred to six hundred red cells. This proportion is, however, subject to wide variation.

Leucocytes may be classified as follows: (a) Lymphocytes; (b)

mononuclear leucocytes; (c) transitional leucocytes; (d) polymorphonuclear or polynuclear leucocytes.

- (a) Lymphocytes (Fig. 49, 4).—These vary in diameter from 5 to  $8\mu$ , and are sometimes subdivided into small lymphocytes and large lymphocytes. The nucleus is spherical, stains deeply, and almost completely fills the cell, the cytoplasm being confined to a narrow zone around the nucleus. Lymphocytes constitute about 20-per-cent. of the white blood cells.
- (b) Mononuclear leucocytes (Fig. 49, 5 and 9) are of about the same size as large lymphocytes. The nucleus, however, stains more faintly and is smaller, while the cytoplasm is greater in amount. From 2-per-cent. to 4-per-cent. of the white cells are mononuclear leucocytes.
- (c) Transitional leucocytes (Fig. 49, 6) occur in about the same numbers as the preceding, and are of about the same size. There is relatively more cytoplasm, and the nucleus, instead of being spherical, is crescentic or horseshoe or irregular in shape. These cells represent a traditional stage between the mononuclear and the polymorphonuclear and polynuclear varieties.
- (d) Polymorphonuclear and polynuclear leucocytes (Fig. 49, 7, 8) constitute about 70-per-cent. of the white blood cells. Their size is about the same as that of the mononuclear form, but they are somewhat more irregular in shape. The appearance of the nucleus is characteristic. In the polymorphonuclear form the nucleus consists of several round, oval, or irregular nuclear masses connected with one another by cords of nuclear substance. These cords are frequently so delicate as to be distinguished with difficulty. The polynuclear form is derived from the polymorphonuclear by breaking down of the connecting cords, leaving several separate nuclei or nuclear segments.

The protoplasm of about 70-per-cent. of leucocytes is granular, and these granules present very definite reactions when subjected to certain aniline dyes.

Aniline dyes may be divided into acid, basic, and neutral, according to whether the coloring matter is an acid, a base, or a combination of an acid and a base.

Upon the basis of their reaction to these dyes, Ehrlich divides these granules into five groups, which he designates by the first five letters of the Greek alphabet.

α-Granules (acidophile, or, because the most common acid dye

used is eosin, eosinophile—Fig. 49, 8). These are coarse, sharply defined granules which stain intensely with acid dyes. Eosinophile cells are mainly of the polynuclear and polymorphonuclear types. More rarely transitional forms contain eosinophile granules. They are actively amœboid. Eosinophile cells constitute from 1-per-cent. to 4-per-cent. of the leucocytes of normal blood. Under certain pathological conditions the number of eosinophile leucocytes is greatly increased.

 $\beta$ -Granules (amphophile). These are very fine granules, which react to both acid and basic dyes.  $\beta$ -Granules are not found in normal human blood. They are found in the blood cells of some of the lower animals.

 $\gamma$ -Granules (basophile) are small granules which stain with basic dyes. They occur in the so-called Mastzellen (p. 75), which are of rare occurrence in normal blood. They are present in certain pathological conditions, and are found normally in the blood cells of some of the lower animals, and in some of the cells of connective tissue.

 $\delta$ -Granules (basophile) are small granules, which stain with basic dyes (Fig. 49, 9). They are found mainly in the mononuclear leucocytes.

ε-Granules (*neutrophile*) react to mixtures of acid and basic dyes. ε-Granules are the most common of all granules, occurring in most of the polynuclear and polymorphonuclear forms, being thus present in about 68-per-cent. of all white blood cells (Fig. 49, 7).

Through their powers of amœboid movement leucocytes are able not only to pass through the walls of the vessels—diapedesis—and out into the tissues, but to wander about more or less freely in the tissues. Both inside and outside of the vessels the leucocytes have an important function to perform in the taking up and disposal of waste or superfluous materials and foreign particles. This is known as phagocytosis, and the cells thus engaged are known as phagocytes. Phagocytosis plays an extremely important rôle both in normal and in certain pathological processes.

3. The blood platelets (thrombocytes) are minute round or oval bodies about  $2\mu$  in diameter. They are clear (colorless), and are described by some as containing chromatin granules, by others as having distinct nuclear structures. They may be separated by the action of a 10-per-cent. saline solution into two elements—one hyaline, the other granular. They are said to possess amœboid properties

and to be concerned in the coagulation of the blood. They number about 200,000 per cubic millimetre.

4. The blood dust (hæmatokonia) occurs in the form of small refractive granules.

In the blood of the lower mammals and in herbivorous animals small droplets of fat derived from the chyle are found. They are known as *elementary granules* and are not present in normal human blood.

# DEVELOPMENT OF THE BLOOD.

At an early stage of embryonic development certain mesodermic cells of the area vasculosa, which surrounds the embryo, become arranged in groups known as blood islands. It is from these "islands" that both blood and blood-vessels develop. The peripheral cells arrange themselves as the primitive vascular wall, within which the central cells soon become free as the first blood corpuscles. In this way vascular channels are formed, inside of which are developing blood cells. These channels, which are at first unconnected, anastomose and give rise to a network of channels which are the earliest capillaries. As regards the origin of the later vessels both within the embryo and in the extraembryonic area, two views are held; (1) that they are outgrowths from the earliest capillaries; (2) that they arise in situ in the same manner as the earliest capillaries and unite secondarily to form networks. The weight of evidence at present favors the latter view. These networks of capillaries at first constitute the entire vascular system. As development proceeds some of the channels enlarge to form the arteries and veins, the smooth muscle and connective tissue of their walls differentiating from the surrounding mesoderm. At first the formed elements of blood consist almost wholly of nucleated red cells. These undergo mitotic division and multiply within the vessels. Two views are held in regard to the manner in which the embryonic nucleated red cell gets rid of its nucleus in becoming the non-nucleated red cell of the adult. According to one the nucleus is absorbed within the cell; according to the other the nucleus, as a whole, is extruded.

In early embryonic life especially active proliferation of red cells occurs in the blood-vessels of the liver. This has led to the considering of the liver as a blood-forming organ. The liver cells themselves, however, taken no actual part in the formation of blood cells, the blind pouch-like venous capillaries of the liver, with their slow-moving blood

currents, merely furnishing a peculiarly suitable place for cellular proliferation. Before birth the splenic pulp and bone marrow become blood-forming organs. In the adult the bone marrow is probably, under normal conditions, the main if not the sole seat of red-cell formation.

During fœtal life the number of nucleated red cells constantly diminishes while the number of non-nucleated red cells increases. At birth there are usually but few nucleated red cells in the general circulation, although even in the adult they are always found in the red bone-marrow.

The earliest embryonic blood contains no white cells.

The origin of the leucocytes is not well understood. It seems probable that the earliest leucocytes are derived like the red cells from the cells of the blood islands of the area vasculosa. Later they are formed in widely distributed groups of cells, lymph nodules, which are found in various tissues and organs. These cells enter the circulation as lymphocytes. According to some, the mononuclear, transitional, polymorphonuclear, and polynuclear forms are later stages in the development of these cells. According to others, the polymorphonuclear and polynuclear forms are derived from the myelocytes of bone marrow.

The origin of the blood platelets is not known. It is possible that they represent extrusion products of the blood cells.

### TECHNIC.

- (1) Fresh Blood.—Prick a finger with a sterile needle. Touch the drop of blood to the centre of the slide and cover quickly. For immediate examination of fresh blood no further preparation is necessary. Evaporation may be prevented by cementing, or by smearing a rim of vaseline around the cover-glass.
- (2) Blood Smears.—From the same or a second prick take up a drop of blood along the edge of a mounting slide. Quickly place the edge against the surface of a second slide and draw the edge across the surface in such a manner as to leave a thin film or smear of blood. Allow the smear to become perfectly dry and stain by technic 9, p. 28. By this method the acidophile granules are stained red, basophile granules purple, and neutrophile granules a reddish-violet.

Good results may also be obtained by fixing the dried smear for half an hour in equal parts alcohol and ether and staining first in a strong alcoholic solution of cosin, then in a rather weak aqueous solution of methylene blue.

# CHAPTER V.

### MUSCLE TISSUE.

WHILE protoplasm in general possesses the property of contractility, it is in *muscle tissue* that this property reaches its highest development. Moreover, in muscle this contractility is along definite

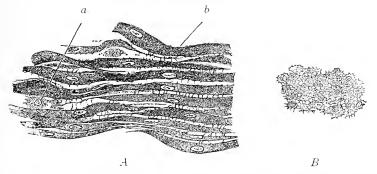


Fig. 50.—Isolated Smooth Muscle Cells from Human Small Intestine. ×400. (Technic 1, p. 109.) Rod-shaped nucleus surrounded by area of finely granular protoplasm; longitudinal striations of cytoplasm.

directions, and is capable of causing motion, not only in the cell itself, but in structures outside the cell.

Muscle may be classified as: (1) Involuntary smooth muscle; (2) voluntary striated muscle; (3) involuntary striated muscle or heart muscle.

1. **Involuntary Smooth Muscle.**—This consists of long spindle-shaped cells (Fig. 50). The length of the cell varies from 30 to 200μ,



F16. 51.—Apparent Intercellular Bridges of Smooth Muscle. A, From longitudinal section of intestine of guinea-pig: B, from transverse section of intestine of rabbit.  $\times$ 420. a, Nerve cell; b, end of muscle cell. (Stöhr.)

its width from 3 to  $8\mu$ , except in the pregnant uterus, where the cells frequently attain a much greater size. At the centre of the cell, which is its thickest portion, is a long rod-shaped nucleus surrounded by an

area of finely granular cytoplasm. The rest of the cytoplasm shows delicate longitudinal striations, which probably represent a longitudinal arrangement of the spongioplasm. The cells are united by a small amount of cement substance. Intercellular "bridges" similar to those connecting epithelial cells have been described (Fig. 51).

Smooth muscle cells may be arranged in layers of considerable thickness, the cells having a definite direction, as in the so-called "musculature" of the intestine (Fig. 52). In such masses of smooth muscle the cells are separated into groups or bundles by connective tissue. Smooth muscle cells may be arranged in a sort of network, the cells crossing and interlacing in all directions, as in the wall of the

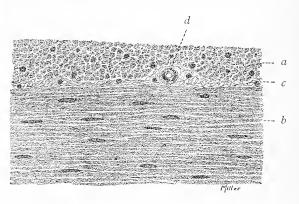


Fig. 52.—Smooth Muscle from Longitudinal Section of Cat's Small Intestine, showing Portions of Inner Circular and Outer Longitudinal Muscle Coats with Intervening Connective Tissue.  $\times$  350. (Technic 3, p. 109.) a, Transversely cut cells of inner circular layer; in comparatively few has the plane of section passed through the nucleus; b, longitudinally cut cells of outer longitudinal layer. In many of the cells the plane of section has not passed through the nucleus; c, intermuscular septum (connective tissue); d, small artery.

frog's bladder. Again, they may be scattered in small groups or singly among connective-tissue elements, as in the villi of the small intestine.

2. Voluntary Striated Muscle.—This consists of cylindrical fibres from 50 to 130 mm. in length and from 10 to 100 $\mu$  in diameter.

Each muscle fibre consists of (a) a delicate sheath, the *sarcolemma*, enclosing (b) the *muscle substance proper*, in which lie (c) the *muscle nuclei*.

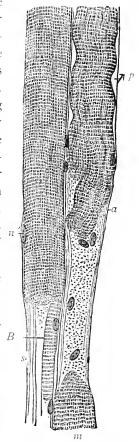
The *sarcolemma* is a clear, apparently structureless, membrane, which adheres so closely to the underlying muscle substance as to be indistinguishable in most preparations. In teased specimens it may frequently be seen at the torn ends of the fibres (Fig. 53).

The muscle substance consists of ergastoplasm (fibrillæ) and sarco-

plasm, and shows two sets of striations (Fig. 54), longitudinal striations and cross striations. The longitudinal striations are due to parallel

running ultimate fibrillæ, of which the muscle fibre is composed. These fibrillæ are united by a minute amount of interfibrillar cement substance. The transverse striations appear in the unstained fibre examined by reflected light as alternate light and dark bands (Figs. 54 and 55). The light band is composed of a singly refracting (isotropic) substance, the dark band of a doubly refracting (anisotropic) substance. Through the middle of the light band runs a fine dark (anisotropic) line (Krause's line), while an even finer light (isotropic) line (Hensen's line) runs through the middle of the dark band. As both dark and light substances run through the entire thickness of the fibre, they in reality constitute discs of muscle substance (Fig. 55). By means of certain chemicals these discs may be separated, the separation taking place along the lines of Krause. Each "muscle disc" thus consists of that portion of a fibre included between two adjacent lines of BKrause and is composed of a central dark disc, and on either side one-half of each adjacent light disc. A muscle fibre is thus seen to be divisible longitudinally into *ultimate fibrilla*, transversely into muscle discs. What is known as the sarcous element of Bowman is that portion of a single fibrilla which is included in a single disc, i.e., be-Fig. 53.—Semidiagrammatween two adjacent lines of Krause (Fig. 55).

The *sarcoplasm* is not evenly distributed throughout the fibre. On cross section irregular trabeculæ of sarcoplasm are seen extending in from the sarcolemma (Fig. 56). These separate the fibrillæ into bundles, the muscle columns of Kölliker. A transverse section of one of these columns presents the appearance of a network of sarcoplasm and of interfibrillar cement substance enclosing the fibrillæ. This appearance is known as Cohnheim's field (Figs. 55 and 56).



tic Drawing of Parts of two Muscle Fibres which have been broken, showing the relations between Muscle Substance Proper and Sarcolemma. (Ranvier.) m, a, Retracted ends of muscle substance, between which is seen the sarcolemma with several adherent muscle nuclei: B, thin layer of muscle substance which has adhered to the sarcolemma: n, muscle nucleus; s, sarcolemma: p, space between sarcolemma and muscle substance.

The contractile element of the fibre, the fibrilla, is anisotropic, the sarcoplasm isotropic; the former, therefore, appears dark, the latter light by polarized light. Upon this is based Rollet's theory of the structure of the striated muscle fibre (Fig. 57). According to this theory, each fibrilla consists of a number of rod-shaped segments joined end to end. Each segment consists of a thicker central portion,

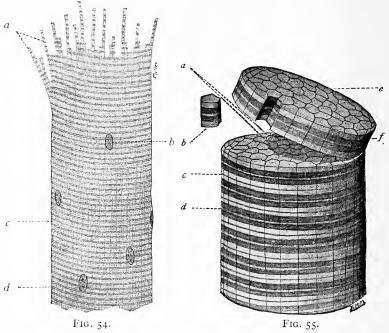


Fig. 54.—Portion of Striated Voluntary Muscle Fibre. X350. (Technic 4, p. 109.) The fibre is seen to be marked transversely by alternate light and dark bands. Through the centre of the light band is a delicate dark line (Krause's line); through the centre of the dark band a fine light line indicates Hensen's line. The black line outlining the fibre represents the sarcolemma. *a*, Fibrillæ; *b*, muscle nucleus; *c*, Krause's line; *d*, Hensen's line. Fig. 55.—Diagram of Structure of a Muscle Column of Kölliker. The appearance

Fig. 55.—Diagram of Structure of a Muscle Column of Kölliker. The appearance presented by the cross-cut muscle column = Cohnheim's field. a, Muscle fibrillæ, b, sarcous element; c, Krause's line; d, Hensen's line; e, Cohnheim's field; f, muscle disc.

which tapers almost to a point where it joins the next adjacent segment. The point of union is marked by a minute globular swelling. Between the fibrillæ is the semi-fluid sarcoplasm. In the formation of a fibre similar parts of each fibril-segment lie in the same transverse plane. The thicker portions lying side by side form the dark disc in which there is comparatively little sarcoplasm. The attenuated portions, with their relatively large amount of sarcoplasm, form the light disc. The row of globular swellings forms the line of Krause.

Two varieties of striated voluntary muscle fibres are distinguished, white fibres and red fibres. The difference between the two is due to the amount of sarcoplasm—the red fibres being rich in sarcoplasm, the white fibres poor. Red fibres contract less rapidly than white, but are less easily fatigued. In man white fibres are in the large majority, red fibres never occurring alone, but mingled with white fibres in some of the more active muscles, such as those of respiration

and mastication. In some of the lower animals are found muscles made up wholly of red fibres.

Muscle fibres ending within the substance of a muscle have pointed extremities. Where muscle fibres join tendon, the fibre ends in a rounded



Fig. 56.

Fig. 57.

Fig. 56.—Semidiagrammatic Drawing of Transverse Section of a Voluntary Muscle Fibre, showing Sarcolemma; sarcoplasm separating fibrils into bundles, each bundle constituting a muscle column of Kölliker and the appearance of its cross-cut end being Cohnheim's field. *a*, Sarcoplasm; *b*, Cohnheim's fields; *c*, sarcolemma.

Fig. 57.—Diagram representing Rollet's Theory of the Structure of a Voluntary Muscle Fibre. a, Dark disc; b, light disc; c, sarcoplasm; d, fibrilla; e, Krause's line.

or blunt extremity, the sarcolemma being continuous with the tendon fibres (Figs. 58 and 59).

Muscle fibres are usually unbranched. In some muscles—e.g., those of the tongue and of the eye—anastomosing branches occur. When muscle fibres end in mucous membranes—e.g., the muscle fibres of the tongue—their terminations are often branched.

Muscle fibres are multinuclear, some of the large fibres containing a hundred or more nuclei. In the white fibres the nuclei are situated at the periphery just beneath the sarcolemma. In red fibres they are centrally placed. 3. Involuntary Striated Muscle (Heart Muscle).—This occupies an intermediate position, both morphologically and embryo-



Fig. 58.—Semidiagrammatic Illustration of Endings of Muscle Fibres within a Muscle and in Tendon. (Gage.) a, Tapering end of fibre terminating within the muscle; the lower end of the central fibre shows the same method of termination: c, c, each fibre terminates above in pointed intramuscular ending, below in blunt ending connected with tendon.

logically, relative to smooth muscle and to striated voluntary muscle. Like the former, it is composed of cells. Like the latter, it is both longitudinally and transversely striated. Heartmuscle cells are short, thick cylinders. These are joined end to end to form long fibres. By means of lateral branches the cells of one fibre anastomose with cells of adjacent fibres. Each heart-muscle cell usually contains one nucleus; some cells contain several nuclei. While there is no distinct sarcolemma, the sarcoplasm is more abundant at the surface of the cell, thus giving much the appearance of an enclosing membrane. The amount of sarcoplasm throughout the cell is large. Around the nucleus is an area of sarcoplasm free from fibrillæ. This area often extends some distance toward the ends of the cell.

The striations of heart muscle are less distinct than are those of voluntary muscle. According to McCallum, they represent very similar structures. The longitudinal striations indicate fibrillæ united by cement substance. From the central mass of sarcoplasm which surrounds the nucleus, strands radiate toward the periphery. These strands, anastomosing, separate the fibrillæ into columns, the muscle columns of Kölliker. In cross section these present the appearance described under voluntary muscle as Cohnheim's fields. The disposition of the sarcoplasm, extending outward from the region of the nucleus like the spokes of a wheel, gives to the cross section a characteristic radiate appearance (Fig. 61). The transverse markings represent, as in voluntary muscle, alternate light and dark discs. Through the middle of the light disc can be seen the membrane of Krause. McCallum describes Krause's membrane as belonging not only to the fibrillar element, but

also to the sarcoplasm. The latter he describes as further subdivided by membranes, which are transversely continuous with Krause's membranes, into minute discs. The centre of the cell around the nucleus is wholly composed of these little discs of sarcoplasm.

McCallum describes two appearances which the lines of union between the muscle cells present. In one each fibrilla shows a thickening at the cement line, from which one or more delicate filaments

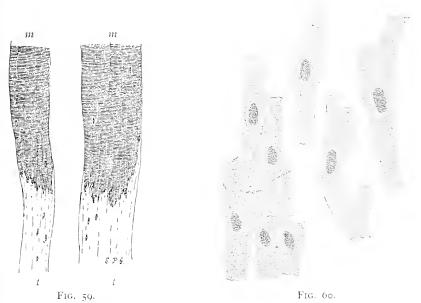


FIG. 59.—Two Muscle Fibres from Upper End of Human Sartorius, to show connection of muscle and tendon.  $\times$  350. (Gage.) m, Muscle fibres; t, tendon fibres. FIG. 60.—Muscle Cells from the Human Heart (technic 6, p. 110), showing lateral branches and lines of union between cells.  $\times$  500.

cross the cement to unite with similar filaments from an opposite fibrilla. In the other form of union the cement substance is crossed by intercellular bridges similar to those described under epithelium.

Recent investigations tend to prove that what have been described as heart-muscle cells are not separate units, but that heart muscle is a syncytial tissue, each cell representing only a growth segment of the whole muscle fibre. The occurrence of non-nucleated segments and the fact that the longitudinal fibrillæ are described by some observers as passing uninterruptedly through the "intercellular" cement substance favor this view. On the other hand, the ease with which heart muscle may be separated into cells, especially in young animals

and in the lower vertebrates, and the definite staining reaction which intercellular substance gives when subjected to the action of silver nitrate are in favor of a cellular structure.

## Development of Muscle Tissue.

In the higher animals muscle tissue, with the single exception of the sweat-gland muscles (page 62), is derived wholly from mesoderm.

The smooth muscle cell shows the least differentiation. In becoming a smooth muscle cell the embryonal cell changes its shape,

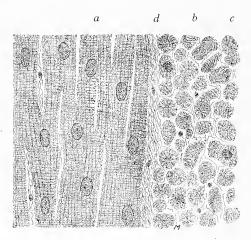


Fig. 61.—Section of Heart Muscle.  $\times$  350. (Technic 7, p. 110.) a, Cells cut longitudinally; b, cells cut transversely (only three nuclei have been included in the plane of section); c, cells cut obliquely; d, connective-tissue septum.

becoming greatly elongated, while at the same time its spongioplasm is arranged as longitudinally disposed contractile fibrils.

A voluntary muscle fibre is a highly differentiated multinuclear cell or syncytium. Each fibre is developed from a single cell (myoblast) of one of the embryonic muscle segments or myotomes. These cells, which are at first spherical, become elongated and spindle-shaped. The nucleus is at this stage centrally placed, and the spongioplasm occurs in the form of a reticulum. Regular arrangement of the spongioplasm first appears around the periphery, while the central portion of the cell is still occupied by reticular spongioplasm and the nucleus. The fibrils extend toward the centre until they fill the entire cell, which has now become a muscle fibre. During this process of fibrillation the nucleus has been undergoing mitotic

division. In the white fibres these nuclei migrate to the surface and come to lie just beneath the sarcolemma. The cement substance which unites the fibrils, as well as the larger masses of sarcoplasm, represents the remains of still undifferentiated protoplasm (hyaloplasm).

McCallum describes the development of heart muscle in the pig as follows: In embryos 10 mm. long the heart muscle consists of closely packed spindle-shaped cells, each containing an oval nucleus. The spongioplasm is arranged in the form of a network, no fibrils being present. In embryos 25 mm. long the shape of the cell remains unchanged, but on cross section there can be seen around the periphery a row of newly formed fibril bundles which have developed from the spongioplasm. From the periphery fibril bundles spread toward the centre. In embryos 70 mm. long the heart-muscle cell has assumed its adult shape and structure.

Attention has already been called (page 47) to the spongioplasm as the contractile element of protoplasm. It is to be noted that in the development of muscle no new element appears, the contractile fibrillæ representing nothing more than a specialization of the already contractile spongioplosm.

#### TECHNIC.

- (1) Isolated Smooth Muscle Cells.—Place small pieces of the muscular coat of the intestine in 0.1-per-cent. aqueous solution of potassium bichromate, or in 30-percent. alcohol for forty-eight hours. Small bits of the tissue are teased thoroughly and mounted in glycerin. Nuclei may be demonstrated by first washing the tissue and then staining for twelve hours in alum carmine (page 17). This is poured off, the tissue again washed in water and preserved in eosin-glycerin, which gives a pink color to the cytoplasm.
- (2) Potassium hydrate in 40-per-cent, aqueous solution is also recommended as a dissociater of smooth muscle cells. Pieces of the muscular coat of the intestine are placed in this solution for five minutes, then transferred to a saturated aqueous solution of potassium acetate containing 1-per-cent, hydric acetate for ten minutes. Replace the acetate solution by water, shake thoroughly, allow to settle, pour off water, and add alum-carmine solution (page 17). After twelve hours' staining, wash and transfer to eosin-glycerin.
- (3) Sections of Smooth Muscle.—Fix small pieces of intestine in formalin-Müller's (technic 5, p. 7) or in Zenker's fluid (technic 9, p. 8). Thin transverse or longitudinal sections are stained with hæmotoxylin-cosin (technic 1, p. 18), and mounted in balsam. As the two muscular coats of the intestine run at right angles to each other, both longitudinally and transversely cut muscle may be studied in the same section.
  - (4) Striated Voluntary Muscle Fibres.—One of the long muscles removed from

a recently killed animal is kept in a condition of forced extension while a 1-percent. aqueous solution of osmic acid is injected into its substance at various points by means of a hypodermic syringe. Fixation is accomplished in from three to five minutes. The parts browned by the osmic acid are then cut out and placed in pure glycerin, in which they are teased and mounted.

- (5) Sections of Striated Voluntary Muscle.—Fix a portion of a tongue in formalin-Müller's fluid or in Zenker's fluid (page 8). Thin sections are stained with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) and mounted in balsam. As the muscle fibres of the tongue run in all directions, fibres cut transversely, longitudinally, and obliquely may be studied in the same section. The sarcolemma, the pointed endings of the fibres, and the relation of the fibres to the connective tissue can also be seen.
- (6) Isolated heart-muscle cells may be obtained in the same manner as smooth muscle cells. (See technic 1, p. 109.)
- (7) Sections of Heart Muscle.—These are prepared according to technic 3 (above). By including the heart wall and a papillary muscle in the same section, both longitudinally and transversely cut cells are secured. The stain may be either hæmatoxylin-eosin (technic 1, p. 18), or hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19).

## CHAPTER VI.

### NERVE TISSUE.

# The Neurone.

In most of the cells thus far described the protoplasm has been confined to the immediate vicinity of the nucleus. In the smooth muscle cell was seen an extension of protoplasm to a considerable distance from the nuclear region, while in the connective-tissue cells of the cornea the protoplasmic extensions took the form of distinct processes. Processes, often extending long distances from the cell body proper, constitute one of the most striking features of nervecell structure. Some of these processes are known as nerve fibres; and nerve tissue was long described as consisting of two elements, nerve cells and nerve fibres. With the establishment of the unity of the nerve cell and the nerve fibre, the nerve cell with its processes was recognized as the single structural unit of nerve\*tissue. This unit of structure is known as a neurone. The neurone may thus be defined as a nerve cell with all of its processes.

In the embryo the neurone is developed from one of the ectodermic cells which constitute the wall of the primitive neural canal. This embryonic nerve cell, or *neuroblast*, is entirely devoid of processes. Soon, however, from one end of the cell a process begins to grow out. This process is known as the *axone* (axis-cylinder process, neuraxone, neurite). Other processes appear, also as outgrowths of the cell body; these are known as *protoplasmic processes* or *dendrites*.

Each adult neurone thus consists of a *cell body*, and passing off from this cell body two kinds of processes, the *axis-cylinder process* and the *dendritic processes* (Fig. 62).

I. The Cell Body.—Like most other cells, the nerve cell body consists of a mass of protoplasm surrounding a nucleus (Fig. 63). Nerve cell bodies vary in size from very small cell bodies, such as those found in the granule layers of the cerebellum and of the olfactory lobe, to the large bodies of the Purkinje cells of the cerebellum and of the motor cells of the ventral horns of the cord, which are among the largest in the body. There is as much variation in shape

as in size, and some of the shapes are characteristic of the regions in which the cells are situated. Thus, many of the bodies of the cells of the spinal ganglia are spheroidal; of most of the cells of the cortex

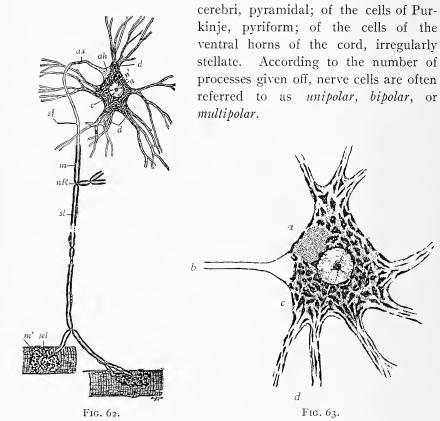


Fig. 62.—Scheme of Lower Motor Neurone. (Barker.) The cell body, protoplasmic processes, axone, collaterals, and terminal arborizations in muscle are all seen to be parts of a single cell and together constitute the neurone. c, Cytoplasm of cell body containing chromophilic bodies, neurofibrils, and perifibrillar substance; n, nucleus; n', nucleolus; d, dendrites; ah, axone hill free from chromophilic bodies; ax, axone; sf, branch (collateral); m, medullary sheath; nR, node of Ranvier where branch is given off; sl, neurilemma (probably not present in central nervous system); m', striated muscle fibre; tel, motor end plate.

Fig. 63.—Large Motor Nerve Cell from Ventral Horn of Spinal Cord of Ox, showing

Chromophilic Bodies. (From Barker, after von Lenhossék.) a, Pigment; b, axone;

c, axone hill; d, dendrites.

The NUCLEUS of the nerve cell (Fig. 63) differs in no essential from the typical nuclear structure. It consists of (1) a nuclear membrane, (2) an intranuclear network of linin and chromatin, (3) an achromatic nucleoplasm, and (4) a nucleolus.

The CYTOPLASM of the nerve cell consists of two distinct elements:

- (1) Neurofibrils, and (2) perifibrillar substance. In most nerve cells a third element is present, (3) chromophilic bodies.
- (1) The *neurofibrils* are extremely delicate fibrils which are continuous throughout the cell body and all of its processes. Within the body of the cell they cross and interlace and probably anastomose (Figs. 64 and 65).

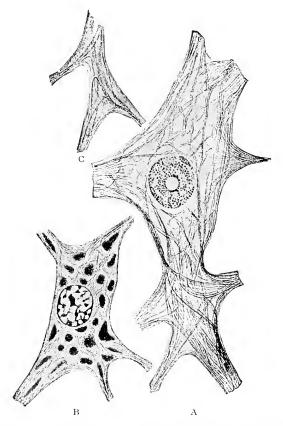


FIG. 64.—Ganglion Cells, Stained by Bethe's Method, showing Neurofibrils. A, Anterior horn cell (human); B, cell from facial nucleus of rabbit; C, dendrite of human anterior horn cell showing arrangement of neurofibrils. (Bethe.)

- (2) The *perifibrillar substance* (Fig. 64) is a fluid or semifluid substance which both in the cell body and in the processes surrounds and separates the neurofibrils. It is believed by some to be like the fibrils, continuous throughout cell body and processes, by others to be interrupted at certain points in the axone (see page 121).
  - (3) The  ${\it chromophilic bodies}$  (Fig. 63) are granules or groups of

granules which occur in the cytoplasm of all of the larger and of many of the smaller nerve cells. They are best demonstrated by means of a special technic known as the method of Nissl (page 35). When subjected to this technic, nerve cells present two very different types of reaction. In certain small cells the amount of cytoplasm is extremely small and only the nuclei stain. Such cells are found in the granule layers of the cerebellum, olfactory lobe, and retina. They are known as *caryochromes*, and apparently consist wholly of neurofibrils

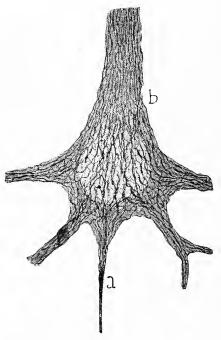


Fig. 65.—Body of Large Pyramidal Cell from Cortex of Cat. Silver Method of Cajal. Shows nucleus pale and arrangement of neurofibrils within the cell; a, axone; b, main or apical dendrite. (Cajal).

and perifibrillar substance. Other cells react, both as to their nuclei and as to their cell bodies, to the Nissl stain. These cells are known as *somatochromes*. Taking as an example of this latter type of cell one of the motor cells of the ventral horn of the cord and subjecting it to the Nissl technic, we note that the cytoplasm is composed of two distinct elements: (a) a clear, unstained *ground substance*, and, scattered through this, (b) deep-blue-staining masses, the *chromophilic bodies* (Fig. 63). These bodies are granular in character and differ in shape, size, and arrangement. They may be large or small, regular

or irregular in shape, may be arranged in rows or in an irregular manner, may be close together, almost filling the cell body, or quite separated from one another. Presenting these variations in different types of cells, the appearance of the chromophilic bodies in a partic-

ular type of cell remains constant, and has thus been used by Nissl as a basis of classification.<sup>1</sup>

It is important to note in studying the nerve cell by this method that somato-chrome cells of the same type frequently show marked variations in staining intensity. This appears to depend upon the size and closeness of arrangement of the chromophilic bodies, and this again seems dependent upon changes in the cytoplasm connected with functional activity.

In cells stained by Nissl's method the cytoplasm between the chromophilic bodies remains unstained and apparently structureless, and it is this part of the cytoplasm that corresponds to the neurofibrils and perifibrillar substance.

The relation which the appearance of the Nissl-stained cell bears to the structure of the living protoplasm is still undetermined. According to some investigators the Nissl bodies exist as such in the living cell. Others believe that they are not present in the living cell, but represent precipitates due either to postmortem changes or to the action of fixatives. The significance of the Nissl picture from the standpoint of pathology lies in the fact that when subjected to a given technic, a particular type of nerve cell always presents the same appearance, and that this appearance furnishes a norm for comparison with cells showing patho-

FIG. 66.—Pyramidal Cell from Human Cerebral Cortex. (Golgi bichlorid method. See 2, p. 33.) Golgi cell type I. a, Cell body: b, main or apical dendrite showing gemmules; c, lateral dendrites showing gemmules; d, axone with collaterals. Only part of axone is included in drawing.

logical changes, and which have been subjected to the same technic.

Many nerve cells contain more or less brownish or yellowish *pig-ment* (Fig. 63). This pigment is not present in the cells of the newborn, but appears in increasing amounts with age. Its significance is not known.

<sup>1</sup>For this classification, the significance of which is somewhat doubtful, the reader is referred to Barker, "The Nervous System and Its Constituent Neurones," p.121.

In addition to its characteristic structure, the nerve cell may contain many elements found in other cells (p. 39). Golgi, Holmgren, and others have also demonstrated a network of canals within the nerve cell similar to that found in other cells (p. 42, Fig. 4).

II. The Protoplasmic Processes or Dendrites.—These have a structure similar to that of the cell body, consisting of neurofibrils, perifibrillar substance, and, in somatochrome cells, chromophilic bodies (Figs. 63 and 64). Dendrites branch dichotomously, become



Fig. 67.—Golgi Cell Type II. from Cerebral Cortex of Cat. (Kölliker.) x, Coarse protoplasmic processes with gemmules easily distinguishable from the more delicate, smoother axone, a. The latter is seen breaking up into a rich plexus of terminal fibres near its cell of origin, practically the entire neurone being included in the drawing.

rapidly smaller, and usually end at no great distance from the cell body (Figs. 66 and 67).

III. The Axone.—This differs from the cell body and dendrites in that it contains no chromophilic bodies (Fig. 63), consisting wholly of neurofibrils and perifibrillar substance. Not only is it entirely achromatic itself, but it always takes origin from an area of the cell body, the axone hill (Fig. 63), which is free from chromophilic bodies. It is as a rule single, and while usually arising from the body of the cell may be given off from one of the larger protoplasmic trunks. Some few cells have more than one axone, and nerve cells without

axones have been described. In Golgi preparations the axone is distinguished by its straighter course, more uniform diameter, and smoother outline (Fig. 66). It sends off few branches (collaterals), and these approximately at right angles. Both axone and collaterals usually end in terminal arborizations. In most cells the axone extends a long distance from the cell body. Such cells are known as Golgi cell type I. (Fig. 66). In others the axone branches rapidly and ends in the gray matter in the vicinity of its cell of origin—Golgi cell type II. (Fig. 67).

As they leave the cell body the neurofibrils of the axone converge to a very narrow portion of the axone, where the perifibrillar substance is much reduced in amount, or according to some, entirely interrupted. Beyond this the fibrils become more separated and the perifibrillar substance more abundant.

Some axones pass from their cells of origin to their terminations as "naked" axones, *i.e.*, uncovered by any sheath. Other axones are enclosed by a thin membrane, the *neurilemma* or *sheath* of *Schwann*. Still others are surrounded by a sheath of considerable thickness known as the *medullary sheath*.

Depending upon the presence or absence of a medullary sheath, axones may thus be divided into two main groups—medullated axones and non-medullated axones.

- 1. Non-medullated Axones (non-medullated nerve fibres) (Fig. 68). These are subdivided into non-medullated axones without a neurilemma and non-medullated axones with a neurilemma.
- (a) Non-medullated axones without a neurilemma are merely naked axones. Present in large numbers in the embryo, they are in the adult confined to the gray matter and to the beginnings and endings of sheathed axones, all of the latter being uncovered for a short distance after leaving the nerve cell body, and also just before reaching their terminations.
- (b) Non-medullated axones with a neurilemma—fibres of Remak (Fig. 68). In these the axone is surrounded by a delicate homogeneous, nucleated sheath, the neurilemma or sheath of Schwann (see p. 119). These axones are described by some writers as having no true neurilemma, but merely a discontinuous covering of flat connective-tissue cells, which wrap around the axone and correspond to the endoneurium of the nerve trunk (see page 382).
- 2. MEDULLATED Axones (medullated nerve fibres).—These, like the non-medullated, are subdivided according to the presence or ab-

sence of a neurilemma into medullated axones with a neurilemma and medullated axones without a neurilemma.

- (a) Medullated axones with a neurilemma constitute the bulk of the fibres of the cerebro-spinal nerves. Each fibre consists of (1) an axone, (2) a medullary sheath, and (3) a neurilemma.
- (1) The axone is composed of neurofibrils continuous with those of the cell body, and like them lying in a perifibrillar substance or neuro-

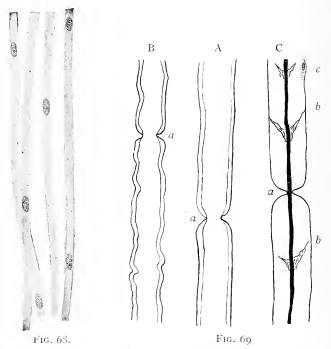


Fig. 68.—Non-medullated Nerve Fibres with Neurilemma, only the nuclei of which

can be seen.  $\times 300$ . Fig. 69.—A, Fresh nerve fibre from sciatic nerve of rabbit teased apart in normal salt solution, showing broad unshrunken axone and comparatively thin medullary sheath. B. Showing crenation of medullary sheath which occurs soon after placing fibres in salt solution. C, Same after fixation and staining with picro-acid-fuchsin, showing shrunken axone and broad medullary space. The latter usually contains irregular clumps of myelin. a, Node of Ranvier; b, incisures of Schmidt; c, nucleus of neurilemma.

plasm (Fig. 72). In the fresh condition the axone is broad, and shows faint longitudinal striations corresponding to the neurofibrils, or appears homogeneous (Fig. 60, A). Fixatives usually cause the axone to shrink down to a thin axial thread, whence its older name of axiscylinder (Fig. 69, C). A delicate membrane has been described by some as enveloping the axone. It is known as the axolemma or periaxial sheath (Fig. 70).

(2) The medullary sheath (Figs. 69 and 72) is a thick sheath composed of a semifluid substance resembling fat and known as mye-

lin. In the fresh state the myelin has a glistening homogeneous appearance. It is not continuous, but is divided at intervals of from 80 to 600 u by constrictions, the nodes or constrictions of Ranvier. That portion of a fibre included between two nodes is known as an internode (Fig. 70). The length of the internode is usually proportionate to the size of the fibre, the smaller fibres having the shorter internodes. In fresh specimens the medullary sheath of an internode appears continuous (Fig. 69, A), but in fixed specimens it is broken up into irregular segments, Schmidt-Lantermann segments, by clefts which pass from neurilemma to the axolemma or axone, and are known as the clefts or incisures of Schmidt-Lantermann (Fig. 69, C). On boiling medullated nerve fibres in alcohol and ether a fine network is brought out in the medullary sheath. the neurokeratin network. Owing to the resistance of neurokeratin to the action of trypsin, it has been considered as possibly similar in composition to horn.

(3) The neurilemma or sheath of Schwann (Figs. 70, B, and 72) is a delicate structureless membrane which encloses the myelin. At the nodes of Ranvier the neurilemma dips into the constriction and comes in contact with the axone or axo-

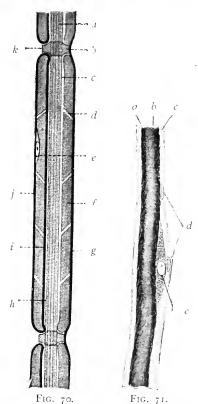


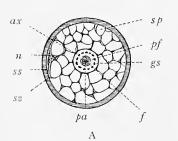
Fig. 70.—Diagram of Structure of a Medullated Nerve Fibre of a Peripheral Nerve showing two different views as to relations of neurilemma and axolemma and their behavior at the nodes of Ranvier. (Szymonowicz.) a. Neurofibrils: b, cement substance: c, axone: d, incisure of Schmidt; c, nucleus of neurilemma: f, medullary sheath: g, sheath of Schwann: h, axone: i, axolemma: j, sheath of Schwann: k, node of Ranvier.

structureless membrane Fig. 71.—Piece of Medullated Nerve Fibre from Human Radial Nerve. ×400. Osmic-acid fixation and stain. (Szymonowicz.) a, Medullary sheath: b, axone; c, sheath of Henle; d, nuclei of Henle's sheath: c, nucleus of neurilemma.

lemma. Against the inner surface of the neurilemma, usually about midway between two nodes, is an oval-shaped nucleus, the nucleus of

the neurilemma (Figs. 69, C, and 71). Each nucleus is surrounded by an area of granular protoplasm, and makes a little depression in the myelin and a slight bulging of the neurilemma (Fig. 69, C). Accord-

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ing to most observers no neurilemma is present in the central nervous system. An important exception is Cajal, who describes the medullated fibre of the central nervous system as having a neurilemma.

In addition to the above-described sheaths, most medullated fibres of peripheral nerves have, outside the neurilemma, a nucleated sheath of connective-tissue origin, known as the sheath of Henle (Fig. 71).

Two views as to the relation of the axolemma to the neurilemma are illustrated in Fig. 70. According to one the neurilemma is continuous, merely dipping into the nodes of Ranvier, where it touches the axolemma or the axone. According to the second both neurilemma and axolemma are interrupted at the node, but unite with each other there to enclose completely the medullary substance of the internode.

Fig. 72.—Scheme of Structure of Medullated Peripheral Nerve Fibre of a Fish (Nemiloff). A, Cross section; B, longitudinal section; on left, fibre is shown as stained intra vitam with methylene blue; on right, myelin is shown black as in osmic acid staining, with the incisures of Schmidt indicated; sz, cells of sheath of Schwann; n, their nuclei; ss, sheath of Schwann or the myelin sheath network; le, larger trabeculae of protoplasmic framework of medullary sheath arranged obliquely to axis-cylinder and forming the so-called "funnels"; leo, clear streaks in fibres treated with osmic acid, corresponding to le, incisures of Schmidt; mo, myelin blackened with osmic acid; ax, axis-cylinder; pa, periaxial space around axis-cylinder; gs, "coagulum sheath," granules probably representing coagulated fluid in periaxial space; pf, peripheral, non-fibrillar, part of axis-cylinder; f, neurofibrils of axis-cylinder; r, ring-like thickening of Schwann's sheath at node of Ranvier; o, cavity in r.

According to the views illustrated in Fig. 72, that part of the axone which lies between two nodes is enveloped by a cell, or by several cells forming a syncytium. The outer homogeneous membrane there pictured would thus be of the nature of a cell membrane or cuticle, and would correspond to the neurilemma. The trabeculæ (neurokeratin network, of which some of the larger strands would represent the incisures of Schmidt) would correspond to the spongioplasm, and just along the outer side of the axone would constitute the axolemma. The myelin would thus be enclosed within the cell in much the same manner as the fat within the fat cell.

Recent experiments of Bethe and others tend to prove an interruption of the perifibrillar substance at the node of Ranvier. They consider the axone at the node as probably crossed by a sieve-like plate, through the holes of which the fibrils pass, but which completely interrupts the perifibrillar substance. The accuracy of these observations has been disputed.

Medullated nerve fibres vary greatly in size. The finer fibres have a diameter of from 2 to  $4\mu$ , those of medium size from 4 to  $10\mu$ , the largest from 10 to  $20\mu$ . They have few branches, and these are always given off at the nodes of Ranvier.

(b) Medullated axones without a neurilemma are the medullated nerve fibres of the central nervous system as described by most observers. Cajal, as already mentioned (p. 120), describes these fibres as having a neurilemma. Their structure is similar to the above-described structure of a medullated nerve fibre with a neurilemma, except for the absence of the latter sheath.

As to the physiological significance of the structural elements of the neurone, we have little absolute knowledge but certain fairly well-grounded theories.

That portion of the neurone which surrounds the nucleus—the cell body—is, as already stated, the *genetic centre* of the neurone, the nucleus as in other cells being probably concerned in the general cell metabolism. From the behavior of the processes when cut off from the cell body it is evident that the latter is the *trophic* or *nutritive centre* of the neurone. It seems probable that from the standpoint of neurone activity, the cell body usually acts as the *functional centre* of the neurone, the processes acting mainly as channels through which impulses are received and distributed. Certain facts, such for example as the entire absence of chromophilic bodies in many nerve cells, which nevertheless undoubtedly functionate; the absence of these bodies in all axones; the diminution of the chromatic substance during functional activity; its much greater diminution if activity be carried to the point of exhaustion; these together with its behavior under certain pathological conditions, all favor the theory that the stainable substance of Nissl is not the active nerve element of the cell, but is rather of the nature of a nutritive element.

There thus remains to be considered as possible factors in the transmission of the nervous impulse the neurofibrils and the perifibrillar substance. While a few investigators are inclined to magnify the importance of the latter, the majority agree in considering the neurofibrils as the principal conducting mechanism of the neurone. The already referred to observations of Bethe regarding the interrup-

tion of the perifibrillar substance at the constricted portion of the axone and at the nodes of Ranvier, thus making the neurofibrils the only continuous structure, are obviously in favor of this view. The neurofibrils are probably a differentiation of the spongioplasm, while the perifibrillar substance and chromophilic bodies are specializations of the hyaloplasm.

As to the manner in which neurones are connected, there are two main theories, the contact theory and the continuity theory.

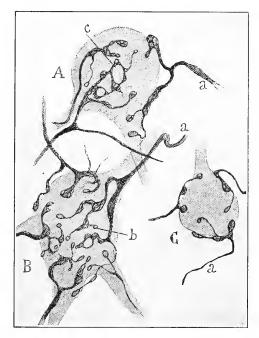


Fig. 73.—A, B, C, Three cells of the Ventral Cochlear Nucleus of Rabbit, showing terminals of fibres of cochlear nerve and their relations to the cell bodies (Cajal). a, a, a, Fibres of the cochlear nerve, which break up into terminal arborizations upon the cells; b, c, terminal rings. The point of contact between the terminals of the one neurone and the cell body of the other neurone constitute a "synapsis."

According to the contact theory each neurone is a distinct and separate entity. Association between neurones is by contact or contiguity of the terminals of the axone of one neurone with the cell body or dendrites of another neurone, and never by continuity of their protoplasm. This theory, which is known as the "neurone theory" and which received general acceptance as a result of the work of Golgi, His, Forel, Cajal, and others, has been recently called in question by such prominent neurologists as Apathy, Bethe, Held, and Nissl, on the ground that in some cases the neurofibrils are continuous throughout a series of neurones. Based upon the contact theory is the so-called "retraction theory," which held that a neurone being associated with other neurones only by contact was able to retract its terminals, thus breaking the association and throwing itself, as it were, out of circuit. The

point of contact between two neurones is called a *synapsis* (Fig. 73), and the conception that there is some kind of interruption or discontinuity in neural circuits involving more than one neurone has proved useful to physiologists. It affords an explanation of certain differences between conduction through a circuit of two or more neurones and through a nerve fibre. For example, an impulse takes longer to traverse the circuit than to traverse a nerve fibre of equal length. Also a stimulus may pass in either direction along a nerve fibre, but cannot be "reversed" along a circuit.

According to the *continuity theory*, while the perifibrillar substance is interrupted as above described, the neurofibrils are continuous. According to this theory the neurofibrils, which form a plexus or network within the cell body and dendrites,

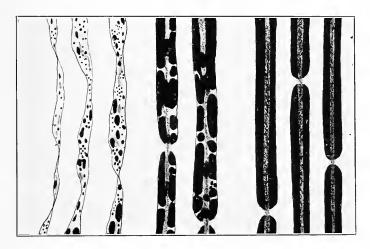


FIG. 74.—A, Normal Nerve Fibres from Sciatic Nerve of Rabbit, osmic acid fixation and stain; each fibre shows node of Ranvier. B, Two fibres from distal part of rabbit's sciatic five days after cutting the nerve; shows segmentation of myelin; C, three fibres from distal part of rabbit's sciatic three weeks after cutting nerve; most of the myelin has been absorbed and only traces of the axones remain.

are connected with a *pericellular network—the Golgi net*—which closely invests the cell body and its dendrites. Externally the Golgi net is further connected with the neurofibrils of the axones and collaterals of other nerve cells. This connection is either direct, or, as some believe, through another general (diffuse) *extracellular network*. The neurofibrils are thus, according to this theory, continuous and form two or possibly three continuous networks: (a) an intracellular network, (b) a pericellular network (Golgi), and (c) a more diffuse extracellular network, lying between the cells. It seems probable that the Golgi network is either nonnervous or an artefact. The main point at issue is whether the neurofibrils, in such pericellular terminals as are illustrated in Fig. 73, are continuous with the neurofibrils within the cell enveloped or are separate from the latter.

The individuality of the neurone and the interdependence of its various parts are strikingly shown by its behavior when injured. That degenerative changes, which progress to complete disappearance of the nerve structures, take place in the distal part of a nerve when that nerve is cut across has long been accepted as one of the fundamental laws of neuropathology (law of Wallerian degeneration). In terms of the neurone concept this would mean that an axone cut off from its cell of origin degenerates and disappears and this behavior of the axone would accord with the already stated fact that the cell body is the trophic center of the neurone. The degenerative changes in the axone are best shown in their earlier stages by an osmic acid (p. 7) or by a Marchi (p. 31) stain. Later, when the degenerated fibres have been largely replaced by connective tissue, the Weigert method is most satisfactory, especially in the central nervous system.

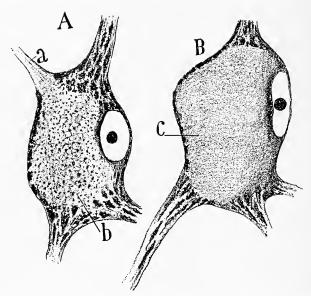
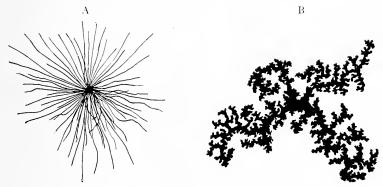


Fig. 75.—Two Motor Cells from Ventral Horn of Dorsal Cord of Rabbit; fifteen days after cutting major sacro-sciatic nerve. A, Cell in which the chromophilic bodies appear disintegrated and nucleus eccentric; B, cell showing more advanced chromatolysis, the chromophilic substance being present only in the dendrites and around the nucleus in the form of a homogeneous mass; nucleus causes bulging of surface of cell.

The degeneration is not progressive from the point of injury distally, but takes place throughout the entire cut off portion at approximately the same time. All parts of the nerve fibre are affected. In the medullary sheath the changes consist in segmentation of the sheath, breaking up of the segments into granules and finally complete absorption (Fig. 74). While undergoing these physical changes chemical changes are also taking place in the myelin which result in its breaking down into simpler fatty substances which give the fat reaction to the Marchi stain. At the same time the neurofibrils become irregular and granular and the axis-cylinder finally disappears. The neurilemma of peripheral nerve fibres is peculiar in that it does not degenerate; instead of this its nuclei proliferate and apparently play an important rôle in the disintegration and absorption of the myelin as well as in any regenerative changes which may occur later. The same rule holds good for dendrites as for axones as far as it has been possible to de-

termine, namely that cut off from their cells of origin they undergo complete degeneration.

At the time the law of Wallerian degeneration was established it was believed that the central portion of the nerve and the cell bodies remained intact after division of the nerve. More recently the method of Marchi (for nerve fibres) and the method of Nissl (for neurone bodies) have shown marked degenerative changes in the parts proximal to the lesion. The extent and rapidity of these changes are dependent mainly upon two factors (1) the type of neurone—some neurones being apparently more resistant than others to injury—and (2) the character and location of the injury—e.g., pulling out the nerve causing the greatest reaction; cutting the nerve, a reaction of less intensity; pinching the



F1G. 76.—A, Neuroglia Cell—Spider Type—Human Cerebrum. B, Neuroglia Cell—Mossy Type—Human Cerebrum.

nerve, the least degree of reaction; an injury near the body of the cell causing more effect centrally than one near the periphery.

In the proximal stump of the nerve the changes are similar to those which take place in the distal stump, but these changes take place more slowly.

In the cell body there is an initial turgescence, followed by disintegration and disappearance of the chromophilic bodies beginning near the center of the cell, and a displacement of the nucleus toward the periphery. This reaction on the part of the cell body to injury to its axone—"central chromatolysis" and "nuclear eccentricity"—is sufficiently characteristic to have led to the designation "axonal degeneration" (Fig. 75).

The importance of these degenerations from the standpoint of anatomy lies in the fact that, combined with such methods as Nissl, Weigert, and Marchi, they enable one to trace the connections between cell bodies and nerve fibres throughout the nervous system.

# Neuroglia.

This is a peculiar form of connective tissue found only in the central nervous system. Unlike the other connective tissues, neuroglia is of ectodermic origin, being developed from the ectodermic cells which line the embryonic neural canal. These cells, at first

morphologically identical, soon differentiate into neuroblasts or future neurones, and spongioblasts or future neuroglia cells, the latter most probably being in the form of a syncytium. Later this spongioblastic syncytium differentiates fibres, the neuroglia fibres, which, according to Weigert and others, may be entirely separate from the cells (Fig. 77). The structure of neuroglia would thus be analogous to that of fibrous connective tissue, i.e., composed of cells, the neuroglia cells, and a fibrillar intercellular substance, the neuroglia fibres. The Golgi method apparently reveals a great variety of neuroglia cells which may be divided into cells with straight radiating unbranched processes,

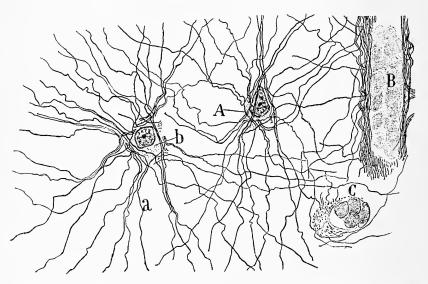


Fig. 77.—Neuroglia Cells and Fibres from the White Matter of the Human Cerebellum stained by Weigert's neuroglia stain. A, Neuroglia cell; B, blood-vessel cut longitudinally, and C, blood-vessel cut transversely, showing enveloping neuroglia fibres; a, neuroglia fibres; b, cytoplasm of neuroglia cell. (Cajal.)

spider cells, and rough thick branching cells, mossy cells. It seems probable that in the former both cells and fibres are stained while in the latter only portions of the cells or syncytium, this method not differentiating between cells and fibres. Some authorities still maintain that the fibres are to be regarded as a part of the cell in the adult. The neuroglia cells and fibres are of marked pathological significance. Spider cells occur chiefly in the white matter, mossy cells in the gray matter in connection with blood-vessels (Fig. 76 A and B).

#### TECHNIC.

- (1) Pieces of the cerebral cortex are stained by one of the Golgi methods. If the rapid or mixed silver method is used, sections must be mounted in hard balsam without a cover; if the slow silver or the bichloride method is used, the sections may be covered. Sections are cut from 75 to 100µ in thickness, cleared in carbol-xylol or oil of origanum and mounted in balsam. This section shows only the external morphology of the neurone. It is also to be used for studying the different varieties of neuroglia cells as demonstrated by Golgi's method (see page 126).
- (2) Thin transverse slices from one of the enlargements of the spinal cord are fixed in absolute alcohol. Thin sections (5 to 10µ) are stained by Nissl's method (page 35) and mounted in balsam. This section is for the purpose of studying the internal structure of the nerve cell and processes as demonstrated by the method of Nissl.
- (3) Medullated Nerve Fibres (fresh).—Place a small piece of one of the sciatic or lumbar nerves of a recently killed frog in a drop of salt solution and tease longitudinally. Cover and examine as quickly as possible. Note the diameter of the axone and of the medullary sheath and the appearance of the nodes of Ranvier. An occasional neurilemma nucleus can be distinguished.
- (4) Medullated nerve fibres—fibres from the cauda equina (this material has the advantage of being comparatively free from fibrous connective tissue)—are fixed in formalin-Müller's fluid (technic 5, p. 7), and hardened in alcohol. Small strands are stained twenty minutes in strong picro-acid-fuchsin solution (technic 2, p. 18), washed thoroughly in strong alcohol, cleared in oil of origanum, thoroughly teased longitudinally and mounted in balsam.

## General References for Further Study of Tissues.

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Ewing: Clinical Pathology of the Blood. Hertwig: Die Zelle und die Gewebe. Kölliker: Handbuch der Gewebelehre.

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# PART IV. THE ORGANS.



#### CHAPTER I.

#### THE CIRCULATORY SYSTEM.

THE circulatory apparatus consists of two systems of tubular structures, the blood-vessel system and the lymph-vessel system, which serve, respectively, for the transmission of blood and lymph.

#### THE BLOOD-VESSEL SYSTEM.

This consists of (a) a central propelling organ, the heart; (b) a series of efferent tubules—the arteries—which by branching constantly increase in number and decrease in calibre, and which serve to carry the blood from the heart to the tissues; (c) minute anastomosing tubules—the capillaries—into which the arteries empty and through the walls of which the interchange of elements between the blood and the other tissues takes place; (d) a system of converging tubules—the veins—which receive the blood from the capillaries, decrease in number and increase in size as they approach the heart, and serve for the return of the blood to that organ.

The entire system—heart, arteries, veins, capillaries—has a common and continuous lining, which consists of a single layer of endothelial cells. Of the capillaries this single layer of cells forms the entire wall. In the heart, arteries, and veins, the endothelium serves simply as the lining for walls of muscle and connective tissue.

## Capillaries.

It is convenient to describe these first on account of their simplicity of structure. A capillary is a small vessel from 7 to 16µ in diameter. Its wall consists of a single layer of edothelial cells. The cells are somewhat elongated in the long axis of the vessel. Their edges are serrated and are united by a small amount of intercellular substance (p. 70), which can be demonstrated by the silver nitrate stain. In certain capillaries—those of the early embryo, of the kidney glomeruli, of the chorioid coat of the eye, of the liver—no cell boundaries can be made out. In these capillaries the endothelium appears to be of the nature of a syncytium (p. 62). Capillaries branch without diminution in

calibre, and these branches anastomose to form capillary networks, the meshes of which differ in size and shape in different tissues and organs (Figs. 78, 79, 80). The largest meshed capillary networks are found in

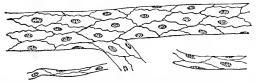


Fig. 78.—Vein and Capillaries. Silver-nitrate and humatoxylin stain (technic 7, p. 72), to show outlines of endothelial cells and their nuclei.

the serous membranes and in the muscles, while the smallest are found in the glands, as, e.g., the liver. As to calibre, the largest are found in the liver, the smallest in muscles.

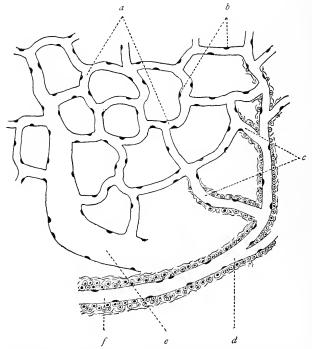


Fig. 79.—Diagram of Capillaries, Small Artery, and Vein, showing their structure and relations. a, Capillaries; b, nuclei of capillary endothelium; c, precapillary arteries; d, arteriole; e, small vein; f, small artery.

In such thin membranous parts as the web of the frog's foot, or the wall of the frog's bladder, the blood may be observed as it flows through the arteries, capillaries, and veins. The current is seen to be fastest in the arteries, and faster in the center of the vessel than at its periphery. It is slower in the veins and slowest in the capil-

laries. In the case of the frog's bladder, the mere exposure to the air acts as a sufficient irritant to cause slight inflammatory changes, and the leucocytes may be seen adhering to the walls of the capillaries and passing through them into the tissues. The capillary, both from the thinness of its wall and from the slowness with which the blood passes through it, is peculiarly adapted for the interchange of material between the blood and the tissues, and it is probable that it is in the capillary that all such interchange takes place.

#### Arteries.

The wall of an artery consists of three coats:

- (1) An inner coat, the intima.
- (2) A middle coat, the media.
- (3) An outer coat, the adventitia.

The intima consists of a single layer of endothelial cells, continuous with and similar to that forming the walls of the capillaries, or, in ar-

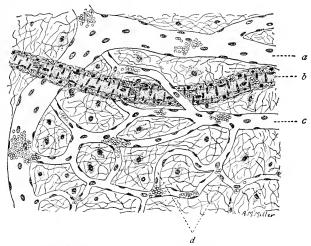


Fig. 80.—Capillary Network from Human Pia Mater, showing also an arteriole in "optical section" and a small vein.  $\times$ 350. (Technic 1, p. 139.) a, Vein; b, arteriole; e, large capillary; d, small capillaries.

teries of considerable size, of this layer plus more or less connective tissue. The middle coat consists mainly of smooth muscle, the outer of connective tissue.

The structure of these three coats varies according to the size of the artery, and while the transition between them is never abrupt, it is convenient, for purposes of description, to distinguish (a) small arteries, (b) medium sized arteries, and (c) large arteries.

Small Arteries.—Passing from a capillary to an artery, the first

change is the addition of a thin sheath of connective tissue around the outside of the endothelial tube. A little farther back isolated smooth muscle cells, circularly arranged, begin to appear between the endothelium and the connective tissue. Such an artery is known as a *precapillary artery*. The next transition is the completion of the muscular coat, the muscle cells now forming a continuous layer. Such an artery, consisting of three distinct coats, the middle coat composed of a single continuous layer of smooth muscle cells, is known as an *arteriole* (Fig. 79, d; Fig. 80, b).

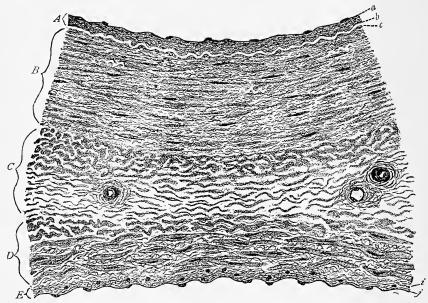


Fig. 81.—From Cross-section through Walls of Medium-sized Artery and its Accompanying Vein.  $\times 75$ . (Technic 3, p. 140.) A, Intima of artery; a, its endothelial layer; b, its intermediary layer; c, its elastic layer; b, media of artery; c, adventitia, the upper part belonging to the artery, the lower to the vein; within the adventitia are seen the vasa vasorum; b, media of vein; b, intima of vein; b, its intermediary layer; b, its endothelial layer.

Medium-sized Arteries.—This group comprises all the named arteries of the body with the exception of the aorta and the pulmonary. Their walls are formed of the same three coats found in the arteriole, but the structure of these coats is more elaborate.

- 1. The Intima consists of three layers (Fig. 81).
- (a) An inner endothelial layer already described.
- (b) A middle layer, the intermediary layer of the intima. This is composed of delicate white and elastic fibrils and connective-tissue cells.

(c) An outer layer, the elastic layer of the intima, or membrana elastica interna—a thin fenestrated membrane of elastic tissue. This membrane is intimately connected with the media and marks the boundary between the latter and the intima. In the smallest of the medium-sized arteries the intermediary layer is often wanting, the endothelial cells resting directly upon the elastic membrane. Owing to the extensive amount of elastic tissue in their walls, there is a post-

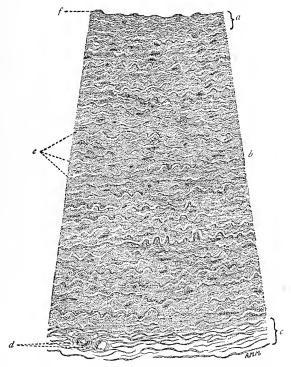


Fig. 82.—From Transverse Section of Dog's Aorta.  $\times$ 60. (Technic 4, p. 140.) a, Intima; b, media; c, adventitia; d, vasa vasorum; c, elastic tissue; f, endothelium.

mortem contraction of arteries which results in the intima being thrown up into folds. For this reason the elastic membrane presents, in transverse sections of an artery, the appearance of a wavy band (Fig. 81).

2. The MEDIA is a thick coat of circularly disposed smooth muscle cells (Fig. 81, B). Its thickness depends largely upon the size of the vessel, though varying somewhat for different vessels of the same size. A small amount of fibrillar connective tissue supports the muscle cells. Elastic tissue is present in the media, the amount

being usually proportionate to the size of the vessel. In the smaller of the medium-sized arteries, the elastic tissue is disposed as delicate fibrils among the muscle cells. In larger arteries many coarse fibres are intermingled with the fine fibrils. When much elastic tissue is present the muscle cells are separated into more or less well-defined groups. In such large arteries as the subclavian and the carotid, elastic tissue occurs not only as fibrils but also as circularly disposed plates or fenestrated membranes.

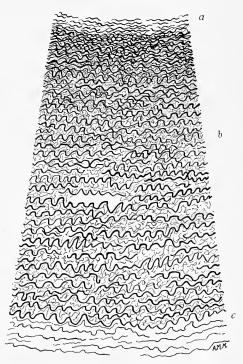


Fig. 83.—From Transverse Section of Dog's Aorta, to show Elastic Tissue. ×60- (Technic 7, p. 140.) Elastic tissue stained black. *a*, Intima; *b*, media; *e*, adventitia.

3. The adventitia (Fig. 81, C) is composed of loose fibrous connective tissue with some elastic fibres. Occasionally there are scattered smooth muscle cells. Both smooth muscle cells and elastic fibres are arranged longitudinally. The adventitia does not form a definitely outlined coat like the media or intima, but blends externally with the tissues surrounding the artery and serves to attach the artery to these tissues. In some of the larger arteries the elastic tissue of the adventitia forms an especially well-defined layer at the outer margin

of the media. This is known as the *membrana elastica externa*. In general, it may be said that the thickness of the adventitia and the amount of elastic tissue present are directly proportionate to the size of the artery.

Large arteries like the aorta (Fig. 82) have the same three coats as small and medium-sized arteries. The layers are not, however, so distinct. This is due mainly to the excessive amount of elastic tissue in the media (Fig. 82), which makes indistinct the boundaries between intima and media, and between media and adventitia. The walls of the aorta are thin in proportion to the size of the vessel, increased strength being obtained by the decided increase in the amount of elastic tissue. Of the intima, the endothelial cells are short and polygonal; the intermediary layer similar to that of a medium-sized artery; the elastic layer less distinct and often broken up into several thin layers. The media consists mainly of elastic tissue arranged in circular plates or fenestrated membranes. Between the elastic-tissue plates are groups of smooth muscle cells and some fibrillated connective tissue. The adventitia resembles that of the medium-sized artery. There is no external elastic membrane.

Certain arteries have structural peculiarities. The arteries of the brain and cord are thin-walled in proportion to their calibre, the inner elastic membrane is especially well defined, and there are few elastic fibres in the media. In the renal, cœliac, mesenteric, and external iliac arteries there is little or no connective tissue separating the endothelium from the media. In the subclavian, the media contains longitudinal muscle cells. Longitudinally running muscle cells occur in the adventitia of the umbilical arteries, in the iliac, splenic, renal, superior mesenteric and dorsalis penis. The radial, femoral and cœliac arteries have comparatively little elastic tissue, while in the common iliac, carotid, and axillary the elastic tissue is in excess of the muscular.

#### Veins.

The walls of veins resemble those of arteries. There are the same three coats, *intima*, *media*, and *adventitia*, and the same elements enter into the structure of each coat (Fig. 81). Venous walls are not, however, so thick as those of arteries of the same calibre, and the coats are not so distinctly differentiated from one another. The transition from capillary through the precapillary vein to the small vein is similar to that described under arteries (page 133). Unlike the artery, the thickness of the wall of a vein and its structure are not directly proportionate to the size of the vessel, but depend also upon other factors such

as the position of the vein and the support given to its walls by surrounding structures.

Of the INTIMA the endothelial layer and the intermediary layer are similar to those of the artery. The elastic layer is not always present, is never so distinct, and is not wavy as in the artery (Fig. 81). The result is a lack of demarcation between intima and media, the connective tissue of the intermediary layer of the intima merging with the mixed muscle and connective tissue of the media. Projecting at intervals from the inner surface of the wall of some veins are valves. These are derived entirely from intima and consist of loose fibrous and elastic tissue covered by a single layer of endothelium. Valves are especially large and strong in the larger veins of the lower limbs. They are absent in the veins of the brain and cord and their membranes, in the veins of bones, in the umbilical vein, and in most of the visceral veins with the exception of some branches of the portal.

The MEDIA of veins is thin as compared with that of arteries of the same size. It consists of fibrous and elastic tissue and smooth muscle cells. The amount of muscle is comparatively small and the cells are arranged in groups through the connective tissue.

The ADVENTITIA is well developed in proportion to the media. It consists of mixed fibrous and elastic tissue and usually contains along its inner margin small bundles of longitudinally disposed smooth muscle cells.

The media is thickest in the veins of the lower extremities and in the veins of the skin. In the veins of the head and abdomen the media is very thin, while in the subclavian and superior vena cava and in the veins of bones, of the pia mater, dura mater, and retina, there is an almost entire absence of media.

Arteries are as a rule empty after death, while veins contain blood. The absence of much elastic tissue in the walls of the veins prevents any such extensive post-mortem contraction as occurs in the arteries. Veins tend to collapse after death, but are usually prevented from doing so by the presence of blood in them.

In the iliac and femoral veins, longitudinally disposed muscle occurs in the inner part of the media. The umbilical vein, like the corresponding artery, has three distinct muscular coats. Longitudinal muscle fibres are present in the adventitia of the superior vena cava (hepatic and abdominal portion) and of the portal and hepatic veins. In the upper portion of the inferior vena cava, in the superior vena cava, the jugular, innominate, and subclavian, there is little muscle tissue in any of the coats, while in the veins of the brain and its membranes, the retina, the placenta and the bones, no muscle is present.

Vasa Vasorum.—Medium and large arteries and veins are supplied with small nutrient vessels—vasa vasorum. These vessels run in the adventitia, small branches penetrating the media (Figs. 81 and 82).

**Lymph channels** are found on the outer surface of many blood-vessels. Some of the smaller vessels are surrounded by spaces lined by endothelium—*perivascular lymph spaces*. These communicate with the general lymphatic system.

Nerves.—The walls of the blood-vessels are supplied with both medullated and non-medullated fibres. The latter are axones of sympathetic neurones. As these nerves control the calibre of the vessels they are known as vasomotor nerves. They form plexuses in the adventitia, from which are given off branches which penetrate the media and terminate on the muscle cells. The medullated fibres are the peripheral arms of spinal or cranial ganglion cells. The larger fibres run in the connective tissue outside the adventitia. From these are given off branches which enter the media, divide repeatedly, lose their medullary sheaths, and terminate mainly in the media, although some fibres have been traced to their terminations in the intima.

#### TECHNIC.

- (1) Capillaries, Arterioles, Small Arteries, and Veins.—Fix an entire brain, or slices about an inch thick from its surface, in formalin-Müller's fluid for twentyfour hours (technic 5, p. 7). Remove the pia mater, especially the thinner parts which lie in the sulci between the convolutions, and harden in graded alcohols. Select a thin piece, stain with hæmatoxylin (lightly) and eosin (strongly) (technic 1, p. 18), and mount in balsam or in eosin-glycerin. The veins, having thin walls and being usually well filled with blood, appear distinct and red from the eosinstained red cells. The arteries, having thicker walls, in which are many hæmoglobin-stained nuclei, have a rather purple color. Between the larger vessels can be seen a network of anastomosing capillaries with their thin walls and bulging nuclei. Some are filled with blood cells; others are empty with their collapsed walls in apposition. Note the appearance of an arteriole, first focusing on its upper surface, then focusing down through the vessel. In this way what is known as an "optical section" is obtained, the artery appearing as if cut longitudinally. Trace the transition from arteriole to precapillary artery and the breaking up of the latter into the capillary network. Similarly follow the convergence of capillaries to form a small vein.
- (2) Instructive pictures of the relations of arteries, capillaries, and veins in living tissues may be obtained by curarizing a frog, distending the bladder with normal saline introduced through a small catheter or cannula, opening the abdomen and drawing out the bladder, which can then be arranged upon the stage of the microscope. The passage of the blood from the arteries through the capillary network and into the veins is beautifully demonstrated.

- (3) For studying the structure of the walls of a medium-sized artery and vein remove a portion of the radial artery, or other artery of similar size, and its accompanying vein, together with some of the surrounding tissues. Suspend the vessels, with a small weight attached, in formalin-Müller's fluid (technic 5, p. 7). Sections should be cut transversely, stained with hæmatoxylin-eosin (technic 1, p. 18), or with hæmatoxylin-picro-acid fuchsin (technic 3, p. 19), and mounted in balsam. The vessels of the adventitia—vasa vasorum—are convenient for studying the structure of arterioles and small veins.
- (4) Fix a piece of aorta in formalin-Müller's fluid, care being taken not to touch the delicate endothelial lining. Stain transverse sections with hæmatoxylineosin or with hæmatoxylin-picro-acid fuchsin and mount in balsam.
- (5) The outlines of the lining endothelial cells may be demonstrated as follows: Kill a small animal, cut the aorta, insert a glass cannula and, under low pressure, thoroughly wash out the entire vascular system with distilled water. Follow the water by a one-per-cent. aqueous solution of silver nitrate. Remove some of the smaller vessels, split longitudinally, mount in glycerine, and expose to the direct sunlight. After the specimen has turned brown examine with the low power. The outlines of the cells should appear brown or black.
- (6) The endothelium of the smaller vessels and capillaries may also be demonstrated in the specimen described under technic 8, p. 72.
- (7) The elastic tissue of the blood-vessels is best demonstrated by means of Weigert's elastic-tissue stain. Prepare sections of medium-sized vessels and of the aorta, as above described (3), and stain as in technic 3, p. 26.

## The Heart.

The heart is a part of the blood-vessel system especially differentiated for the purpose of propelling the blood through the vessels.

The main mass of the heart wall consists of a special form of muscle tissue already described as heart muscle (page 106). This constitutes the *myocardium*. On its inner and outer sides the myocardium is covered by connective-tissue membranes lined, respectively, with endothelium and mesothelium and known as the *endocardium* and *epicardium*.

The MYOCARDIUM varies in thickness in different parts of the heart, being thickest in the left ventricle, thinnest in the auricles. A ring of dense connective tissue, the auriculo-ventricular ring, completely separates the muscle of the auricles from that of the ventricles. The auricular muscle consists of an outer coat common to both auricles, the fibres of which have a transverse direction, and of an inner coat, independent for each auricle, the fibres of which are longitudinally disposed. Between the two coats bundles of muscle fibres are frequently found which run in various directions.

The disposition of the muscle tissue of the ventricles is much

more complicated. It is usually described as composed of several layers, the fibres of which run in different directions. The meaning of these fibre layers becomes apparent when we study the arrangement of the fibres in embryonic hearts in which the connective tissue has been broken down by maceration. Thus dissected, the muscle of the ventricles is seen to consist mainly of two sets of fibres, a *superficial set* and a *deep set*. These run at right angles to each other. Both sets of fibres begin at the auriculo-ventricular rings. The superficial fibres wind around both ventricles in a spiral manner, becoming constantly deeper, to terminate in the papillary muscles of the opposite ventricle. The deeper fibres pass from the auriculo-ventricular ring around the ventricle of the same side, through the interventricular septum and terminate in the papillary muscles of the opposite ventricle.

The ENDOCARDIUM covers the inner surface of the myocardium and forms the serous lining of all the chambers of the heart. At the arterial and venous orifices it is seen to be continuous with and similar in structure to the intima of the vessels. It consists of two layers: (a) an inner composed of a single layer of endothelial cells, corresponding to the endothelial lining of the blood-vessels; and (b) an outer composed of mixed fibrous and elastic tissue and smooth muscle cells. Externally the endocardium is closely attached to the myocardium.

Strong fibrous rings (annuli fibrosi), composed of mixed fibrous and elastic tissue, surround the openings between auricles and ventricles. Similar but more delicate rings encircle the openings from the heart into the blood-vessels.

The *heart valves* are attached at their bases to the annuli fibrosi. They are folds of the endocardium, and like the latter consist of fibrous and elastic tissue continuous with that of the rings and covered by a layer of endothelium.

The EPICARDIUM is the visceral layer of the pericardium. It is a serous membrane like the endocardium, which it resembles in structure. It consists of a layer of mixed fibrous and elastic tissue covered over by a single layer of mesothelial cells. Beneath the epicardium there is usually more or less fat.

**Blood-vessels.**—Blood for the nutrition of the heart is supplied through the coronary arteries. The larger branches run in the connective tissue which separates the bundles of muscle fibres. From these, smaller branches pass in among the individual fibres, where

they break up into a rich capillary network with elongated meshes. From the myocardium, capillaries penetrate the connective tissue of the epicardium and endocardium. The auriculo-ventricular valves are supplied with blood-vessels, while in the semilunar valves blood-vessels are wanting.

Lymphatics.—Lymph channels traverse the epicardium and endocardium and enter the valves. Within the myocardium minute lymph vessels have been demonstrated between the muscle fibres and accompanying the blood-vessels.

Nerves.—These are derived from both cerebro-spinal and sympathetic systems, and consist of both medullated and non-medullated fibres. Sympathetic ganglion cells are distributed in groups throughout the myocardium. Among these cells the nerve fibres form plexuses from which both motor and sensory terminals are given off to the muscle. (For nerve endings in heart muscle see page 393.)

#### TECHNIC.

- (1) The Heart.—Cut pieces through the entire thickness of the wall of one of the ventricles, care being taken not to touch either the serous surface or the lining endothelium. Fix in formalin-Müller's fluid (technic 5, p. 7). Cut transverse and longitudinal sections; stain with hæmatoxylin-eosin (technic 1, p. 18) and mount in balsam.
- (2) Treat the entire heart of a small animal (e.g., guinea-pig or frog) in the same manner as the preceding, making transverse sections through both ventricles.
- (3) An entire heart, human or animal, may be fixed in the distended condition by filling with formalin-Müller's fluid under low pressure and then tying off the vessels. The entire heart thus distended is placed in a large quantity of the same fixative.

## DEVELOPMENT OF THE CIRCULATORY SYSTEM.

The blood-vessels and the heart begin their development separately and afterward become united. Both are derived from mesoderm. The earliest vessels to be formed are the capillaries. These make their appearance in the mesodermic tissue near the periphery of the area vasculosa which surrounds the developing embryo. Here groups of cells known as "blood islands" differentiate from the rest of the mesodermic cells. The superficial cells of these islands become flattened to form the endothelium, while the remaining cells form the crythroblasts. These represent the earliest blood-vessels. These channels, which are at first unconnected, anastomose and give rise to a net-

work of channels which are the earliest capillaries. In regard to the origin of the later vessels in the extraembryonic area, and those within the embryo, there are two views: (1) that they represent outgrowths from the original capillaries; (2) that they arise in situ in the same manner as the earliest capillaries and unite secondarily to form networks. The weight of evidence at present favors the latter view. The entire vascular system is at first represented by a network of capillaries. As development proceeds some of the channels enlarge to form the arteries and veins, the smooth muscle and connective tissue of the walls being differentiated from the surrounding mesoderm.

The heart first appears as an endothelial tube, the primitive endocardium, at a very early age of embryonic life. The origin of the cardiac endothelium is not definitely known. It is believed by some to be of entodermic origin, by others of mesodermic, by still others to be partly derived from each of these lavers. Around this endothelial tube, but separated from it by a space, there develops from mesoderm an entirely distinct muscular tube, the primitive myocardium. These two tubes are at first united only in places by bands of connective tissue. Later they unite so that the inner tube, the endocardium, becomes a lining for the outer tube, the myocardium. The union of the two heart tubes occurs very early. In the human embryo of 2 to 3 mm. the heart is a single, slightly coiled tube connected at its cephalic end with the ventral aorta and caudally with the omphalo-mesenteric veins. The *epicardium*, as the visceral layer of the pericardium, has a separate origin, being constricted off from that portion of the mesoderm which lines the primary body cavity.

#### THE LYMPH-VESSEL SYSTEM.

The larger lymph vessels are similar in structure to veins. Their walls are, however, thinner than those of veins of the same calibre and they contain more valves. They are capable of great distention, and when empty collapse so that their thin walls are in apposition.

The largest of the lymph vessels, the thoracic duct, has three well-defined coats: an *intima* consisting of the usual lining endothelium resting upon a subendothelial layer of delicate fibro-elastic tissue, the outermost elastic fibres having a longitudinal arrangement; a fairly thick *media* of circularly disposed smooth muscle cells; and an *adventitia* which is strengthened by bundles of longitudinal smooth muscle.

Lymph capillaries resemble blood capillaries in that their walls are composed of a single layer of endothelial cells. The cells are rather larger and more irregular than in blood capillaries, the capillaries themselves are larger, and, instead of being of uniform diameter throughout, vary greatly in calibre within short distances. In certain tissues dense networks of these lymph capillaries are found. Cleft-like lymph spaces—perivascular lymph spaces—partially surround the walls of the smaller blood-vessels.

Lymph spaces without endothelial or other apparent lining also occur. Examples of these are the *pericellular lymph spaces* found in various tissues and the *canaliculi* of the cornea and of bone (pages 74 and 93).

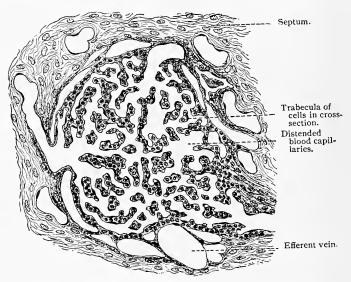


Fig. 84.—Section of human carotid gland.  $\times$  160. (Schaper.)

Similar in character to lymph spaces are the body cavities, peritoneal, pleural, and pericardial, with their linings of serous membranes. These cavities first appear in the embryo as a cleft in the mesoderm—the cælom, body cavity, or pleuroperitoneal cleft. This cleft is lined with mesothelium beneath which the stroma is formed. These membranes not only line the cavities, but are reflected over most of the viscera of the abdomen and thorax. They consist of a stroma of mixed fibrous and elastic tissue, covered on its inner side by a layer of mesothelium, the two being separated by a homogeneous basement membrane. The stroma contains numerous lymphatics. These have been described as communicating with the free surfaces by means of

openings—stomata. Recent observations, however, would seem to indicate that these stomata are artefacts.

That the lymph-vessels form a definite and closed system of channels and are not in direct communication with the lymph spaces has been clearly demonstrated.

The lymphatics apparently originate from the vascular system, starting as four buds, two from the veins of the neck, and two from veins in the inguinal region.

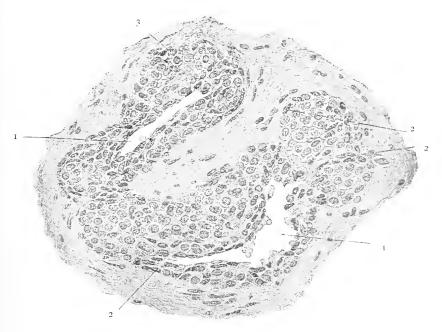


Fig. 85.—Section through coccygeal gland (Walker). 1. Blood space; 2. epithelium; 3. connective tissue.

#### TECHNIC.

- (1) Remove a portion of the central tendon of a rabbit's diaphragm. Rub the pleural surface gently with the finger or with a brush to remove the mesothelium. Rinse in distilled water and treat with silver nitrate as in technic 7, p. 72. Mount in glycerin. If the silver impregnation is successful, the networks of coarser and finer lymphatics can be seen as well as the outlines of the endothelium of their walls. If care has been taken not to touch the peritoneal surface, the peritoneal mesothelium and the stomata are frequently seen.
- (2) The Thoracic Duct.—Remove a portion of the thoracic duct, fix in formalin-Müller's fluid (technic 5, p. 7), and stain sections with hæmatoxylin-cosin (technic 1, p. 18).

#### THE CAROTID GLAND.

This is a small ductless gland, about the size of a rice grain, which lies at the bifurcation of the carotid artery. It is composed of a vascular connective tissue supporting spheroidal groups of polyhedral epithelial cells which are closely associated with tufts of capillaries. Some of the gland cells take a brownish stain with chromic acid similar to the medullary cells of the adrenal (Fig. 84).

#### THE COCCYGEAL GLAND.

This is also a ductless gland similar in structure to the preceding, but with much more irregularly arranged groups of cells. According to some observers, the cells of the coccygeal gland differ from those of the carotid in that they do not give the chromaffin reaction, the gland conforming more to the structure of lymphoid tissue (Fig. 85).

#### TECHNIC.

Technic same as for Thyreoid Gland, page 285.

## General References for Further Study of the Circulatory System.

Kölliker: Handbuch der Gewebelehre des Menschen, vol. iii.

Stöhr: Text-book of Histology.

Schäfer: Histology and Microscopic Anatomy, in Quain's Elements of Anat-

omy, tenth edition.

### CHAPTER II.

#### LYMPHATIC ORGANS.

## The Lymph Nodes.

LYMPH nodes are small bodies, usually oval or bean-shaped, which are distributed along the course of the lymph vessels. In some regions they are arranged in series forming "chains" of lymph nodes as, e.g., the axillary and inguinal.

Each lymph node is surrounded by a *capsule* of connective tissue which sends *trabeculæ* or *septa* into the organ. The capsule and septa

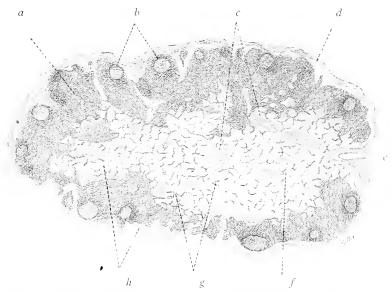


Fig. 86.—Section through Entire Human Lymph Node, including Hilum.  $\times$ 15. (Technic 1, p. 150.) Dark zone, cortex; light central area, medulla. a, Lymph nodule of cortex; b, germinal centres; c, trabecuke containing blood-vessels; d, capsule; e, hilum; f, lymph sinus of medulla; g, lymph cords of medulla; h, lymph sinuses of medulla and cortex.

constitute the *connective-tissue framework* of the node, and serve as a support for the lymphatic tissue (Fig. 86).

The *capsule* is composed of fibrous connective tissue arranged in two layers. In the outer, the fibres are loosely arranged and serve,

like the fibres of the arterial adventitia, to attach the node to the surrounding tissues. The inner layer of the capsule consists of a more dense connective tissue and contains some smooth muscle cells. At one point, known as the *hilum* (Fig. 86), there is a depression where the connective tissue of the capsule extends deep into the substance of the node. This serves as the point of entrance for the main arteries and nerves, and of exit for the veins and efferent lymph vessels.

The connective-tissue septa, which extend from the capsule into the interior of the node incompletely divide it into irregular intercommunicating compartments. In the peripheral portion of the node these compartments are somewhat spheroidal or pear-shaped. Toward the centre of the node the septa branch and anastomose freely, with the result that the compartments are here narrower, more irregular, and less well defined. This arrangement of the connective tissue allows the division of the node into two parts, an outer peripheral part or cortex and a central portion, the medulla (Fig. 86).

Within the compartments formed by the capsule and the septa is the lymphatic tissue (for structure see page 84). In the cortex where the compartments are large and spheroidal or pear-shaped, the lymphatic tissue is of the compact variety, and is arranged in masses which correspond in shape to the compartments. These are known as lymph nodules (Fig. 86). In the centre of each nodule is usually an area in which the cells are larger, are not so closely packed, and show marked mitosis. As it is here that active proliferation of lymphoid cells takes place, this area is known as the germinal centre (Figs. 86 and 87). Immediately surrounding the germinal centre is a zone in which the lymphoid cells are more closely packed than elsewhere in the nodule (Fig. 87). This is apparently due to the active production of new cells at the germinal centre and the consequent pushing outward of the surrounding cells. In stained sections the centre of the nodule is thus lightly stained, while immediately surrounding this light area is the darkest portion of the nodule (Fig. 87). From the inner sides of the nodules strands of lymphoid tissue extend into the medulla. These are known as lymph cords, and anastomose freely in the small irregular compartments of the medulla. In both cortex and medulla the lymphoid tissue is always separated from the capsule or from the septa by a distinct space—the lymph sinus which is bridged over by reticular tissue containing comparatively few lymphoid cells (Fig. 87). These sinuses form a continuous system of anastomosing channels throughout the node.

The reticular connective tissue (page 83), which forms a part of the lymphatic tissue proper, is continuous with the fibrous connective-tissue framework of the organ in such a manner that it is impossible to determine any demarcation between the two tissues. In the lymph nodules, and wherever the lymphoid cells are densely packed, the underlying reticular network is almost completely obscured. Crossing the sinuses, especially those of the medulla, and in specimens

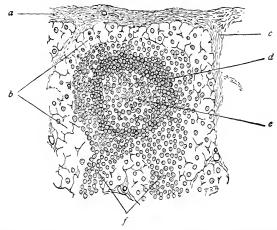


Fig. 87.—Section through Cortex and Portion of Medulla of Human Lymph Node. (Technic 2, p. 150.) a, Capsule; b, lymph sinus; c, trabecula; d, closely packed cells at outer border of lymph nodule; e, germinal centre; f, lymph cords in medulla.

in which the cells have been largely washed out or removed by maceration, the reticular structure is well shown.

The *lymphoid tissue proper*, as represented by the lymph nodules and anastomosing lymph cords, is thus, as it were, *suspended* in the meshes of a reticulum which is swung from the capsule and trabeculæ. As both nodules and cords are everywhere separated from capsule and trabeculæ by the sinuses, and as these latter serve for the passage of lymph through the node, it is seen that the lymphatic tissue of the node is broken up in such a manner as to be bathed on all sides by the circulating lymph.

In addition to the definitely formed lymph nodes and the well-defined collections of lymph nodules, such as those of the tonsil or of Peyer's patches, small nodules or groups of lymphoid cells have a wide distribution throughout the various organs. While many of these collections of lymphatic tissue are inconspicuous, still the aggregate of lymph tissue thus distributed is by no means inconsider-

able. The most important will be described in connection with the organs in which they occur.

Blood-vessels.—Those which enter the hilum carry the main blood supply to the organ. Most of the arteries pass directly into the lymphatic tissue, where they break up into dense capillary networks. Some of the arteries, instead of passing directly to the lymphatic tissue, follow the septa, supplying these and the capsule, and also sending branches to the surrounding lymphatic tissue. A few small vessels enter the capsule along the convexity of the organ and are distributed to the capsule and to the larger septa.

Lymphatics.—The afferent lymph vessels enter the node on its convex surface opposite the hilum, penetrate the capsule, and pour their lymph into the cortical sinuses. The lymph passes through the sinuses of both cortex and medulla, and is collected by the efferent lymph vessels which leave the organ at the hilum. Within the node the lymph comes in contact with the superficial cells of the nodules and of the lymph cords. These cells are constantly passing out into the lymph stream so that the lymph leaves the node much richer in cellular elements.

**Nerves** are not abundant. Both medullated and non-medullated fibres occur. Their exact modes of termination are not known.

#### TECHNIC.

- (1) Remove several lymph nodes from one of the lower animals (ox, cat, dog. rabbit), fix in formalin-Müller's fluid (technic 5, p. 7), and harden in alcohol, Cut thin sections through the hilum, stain with hæmatoxylin-eosin (technic 1, p. 18), or with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19), and mount in balsam.
- (2) Expose a chain of lymph nodules (e.g., the cervical or inguinal of a recently killed dog or cat). Insert a small cannula or needle into the uppermost node and inject formalin-Müller's fluid until the node becomes tense. By now slightly increasing the pressure the fluid may be made to pass into the second node, and so through the entire chain. The nodes are then carefully dissected out and placed for twenty-four hours in formalin-Müller's fluid, then hardened in alcohol. Sections are cut through the hilum, stained with hæmatoxylin-eosin or with hæmatoxylin-picro-acid-fuchsin and mounted in balsam. Near the centre of the chain are usually found nodes in which the lymph sinuses are properly distended. The most proximal nodes are apt to be overdistended, but for this very reason are often excellent for the study of the reticular tissue from which most of the cells have been washed out, especially in the medulla.
- (3) Human lymph nodes may be treated by either of the above methods. Owing to the coalescence of their cortical nodules their structure is not so easily demonstrated as that of the lymph nodes of lower animals.

## Hæmolymph Nodes.

These are lymphoid structures which closely resemble ordinary lymph nodes, but with the essential difference that their sinuses are blood sinuses instead of lymph sinuses.

Each node is surrounded by a *capsule* of varying thickness, composed of fibro-elastic tissue and smooth muscle cells. From the capsule *trabeculæ* of the same structure pass down into the node, forming its framework (Fig. 88). Beneath the capsule is a *blood sinus*, which may be broad or narrow, and usually completely surrounds the node. Less commonly the sinus is interrupted by lymphoid tissue extending

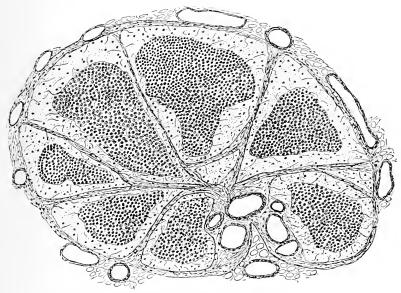


Fig. 88.—Section through Human Hæmolymph Node, including Hilum, showing capsule, trabecuke, sinuses filled with blood, and lymph nodules. (Warthin.)

out to the capsule. From the peripheral sinus branches extend into the interior of the node, separating the lymphoid tissue into *cords* or *islands*. The relative proportion of sinuses and lymphoid tissue varies greatly, some nodes being composed almost wholly of sinuses, while in others the lymphoid tissue predominates. There is usually a fairly distinct *hilum*. In many glands no differentiation into *cortex* and *medulla* can be made. Where there are a distinct medulla and cortex the peripheral lymphoid tissue is arranged in *nodules* as in the ordinary lymph node. *Reticular connective tissue* crosses the sinuses and supports the cells of the lymph nodules and cords (Fig. 89).

The cellular character of the lymphoid tissue has led to the subdivision of hæmolymph nodes into *splenolymph nodes* and *marrow-lymph nodes*. In the *splenolymph node* the lymphoid tissue resembles that of the ordinary lymph node of the spleen. In the *marrow-lymph node*, which is the much less common form, the lymphoid tissue resembles red marrow. There are no distinct nodules, and there is a quite characteristic distribution of small groups of fat cells. The most numerous cells are eosinophiles and mast cells (see page 98). Polynuclear leucocytes and large leucocytes with a single

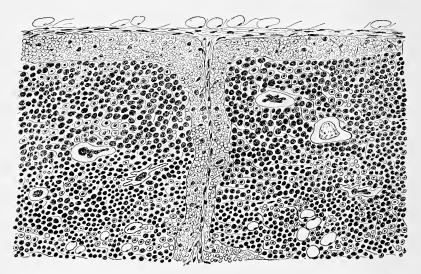


Fig. 89.—Section through Superficial Portion of Human Hæmolymph Node (Marrow-lymph Node). (Warthin.) Capsule, trabeculæ, and parts of two adjacent nodules; sinuses filled with blood; among the lymph cells are large multinuclear cells resembling those of marrow, nucleated red blood cells, etc.

lobulated nucleus are less numerous. The very large multinuclear cells of red marrow are also found, but usually in small numbers.

Large *phagocytes* containing blood pigment and disintegrating red blood cells are found in both forms of hæmolymph nodes, but are most numerous in the splenolymph type. In nodes which have a brownish color when fresh, these phagocytes frequently almost completely fill the sinuses.

Further classification of hæmolymph nodes has been attempted, but is unsatisfactory, owing to the large number of transitional forms. Thus many nodes are transitional in structure between the hæmolymph node and the ordinary lymph node, between the splenolymph

node and the marrowlymph node, and between the splenolymph node and the spleen.

Under normal conditions the hæmolymph nodes appear to be concerned mainly in the destruction of red blood cells; possibly also in the formation of leucocytes. Under certain pathological conditions they probably become centres for the formation of red blood cells.

Blood-vessels.—An artery or arteries enter the node at the hilum, and break up within the node into small branches, which communicate with the sinuses where the blood comes into intimate association with the lymphoid tissue. From the sinuses the blood passes into veins, which leave the organ either at the hilum or at some other point on the periphery. The course which the blood takes in passing through the hæmolymph node is thus apparently similar to that taken by the lymph in passing through the ordinary lymph node.

The relation of the hæmolymph node to the *lymphatic system* is not known, and like ignorance exists as to its *innervation*.

#### TECHNIC.

Same as for lymph nodes (technic 1, p. 150). The nodes are found in greatest numbers in the prevertebral tissue, and are often difficult to recognize. Fixing the tissues in 5-per-cent. formalin aids in their recognition as it darkens the nodes while bleaching the rest of the tissues.

# The Thymus.

The thymus is an organ of fœtal and early extra-uterine life; reaching in man its greatest development at the end of the second year. After this age it undergoes a slow retrograde change into fat and connective tissue, until by the twentieth year scarcely a vestige of glandular tissue remains.

The thymus originates in the entoderm and begins its feetal existence as a typical epithelial gland. Into this epithelial structure mesodermic cells grow and differentiate into *lymphatic tissue*. This almost completely replaces the epithelial tissue, only rudiments of which remain.

Morphologically the fully developed thymus consists of *lobes* and *lobules* (Fig. 90). The whole gland is surrounded by a connective-tissue *capsule*, and the lobes are separated from one another by strong extensions of capsular tissue. Smaller connective-tissue septa extend

into the lobes, subdividing them into lobules. From the perilobular connective tissue, septa extend into the lobule, incompletely separating it into a number of *chambers*. Each lobule consists of a *cortical portion* and a *medullary portion*. The cortex consists of *nodules* of compact lymphatic tissue similar to those found in the lymph node. These occupy the chambers formed by the connective-tissue septa. The medulla consists of a more diffuse lymphatic tissue with no connective-tissue septa. It is common for the medullary tissue to extend to the surface of a nodule at one or more points and to be there

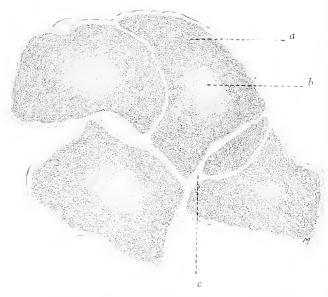


Fig. 90.—From Section of Human Thymus, showing parts of five lobules and interlobular septa. ×20. (Technic, page 155.) a, Cortex; b, medulla; c, interlobular septum.

continuous with the medullary substance of an adjacent lobule. In the medulla are found a number of spherical or oval bodies composed of concentrically arranged epithelial cells. These are known as *Hassall's corpuscles* (Fig. 91), and represent the only remains of the original glandular epithelium. They are characteristic of the thymus. The central cells of the corpuscles are usually spherical and contain nuclei, while the peripheral cells are flat and non-nucleated. As the entire corpuscle takes a bright red stain with cosin-hæmatoxylin, the corpuscles stand out sharply from the surrounding bluish lymphatic tissue. With low magnifications they are apt to be mistaken for blood-vessels.

Unlike the other lymphatic organs, the lymph nodules of the thymus contain no germinal centres. Mitosis can, however, usually be seen in the lymphoid cells. Nucleated red blood cells also occur in the thymus. The thymus must therefore be considered one of the

sources of lymphoid cells and of red blood cells.

Blood-vessels.—The larger arteries run in the connective-tissue septa. From these, smaller intralobular branches are given off, which break up into capillary networks in the cortex and medulla. The capillaries pass over into veins. These converge to form larger veins, which accompany the arteries.

Of the **lymphatics** of the thymus little is known. They



Fig. 91.—Hassall's Corpuscle and Small Portion of Surrounding Tissue. ×600. (See Technic below.)

appear to originate in indefinite sinuses within the lymphoid tissue, whence they pass to the septa where they accompany the blood-vessels.

**Nerves.**—These are distributed mainly to the walls of the blood-vessels. A few fine fibres, terminating freely in the lymphatic tissue of the cortex and of the medulla, have been described.

#### TECHNIC.

Fix the thymus of a new-born infant in formalin-Müller's fluid (technic 5, p. 7), and harden in alcohol. Stain sections with hæmatoxylin-eosin (technic 1, p. 18), or with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19), and mount in balsam.

#### The Tonsils.

The Palatine Tonsils or True Tonsils.—These are compound lymphatic organs, essentially similar in structure to the lymphatic organs already described. The usual fibrous capsule is present only over the attached surface, where it separates the tonsil from surrounding structures. From the capsule, connective-tissue trabeculæ extend into the substance of the organ and branch to form its framework. The free surface of the tonsil is covered by a reflection of the stratified squamous epithelium of the pharynx (Fig. 92). The epithelium is sepa-

rated from the underlying lymphatic tissue of the tonsil by a more or less distinct basement membrane. At several places on the surface of the tonsil deep indentations or pockets occur. These are known as the crypts of the tonsil (Fig. 92), and are lined throughout by a continuation of the surface epithelium which becomes thinner as the deeper part of the crypt is reached. Passing off from the bottoms and sides of the main or primary crypts are frequently several secondary crypts, also lined with the same type of epithelium.

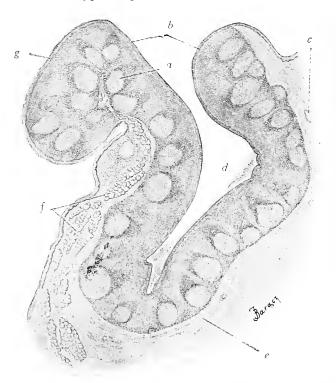


Fig. 92.—Vertical Section of Dog's Tonsil through Crypt.  $\times 15$ . (Szymonowicz.) a, Lymph nodule; b, epithelium of crypt; c, blood-vessel; d, crypt; e, connective-tissue capsule; f, mucous glands; g, epithelium of pharynx.

Beneath the basement membrane is the lymphoid tissue of the tonsil. This consists of diffuse lymphatic tissue in which are found nodules of compact lymphatic tissue similar to those in the lymph node. Each nodule has a germ centre, where active mitosis is going on, and a surrounding zone of more densely packed cells. The nodules have a fairly definite arrangement, usually forming a single layer beneath the epithelium of the crypts. At various points on the surface of the

tonsil, and especially in the crypts, occurs what is known as *lymphoid* infiltration of the epithelium (Fig. 93). This consists in an invasion of the epithelium by the underlying lymphoid cells. It varies from the presence of only a few lymphoid cells scattered among the epithelial, to an almost complete replacement of epithelial by lymphoid tissue. In this way the latter reaches the surface and lymphoid cells are discharged upon the surface of the tonsil and into the crypts. These cells probably form the bulk of the so-called *salivary corpuscles*. In the connective tissue adjacent to the tonsil are numerous mucous glands, the ducts of which empty into the tonsillar crypts.

The Lingual Tonsils—Folliculi Linguales.—These are small lymphatic organs situated on the dorsum and sides of the back part of the tongue between the circumvallate papillæ and the epiglottis.

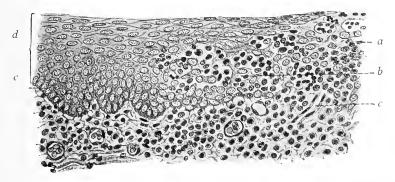


Fig. 93.—Vertical Section through Wall of Crypt in Dog's Tonsil, showing lymphoid infiltration of epithelium.  $\times 150$ . (Böhm and von Davidoff.) a, Leucocytes in epithelium; b, space in epithelium filled with leucocytes and changed epithelial cells; c, blood-vessel; d, epithelium beyond area of infiltration; e, basal layer of cells.

They are similar in structure to the true tonsils. Each lingual tonsil has usually one rather wide-mouthed deep crypt (the *foramen cæcum lingui*) which may be branched and which is lined with a continuation of the surface stratified squamous epithelium. Into these crypts frequently open the ducts of some of the mucous glands of the tongue.

The Pharyngeal Tonsils.—These are lymphatic structures which lie in the naso-pharynx. They resemble the lingual tonsils, except that they are, as a rule, not so sharply circumscribed. Hypertrophy of the pharyngeal tonsils is common especially in children, giving rise to what are known as *adenoids*.

The tonsils make their first appearance toward the end of the fourth month of intra-uterine life. The earliest of the tonsillar lymphoid cells are white blood cells which have migrated from the ves-

sels of the stroma of the mucosa and have infiltrated the surrounding connective tissue. Further development of the tonsil is by proliferation of these cells. The crypts are at first solid ingrowths of surface epithelium. These later become hollowed out.

The **blood-vessels** and **nerves** have a distribution similar to those of the lymph nodes, but enter the organ along its entire attached side and not at a definite hilum.

Of the lymphatics of the tonsil little is known.

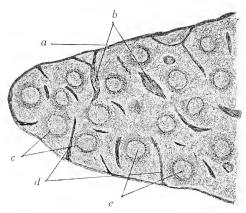
## TECHNIC.

Normal human tonsils are so rare, owing to the frequency of inflammation of the organ, that it is best to make use of tonsils from one of the lower animals (dog, cat, or rabbit). Treat as in technic 1, p. 150, care being taken that sections pass longitudinally through one of the crypts.

# The Spleen.

The spleen is a *lymphatic organ*, the peculiar structure of which appears to depend largely upon the arrangement of its blood-vessels.

The surface, except where the organ is attached, is covered by a



F16. 94.—Section through Portion of Cat's Spleen, to show general topography.  $\times$  15. (Technic 1, p. 163.) *a*, Capsule; *b*, septa containing blood-vessels; *c*, germinal centres; *d*, septa; *e*, lymph nodules.

serous membrane, the *peritoneum* (page 235). Beneath this is a *capsule* of fibrous tissue containing numerous elastic fibres and smooth muscle cells. From the capsule strong connective-tissue *septa*, similar to the capsule in structure, extend into the interior of the organ. These branch and unite with one another to form very incomplete

anastomosing chambers. The capsule and septa form, as in the lymph node, the *connective-tissue framework* of the organ (Fig. 94).

The chambers incompletely bounded by the connective-tissue septa are filled in with tissue resembling lymphatic tissue, composed of reticular connective tissue, lymphoid cells, and other varieties of cells described on p. 161. This tissue constitutes the *substantia propria* of the organ and is everywhere traversed by thin-walled vascular channels, the tissue and vascular channels together constituting the *splenic pulp* (Fig. 95). Compact lymphatic tissue occurs in the spleen as spherical, oval, or cylindrical aggregations of closely packed

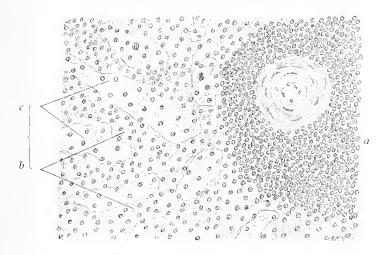


Fig. 95.—Section of Human Spleen, including portion of Malpighian body with its artery and adjacent splenic pulp.  $\times$ 300. (Technic 2, p. 163.) a, Malpighian body; b, pulp cords,  $\epsilon$ , cavernous veins; b and  $\epsilon$  together constituting the splenic pulp.

lymphoid cells. These are known as *Malpighian bodies* or *splenic corpuscles* (Figs. 94 and 95) and are distributed throughout the splenic pulp. Each splenic corpuscle contains one or more small arteries. These usually run near the periphery of the corpuscle; more rarely they lie at the centre. Except for its relation to the blood-vessels, the splenic corpuscle is quite similar in structure to a lymph nodule. It consists of lymphoid cells so closely packed as completely to obscure the underlying reticulum. In a child's spleen the centre of each corpuscle shows a distinct *germinal centre* (see page 148). In the adult human spleen germ centers are rarely seen. The blood-vessels of the spleen have a very characteristic arrangement, which must be described before considering further the minute structure of the organ.

The arteries enter the spleen at the hilum and divide, the branches following the connective-tissue septa. The arteries are at first accompanied by branches of the *splenic veins*. Soon, however, the arteries leave the veins and the septa, and pursue an entirely separate course through the splenic pulp. Here the adventitia of the smaller arteries assumes the character of reticular tissue and becomes infiltrated with lymphoid cells. In certain animals, as, *e.g.*, the guinea-

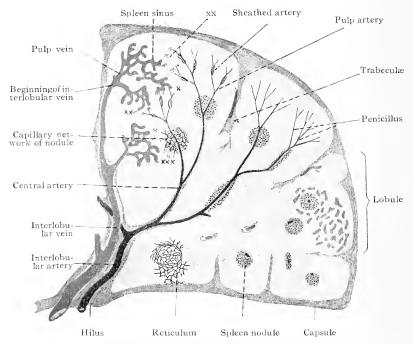


Fig. 96.—Scheme of Human Spleen. x, Opening of arterial capillaries into spleen sinus; xx,interruption of closed blood course at ends of arterial capillaries, at margin of nodule, xxx. For sake of clearness, sinus is placed too far from margin of nodule. (Stöhr).

pig, this infiltration is continuous, forming long cord-like masses of compact lymphoid tissue. In man, the adventitia is infiltrated only at points along the course of an artery. This may take the form of elongated collections of lymphoid cells—the so-called *spindles*—or of distinct lymph nodules, the already mentioned *splenic corpuscles*. Although usually eccentrically situated with reference to the nodules, these arteries are known as *central arteries*. They give rise to a few capillaries in the spindles, to a larger number in the nodules. Beyond the latter the arteries divide into thick sheathed terminal arteries—

ellipsoids—which do not anastomose, but lie close together like the bristles of a brush or penicillus. The terminal arteries break up into arterial capillaries which still retain an adventitia, and which empty into broader spaces—sinuses or ampullæ—which in turn empty into the cavernous veins of the splenic pulp (Fig. 95).

THE SPLENIC PULP.—The anastomosing cavernous veins break up the diffuse lymphatic tissue of the spleen into a series of anasto-

mosing cords similar to those found in the medulla of the lymph node. These are known as pulp cords (Fig. 95), and with the cavernous veins constitute, as already mentioned, the splenic pulp. The pulp cords consist of a delicate framework of reticular connective tissue, in the meshes of which are found, in addition to lymphoid cells, the following (Fig. 97):

- (1) Red blood cells.
- (2) Nucleated red blood cells.
- (3) White blood cells.
- (4) Mononuclear cells, the socalled spleen cells. These are

Fig. 97.—Isolated Spleen Cells. ×700. (Kölliker.) A, Cell containing red blood cells; b, blood cell; k, nucleus; B, leucocyte with polymorphous nucleus; C, "spleen" cell with pigment granules; D, lymphocyte; E, large cell with lobulated nucleus (megalocyte): F, nucleated red blood cells; G, red blood cell; H, multinuclear leucocyte: J, cell containing eosinophile granules.

rather large, granular, spherical, or irregular cells. From the fact that blood pigment and red blood cells in various stages of disintegration are found in their cytoplasm, these cells are believed to be concerned in the destruction of red blood cells.

(5) Multinuclear cells. These are most common in young animals. Each cell contains a single large lobulated nucleus, or more frequently several nuclei. These cells resemble the osteoclasts of developing bone and the multinuclear cells of bone-marrow.

In macerated splenic tissue or in smears from the spleen, there are found, in addition to the above varieties of cells, long spindle-shaped cells with bulging nuclei. These come from the walls of the cavernous veins.

Two views are held regarding the vascular channels of the splenic pulp. According to one, these channels have complete walls, the arterial capillaries passing over into venous capillaries in the usual manner; according to the other, the arterial capillaries open into spaces, the cavernous veins or spleen sinuses, which have

fenestrated walls, thus allowing the blood to come into direct contact with the surrounding tissues. From these open-walled sinuses, the veins proper take origin. These uniting form veins which enter the septa and ultimately converge to form the splenic veins which leave the organ at the hilum.

According to Mall, the spleen, like the liver, is composed of a large number of lobules, which may be considered its anatomical units (Fig. 98). Each lobule is separated from its neighbors by several (usually three) connective-tissue septa (interlobular septa). Each interlobular septum gives off about three secondary

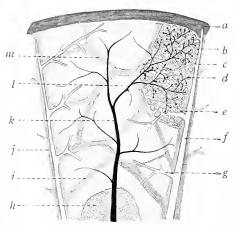


FIG. 98.—Diagram of Splenic Lobule, according to Mall. *a*, Capsule; *b*, intralobular venous spaces; *c*, intralobular vein; *d*, ampulla of Thoma; *e*, pulp cord; *f*, interlobular vein; *g*, intralobular vein; *h*, Malpighian body; *i*, intralobular trabecula; *j*, interlobular trabecula; *j*, interlobular trabecula; *k*, intralobular artery; *l*, artery to one of the ten compartments; *m*, intralobular trabecula.

septa (intralobular septa) which pass into the lobule and, anastomosing, divide it into about ten chambers, which are filled with splenic pulp. As the splenic pulp of neighboring chambers anastomoses, cord-like structures are formed which Mall designates pulp cords. It will be seen that the pulp cords of Mall are altogether different from the pulp cords previously mentioned. An artery passes through the centre of each lobule, giving off a branch to each of its chambers. branch repeatedly in the pulp cords of Mall and end in small dilatations, the ampullæ of Thoma. The ampullæ pass over into minute veins which converge and empty into the interlobular veins. Mall believes the walls of the ampullæ

and beginning venous plexuses to be very porous, "allowing fluids to pass through with great ease, and granules only with difficulty." He further states that "in life the plasma constantly flows through the intercellular spaces of the pulp cords, while the blood corpuscles keep within fixed channels."

Lymphatics are not numerous. In certain of the lower animals large lymph vessels occur in the capsule and septa. These are not well developed in man. Lymph vessels are present in the connective tissue of the hilum. They probably do not occur in the splenic pulp or in the splenic corpuscles.

Nerves.—These are mainly non-medullated, although a few medullated fibres are present. Among the latter are dendrites of sensory neurones whose cell bodies are situated in the spinal ganglia. They supply the connective tissue of the capsule, septa, and blood-vessels. The non-medullated fibres—axones of sympathetic

neurones—accompany the arteries, around which they form plexuses. From these plexuses terminals pass to the muscle cells of the arteries, to the septa, to the capsule, and possibly also to the splenic pulp. The exact manner in which both medullated and non-medullated fibres terminate is as yet undetermined.

### TECHNIC.

- (1) The spleen of a cat is more satisfactory for topography than the human spleen, as it is smaller, contains more connective tissue, and its Malpighian bodies are more evenly distributed and more circumscribed. Fix in formalin-Müller's fluid (technic 5, p. 7), and harden in alcohol. Cut sections through the entire spleen. Stain with hæmatoxylin-eosin (technic 1, p. 18), or with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19).
  - (2) Human Spleen.—Small pieces are treated as in technic (1).
- (3) Human Spleen (Congested).—Congested human spleens are usually easy to obtain from autopsies. Treat as in technic  $(\tau)$ . The cavernous veins being distended with blood, the relations of the veins to the pulp cords are more easily seen than in the uncongested spleen. The contrasts are especially sharp in sections stained with hæmatoxylin-picro-acid-fuchsin.
- (4) The cells of the spleen may be studied along the torn edges or in the thinner parts of any of the spleen sections. Or a smear may be made in a manner similar to that described in technic (page 100), by drawing the end of a slide across a freshly cut spleen surface and then smearing the tissue thus obtained across the surface of a second slide. Dry, fix in equal parts alcohol and ether (one-half hour), stain with hæmatoxylin-eosin and mount in balsam. Or the cut surface of the spleen may be scraped with a knife, the scrapings transferred to Zenker's fluid, hardened in alcohol, stained with alum-carmine (pages 17 and 57) and mounted in eosin-glycerin.

# General References for Further Study.

Kölliker: Handbuch der Gewebelehre des Menschen, vol. iii.

Szymonowicz and MacCallum: Histology and Microscopic Anatomy.

Warthin: Hæmolymph Glands (with bibliography). Reference Handbook of the Medical Sciences, vol. iv.

Mall: Lobule of the Spleen. Bul. Johns Hopkins Hospital, vol. ix.—Architecture and Blood-vessels of the Dog's Spleen. Zeit. f. Morph. u. Anth., Bd. ii.

Oppel: Ueber Gitterfasern der menschlichen Leber und Milz. Anat. Anz., 6 Jahrg., S. 165.

# CHAPTER III.

# THE SKELETAL SYSTEM.

THE skeletal system consists of a series of bones and cartilages which are united by special structures to form the supporting framework of the body. Under this head are considered: (1) bones, (2) marrow, (3) cartilages, (4) articulations.

# The Bones.

A bone considered as an organ consists of bone tissue laid down in a definite and regular manner. If a longitudinal section be made through the head and shaft of a long bone, the head of the bone and also part of the shaft are seen to be composed of anastomosing bony trabeculæ enclosing cavities. This is known as *cancellous* or *spongy* 

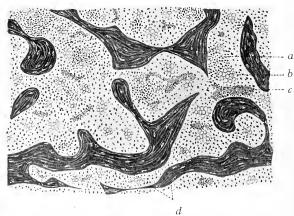


Fig. 99.—Section of Spongy Bone.  $\times$  75. (Technic 3, p. 172.) a, Marrow space; b, group of fat cells; c, blood-vessel; d, trabecuke of bone.

bone. The shaft of the bone consists of a large central cavity surrounded by spongy bone, which, however, passes over on its outer side into a layer of bone of great density and known as hard or compact bone. Spongy bone forms the ends and lines the marrow cavities of the long bones, and occurs also in the interior of short bones and flat

bones. Compact bone forms the bulk of the shafts of the long bones and the outer layers of the flat and short bones.

In *compact bone* the layers or lamellæ of bone tissue have a definite arrangement into systems, the disposition of which is largely dependent upon the shape of the bone and upon the distribution of its blood-vessels.

In *spongy bone* (Fig. 99) there is no arrangement of the bone tissue into systems. The trabeculæ consist wholly of bony tissue laid down

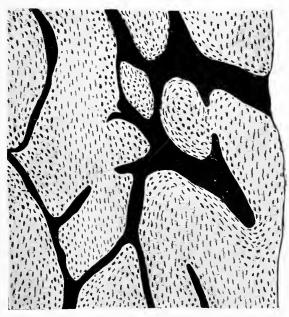


FIG. 100.—Longitudinal Section of Hard (Undecalcified) Bone: Shaft of Human Ulna. × 00. (Szymonowicz.) Haversian canals, lacunæ, and canaliculi in black.

in lamellæ. These trabeculæ anastomose and enclose spaces which contain marrow and which serve for the passage of blood-vessels, lymphatics, and nerves.

On examining a longitudinal section of compact bone (Fig. 100) there are seen running through it irregular channels, the general direction of which is parallel to the long axis of the bone. These channels anastomose by means of lateral branches, and form a complete system of intercommunicating tubes. They are known as *Haversian canals*, contain marrow elements, and serve for the transmission of blood-vessels, lymphatics, and nerves. They anastomose not only with one another, but are in communication with the surface of the

bone and with the central marrow cavity. Between the Haversian canals most of the lamellæ run parallel to the canals.

In a cross section through the shaft of a long bone (Fig. 101), three distinct systems of lamellæ are seen. These are known as *Haversian lamellæ*, interstitial lamellæ, and circumferential lamellæ.

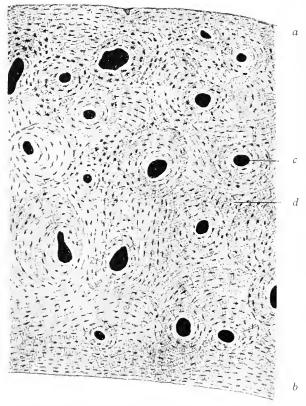


Fig. 101.—Cross-section of Hard (Undecalcified) Bone from Human Metatarsus.  $\times$  90. (Szymonowicz.) Haversian canals, lacunæ, and canaliculi in black. a, Outer circumferential lamelæ; b, inner circumferential lamelæ; c, Haversian lamelæ; d, interstitial lamelæ.

(1) Haversian Lamellæ (Fig. 102).—These are arranged in a concentric manner around the Haversian canals. Between the lamellæ, their long axes corresponding to the long axes of the Haversian canals, are the *lacunæ* with their inclosed *bone cells* (page 93). The lacunæ of adjacent lamellæ are usually arranged alternately. In a section of ordinary thickness the lacunæ are not nearly so numerous as the lamellæ, and are seen only between some of the lamellæ. The lacunæ of a

Haversian system communicate with one another and with their Haversian canal by means of the *canaliculi*. In Haversian systems the fibres of the matrix (see page 93) run in some lamellæ parallel to the canal, in others concentrically. Adjacent fibres thus frequently cross at right angles.

(2) Interstitial (Intermediate or Ground) Lamellæ (Figs. 101 and 102).—These are irregular short lamellæ, which occupy the

spaces left between adjacent Haversian systems.

(3) CIRCUMFERENTIAL LAMELLÆ (Fig. 101).—These are parallel lamelæ which run in the long axis of the bone, just beneath the periosteum

just beneath the periosteum and at the outer edge of the central marrow cavity. Occasionally circumferential lamellæ are absent, the Haversian systems abutting directly upon periosteum.

Channels for the passage of blood-vessels from the periosteum to the Haversian canals pierce the circumferential lamellæ. They are known as *Volkmann's canals*, and are not surrounded by concentric lamellæ as are the Haversian lamelæ, but are mere channels through the bone. Similar

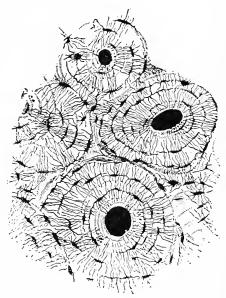


FIG. 102.—Transverse Section of Compact Bone from Shaft of Humerus. × 150 and slightly reduced. (Sharpey.) (Technic 1, p. 171.) Three Haversian canals with their concentric lamelle and lacunæ; canaliculi connecting lacunæ with each other and with Haversian canal. Between the Haversian systems of lamellæ are seen the interstitial lamellæ.

canals pass from the inner Haversian canals into the marrow cavity.

The Periosteum.—This is a fibrous connective-tissue membrane which covers the surfaces of bones except where they articulate. It is firmly adherent to the superficial layers of the bone and consists of two layers. The outer layer is composed of coarse fibrillated fibres and contains the larger blood-vessels. The inner layer consists of fine white fibres and delicate elastic fibres which support the smaller blood-vessels.

From the periostcum distinct bundles of white fibres, with often some elastic fibres, pierce the outer layers of the bone. These are

known as the *perforating fibres of Sharpey*. When tendons and ligaments are attached to bone, their fibres are prolonged through the periosteum into the bone as *perforating fibres*.

# Bone Marrow.

Bone marrow is a soft tissue which occupies the medullary and Haversian canals of the long bones and fills the space between the trabeculæ of spongy bone. Marrow occurs in two forms—red marrow and yellow marrow.

Red marrow is found in all bones of embryos and of young animals, also in the vertebræ, sternum, ribs, cranial bones, and epiphyses of long bones in the adult. In the diaphyses of adult long bones the marrow is of the yellow variety. The difference in color between red marrow and yellow marrow is due to the much greater proportion of fat in the latter, yellow marrow being developed from the red by an almost complete replacement of its other elements by fat cells.

Red marrow is of especial interest as a blood-forming tissue, being in the healthy adult the main if not the sole source of red blood cells, and one of the sources from which the leucocytes are derived. The blood-forming function of marrow must be borne in mind in studying the various forms of marrow cells.

Red marrow (Fig. 103) consists of a delicate reticular connective tissue which supports the following varieties of cells:

- (1) Marrow Cells—Myelocytes.—These resemble the mononuclear and some of the transitional forms of leucocytes. The nucleus is large and may be lobulated. It contains a comparatively small amount of chromatin and therefore stains faintly. The cytoplasm is finely granular and stains with neutrophile dyes. Myelocytes are not present in normal blood, but occur in large numbers in leukæmia. It is from the myelocytes that those leucocytes, which are of bonemarrow origin, are derived.
- (2) Nucleated Red Blood Cells.—These are divisible into erythroblasts and normoblasts. The former represents an earlier, the latter a later stage in the evolution of the non-nucleated adult red blood cell.

The *erythroblast*, the younger of the two, has a well-formed nucleus with a distinct intranuclear network. The protoplasm contains but little hæmoglobin. In the *normoblast* the intranuclear network has disappeared and the protoplasm has become much richer in

hæmoglobin. The normoblast is converted into the adult red blood cell either by extrusion of its nucleus or by the disintegration of the nucleus within the cell body.

- (3) Non-nucleated Red Blood Cells.—These are the same as are found in the blood (page 95).
- (4) Multinuclear Cells—Myeloplaxes.—These are large cells with abundant protoplasm. Each cell may contain a single large spheri-

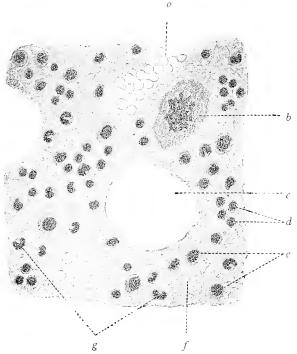


Fig. 103.—Section of Red Bone-marrow from Rabbit's Femur.  $\times$  700. (Technic 49 p. 172.) a, Red blood cells; b, myeloplax; c, fat space; d, nucleated red blood cells; e, myelocytes; f, reticular connective tissue; g, leucocytes.

cal nucleus or a much lobulated nucleus or several nuclei. Myeloplaxes are probably derived from leucocytes, and are closely related to, if not identical with, the osteoclasts of developing bone.

- (5) Leucocytes of all kinds are found in marrow. They have the same structure as in blood (page 96).
- (6) Mast cells may be present. They are usually not numerous. (For description see page 98.)
- (7) Fat Cells.—These are usually round and rather evenly distributed throughout the marrow.

Yellow marrow (Fig. 104) consists almost wholly of fat cells, which have gradually replaced the other marrow elements. Under certain conditions the yellow marrow of the bones of the old or greatly emaciated undergoes changes due for the most part to the absorption of its fat. Such marrow becomes reddish and assumes a somewhat gelatinous appearance. It is known as "gelatinous marrow."

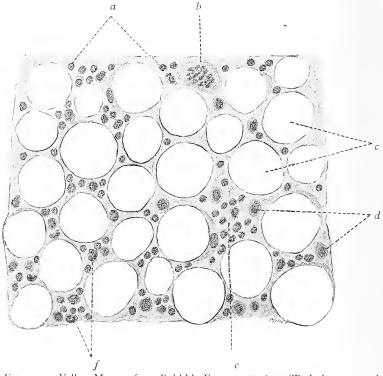


Fig. 104.—Yellow Marrow from Rabbit's Femur.  $\times$ 560. (Technic 4, p. 172.) a, nucleated red blood cells; b, myeloplax, c, fat cells; d myelocytes; e, reticular connective tissue; f, leucocytes.

The large marrow cavities, such as those of the shafts of the long bones, are lined by a layer of fibrous connective tissue, the *endosteum*.

Blood-vessels.—The blood-vessels of bone pass into it from the periosteum. Near the centre of the shaft of a long bone a canal passes obliquely through the compact bone. This is known as the *nutrient canal* and its external opening as the *nutrient foramen*. This canal serves for the passage of the nutrient vessels—usually one artery and two veins—to and from the medullary cavity. In its passage through the compact bone the nutrient artery gives off branches to,

and the veins receive branches from, the vessels of the Haversian canals.

Each of the flat and of the short bones has one or more nutrient canals for the transmission of the nutrient vessels.

In addition to the nutrient canals the surface of the bone is everywhere pierced by the already mentioned (page 167) Volkmann's canals, which serve for the transmission of the smaller vessels. In compact bone these vessels give rise to a network of branches which run in the Haversian canals. In spongy bone the network lies in the marrow spaces. Branches from these vessels pass to the marrow cavity, and there break up into a capillary network, which anastomoses freely with the capillaries of the branches of the nutrient artery.

The *capillaries* of marrow empty into wide veins without valves, the walls of which consist of a single layer of endothelium. So thin are these walls that the veins of marrow were long described as passing over into open or incompletely walled spaces in which the blood came into direct contact with the marrow elements. These veins empty into larger veins, which are also valveless. Some of these converge to form the vein or veins which accompany the nutrient artery; others communicate with the veins of the Haversian canals.

**Lymphatics** with distinct walls are present in the outer layer of the periosteum. Cleft-like lymph capillaries lined with endothelium accompany the blood-vessels in Volkmann's and in the Haversian canals. The *lacunæ* and *canaliculi* constitute a complete system of lymph channels which communicate with the lymphatics of the periosteum, of Volkmann's and the Haversian canals, and of the bonemarrow.

**Nerves.**—Both medullated and non-medullated nerves accompany the vessels from the periosteum through Volkmann's canals, into the Haversian canals and marrow cavities. Pacinian bodies (page 388) occur in the periosteum. Of nerve endings in osseous tissue and in marrow little definite is known.

#### TECHNIC.

(1) Decalcified Bone.—Fix a small piece of the shaft of one of the long bones—human or animal—in formalin-Müller's fluid (technic 5, p. 7), and decalcify in hydrochloric or nitric acid solution (page 10). After decalcifying, wash until all traces of acid are removed, in normal saline solution to which a little ammonia has been added. Dehydrate, and embed in celloidin. Transverse and longitudinal sections are made through the shaft, including periosteum and edge of marrow

cavity. Stain with hæmatoxylin-eosin (technic 1, p. 18) and mount in eosin-glycerin.

- (2) Hard Bone.—Transverse and longitudinal sections of undecalcified bone may be prepared as in technic 1, p. 94.
- (3) Spongy Bone.—This may be studied in the sections of decalcified bone, technic (1), where it is found near the marrow cavity. Or spongy bone from the head of one of the long bones or from the centre of a short bone may be prepared as in technic (2).
- (4) Red Marrow.—Split longitudinally the femur of a child or young animal, and carefully remove the cylinder of marrow. Fix in formalin-Müller's fluid and harden in graded alcohols. Cut sections as thin as possible, stain with hæmatoxylin-eosin, and mount in balsam.
- (5) Marrow: fresh specimen.—By means of forceps or a vice, squeeze out a drop of marrow from a young bone, place on the centre of a mounting slide, cover and examine it immediately.
- (6) Place a similar drop of marrow on a cover-glass and cover with a second cover-glass. Press the covers gently together, slide apart and fix the specimen by immersion for five minutes in saturated aqueous solution of mercuric chlorid. Wash thoroughly, stain with hæmatoxylin-eosin, and mount in balsam.

## DEVELOPMENT OF BONE.

The forms of bones are first laid down either in cartilage or in embryonic connective tissue. The bones of the trunk, extremities, and parts of the bones of the base of the skull develop in a matrix of cartilage. This is known as intracartilaginous or endochondral ossification. The flat bones, those of the vault of the cranium and most of the bones of the face, are developed in a matrix of fibrillar connective tissue—intramembranous ossification. A form of bone development, similar in character to intramembranous, occurs in connection with both intramembranous ossification and intracartilaginous ossification. This consists in the formation of bone just beneath the perichondrium—subperichondrial ossification—or, as with the development of bone perichondrium becomes periosteum—subperiosteal ossification.

There are thus three forms of bone development to be considered: (1) Intramembranous, (2) intracartilaginous, and (3) subperiosteal.

1. Intramembranous Development (Fig. 105).—In intramembranous ossification the matrix in which the bone is developed is connective tissue. The process of bone formation begins at one or more points in this matrix. These are known as ossification centres. Here some of the bundles of white fibres become calcified, i.e., become impregnated with lime salts. There is thus first established a centre

or centres of calcification. Between the bundles of calcified fibres the connective tissue is rich in cells and vascular, and from its future rôle in bone formation is known as osteogenetic tissue (Fig. 105). Along the surfaces of the calcified fibres certain of the osteogenetic cells arrange themselves in a single layer (Figs. 105 and 106). These are now known as osteoblasts or "bone formers." Under the influence of these osteoblasts a thin plate of bone is formed between them-

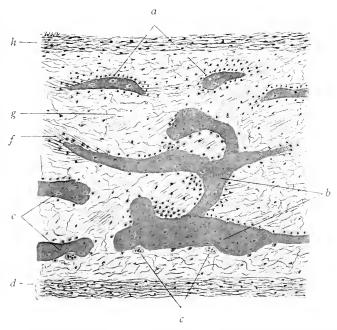


Fig. 105.—Intramembranous Bone Development. Vertical section through parietal bone of human fœtus.  $\times$ 160. (Technic 1, p. 179.) a, Osteoblasts; b, bone trabeculæ; c, osteoclasts lying in Howship's lacunæ; d, internal periosteum; c, bone cells; f, calcified fibres; g, osteogenetic tissue; h, external periosteum (pericranium).

selves and the calcified fibres. This plate of bone at first contains no cells, but as the lamella of bone grows in thickness, the layer of osteo-blasts becomes completely enclosed by bone. The osteoblasts are thus transformed into bone cells (Fig. 106), the spaces in which they lie becoming bone lacunæ. The bone cell is thus seen to be derived from the embryonic connective-tissue cell, the osteoblast being an intermediate stage in its development. In this way irregular anastomosing trabeculæ of bone are formed enclosing spaces (Fig. 105). The bony trabeculæ at first contain remains of calcified connective-tissue fibres, while the spaces, which are known as primary marrow

spaces, contain blood-vessels, osteogenetic tissue, and developing marrow. The osteoblasts ultimately disappear and the spaces are then occupied by blood-vessels and marrow. The connective-tissue membrane has now been transformed into cancellous or spongy bone (Fig. 99).

The bone thus formed is covered on its outer surface by a layer of connective tissue, a part of the membrane in which the bone was formed, but which from its position is now known as the *periosteum*, or, in the case of the cranial bones, as the *peri-* or *epicranium* (Fig. 105).

In this form of bone development, occurring as it does in the bones of the skull, provision must be made for increase in the size of the

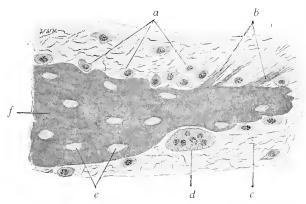


Fig. 106.—Intramembranous Bone Development. Vertical section through parietal bone of human fœtus.  $\times$  350. (Technic 1, p. 179.) a, Osteoblasts; b, calcified fibres; c, osteogenetic tissue; d, osteoclast lying in Howship's lacuna; e, bone lacunæ; f, bone.

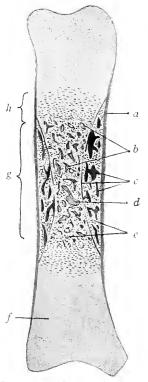
cranial cavity to accomodate the growing brain. This is accomplished in the following manner: Along the surface of the bone, directed toward the brain, large multinuclear cells—osteoclasts or "bone breakers"—make their appearance (Fig. 106). The origin of these cells is not clear. Similar cells are conspicuous elements of adult marrow. They have been variously described as derived from leucocytes, from osteoblasts, or directly from the connective-tissue cells. A recent theory holds that they are derived by a process of budding from the endothelial cells, which form the walls of the capillaries. These osteoclasts apparently possess the power of breaking down bone. They are found mainly along its inner surface, and can be seen lying in little depressions—Howship's lacunæ (Fig. 106)—which they have hollowed out in the bone. Between the outer surface of the bone and the pericranium is a layer of osteogenetic tissue, the innermost cells of which are

arranged as osteoblasts along the outermost osseous lamellæ. Here they are constantly adding new bone beneath the pericranium. new bone is laid down, not in flat, evenly disposed layers, but in the form of anastomosing trabeculæ enclosing marrow spaces.

It is thus seen that subperiosteal bone, like intramembranous, is at first of the spongy variety, and that with the development of the cranium the original intramembranous bone is entirely absorbed, together with much of the subperiosteal.

2. Intracartilaginous Development.— In this form of ossification an embryonal type of hvaline cartilage precedes the formation of bone, the cartilage corresponding more or less closely in shape to the future bone (Fig. 107). Covering the surface of the cartilage is a membrane of fibrillar connective tissue, the perichondrium or primary periosteum.

In most of the long bones the earliest changes take place within the cartilage at about the centre of the shaft (Fig. 107). Here the cartilage cells increase in size and in number in such a way that several enlarged cartilage cells come to lie in a single enlarged cell space, and the cartilage assumes the character of hyaline cartilage. The cell Fig. 107.—Intracartilaginous groups next arrange themselves in rows or columns, which at first extend outward in a radial manner from a common centre, but later lie in the long axis of the bone. During these changes in the cells there is an increase in the intercellular matrix and a deposit there of calcium salts. In this way the cartilage becomes calcified, the area involved being



Bone Development. Longitudinal section of one of the bones of embryo sheep's foot, showing ossification centre. ×20. (Technic 2, p. 179.) a, Periosteum; b, blood-vessels; c, subperiosteal bone; d, intracartilaginous bone; e. osteogenetic tissue: f, cartilage; g, ossification centre; h, calcification zone.

known as the calcification centre. Further growth of cartilage at the calcification centre now ceases and, as growth of cartilage at the ends of the bone continues, the central portion of the shaft appears constricted. The changes up to this point seem to be preparatory to actual bone formation.

Ossification proper begins by blood-vessels from the periosteum<sup>1</sup> pushing their way into the calcified cartilage at the calcification centre, carrying with them some of the osteogenetic tissue from beneath the periosteum. These blood-vessels with their accompanying osteogenetic tissue are known as *periosteal buds* (Fig. 108). Osteoblasts now develop from the osteogenetic tissue and appear to dissolve the

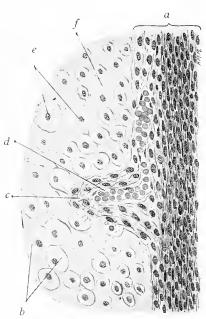


FIG. 108.—Intracartilaginous Bone Development. ×350. Showing osteogenetic tissue pushing its way into the cartilage (periosteal bud) at the ossification centre. *a*, Periosteum; *b*, cartilage cell spaces; *c*, periosteal bud; *d*, blood-vessel; *e*, cartilage cells: *f*, cartilage matrix.

calcified cartilage from in front of the advancing vessels. In this way the septa between the cartilage cell spaces are broken down, the cartilage cells disappear, and a central cavity is formed—the *primary marrow* cavity. From the region of the primary marrow cavity bloodvessels and osteogenetic tissue push in both directions toward the ends of the cartilage which is to be replaced by bone. These break down the transverse septa between the cell spaces, while many of the longitudinal septa at first remain to form the walls of long anastomosing channels, the primary marrow spaces (Fig. 100). As in intramembranous bone, these contain blood-vessels, embryonal marrow, and osteoblasts, all of which are derived from the osteogenetic tissue

brought in from the periosteum by the periosteal buds. The osteoblasts next arrange themselves in a single layer along the remains of the calcified cartilage, where they proceed to deposit a thin layer of bone between themselves and the cartilage (Fig. 110). As this increases in thickness some of the osteoblasts are enclosed within the newly formed bone to become *bone cells*, while the remains of the cartilage dimishes in amount and finally disappears. The *calcification centre* has now become the *ossification centre*, and its anastomosing

<sup>&</sup>lt;sup>1</sup>The term "periosteum" is admissible from the fact that the first bone actually formed is beneath the perichondrium, which thus becomes converted into periosteum.

osseous trabeculæ, with their enclosed spaces containing osteogenetic tissue and marrow, constitute primary spongy bone.

At either end of the ossification centre the cartilage presents a special structure. Nearest the centre the cell spaces are enlarged, flattened, arranged in rows and contain shrunken cells. Some of the walls break down and irregular spaces are formed. The ground

substance is calcified. Passing away from the ossification centre. the cell spaces become less flattened, still arranged in rows, the contained cells larger, and there is a lesser degree of calcification. This area passes over into an area of hvaline cartilage which blends without distinct demarcation with the ordinary embryonal cartilage of the rest of the shaft. The area of calcified cartilage at either end of the ossification centre is known as the calcification zone and everytrue bone (Fig. 107).

3. Subperiosteal or subperichondrial development (Fig. 107) has already been largely described in connection with intramembranous ossification. and

where precedes the formation of Fig. 100.—Intracartilaginous Bone Development. Same specimen as Fig. 107 ( $\times 350$ ), showing osteogenetic tissue pushing its way into the cartilage and breaking it up into trabeculæ; also formation of primary marrow spaces and disintegration of cartilage cells. a, Disintegrating cartilage cells; b, cartilage trabecula; c, osteogenetic tissue in primary marrow space; d, blood-vessels; e, cell spaces; f, cartilage cells.

differs in no important respect from the latter. It always accompanies one of the other forms of ossification. Bone appears beneath the perichondrium somewhat earlier than within the underlying cartilage. Beneath the perichondrium is a layer of richly cellular osteogenetic tissue. The cells of this tissue nearest the cartilage become osteoblasts and arrange themselves in a single layer along its surface. Under their influence bone is laid down on the surface of the cartilage in the same manner as in intramembranous ossification.

Intracartilaginous and subperiosteal bone can be easily differentiated by the presence of cartilaginous remains in the former and their absence in the latter.

All bone is at first of the spongy variety. When this is to be converted into compact bone, there is first absorption of bone by osteoclasts,

with increase in size of the marrow spaces and reduction of their walls to thin plates. These spaces are now known as *Haversian spaces*.

Within these new bone is deposited. This is done by osteoblasts which lay down layer within layer of bone until the Haversian space is reduced to a mere channel, the Haversian canal. In this way are formed the Haversian canals and the Haversian systems of lamellæ. Some of the interstitial lamellæ are the remains of the spongy bone which was not quite removed in the enlargement of the primary marrow spaces to form the Haversian spaces; other interstitial lamellæ appear to be early formed Haversian lamellæ which have been more or less replaced by Haversian lamellæ formed later.

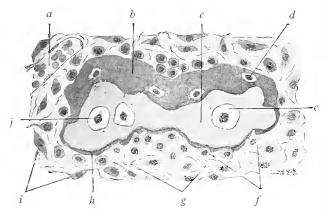


Fig. 110.—Intracartilaginous Bone Development. Same specimen as Fig. 107 ( $\times$ 350), showing bone being deposited around one of the trabeculæ of cartilage. a, Blood-vessel; b, bone; c, cartilage remains; d, bone cell; e, cartilage cell space; f, osteoblasts; g, osteogenetic tissue; h, lamella of bone; i, connective-tissue cells; f, cartilage cell.

While these varieties of ossification have been described, we would emphasize the *essential unity* of the process. The likeness between intramembranous and subperiosteal ossification has been already noted. The differences observed in intracartilaginous ossification are more apparent than real. In intracartilaginous ossification the bone is developed *in* cartilage but not *from* cartilage. As in intramembranous and in subperiosteal ossification, intracartilaginous bone is developed *from osteogenetic tissue*. This osteogenetic tissue is a differentiation of embryonal connective tissue, in this case *carried into* the cartilage from the periosteum in the *periosteal buds*. In intramembranous ossification the bone is developed *within* and *directly* 

from the embryonal connective tissue of which the membrane is composed. In intracartilaginous ossification there is the same embryonal connective-tissue membrane, but within this membrane the form of the bone is first laid down in embryonal cartilage. Surrounding the cartilage there remains the embryonal connective tissue of the membrane, now perichondrium. It is from tissue which grows into the cartilage from this membrane—embryonal connective tissue—that the bone, although developed in cartilage, is formed.

# GROWTH OF BONE.

The growth of intramembranous bone by the formation of successive layers beneath the periosteum has been already described (page 174).

Intracartilaginous bones grow both in diameter and in length.

Growth in diameter is accomplished by the constant deposition of new layers of bone beneath the periosteum. During this process, absorption of bone from within by means of osteoclasts leads to the formation of the marrow cavity. The hard bone of the shaft of a long bone is entirely of subperiosteal origin, the intracartilaginous bone being completely absorbed.

Growth in length takes place in the following manner: Some time after the beginning of ossification in the shaft or diaphysis, independent ossification centres appear in the ends of the bone (epiphyses). So long as bone is growing, the epiphyses and diaphysis remain distinct. Between them lies a zone of growing cartilage, the epiphyseal or intermediate cartilage. Increase in length of the bone takes place by a constant extension of ossification into this cartilage from the ossification centers of the epiphyses and diaphysis. After the bone ceases to grow in length, the epiphyses and diaphysis become firmly united.

## TECHNIC.

- (1) Developing Bone—Intramembranous.—Small pieces are removed from near the edge of the parietal bone of a new-born child or animal. These pieces should include the entire thickness of bone with the attached scalp and dura mater. Treat as in technic 1, p. 171, except that the sections which are cut perpendicular to the surface of the bone should be stained with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) and mounted in balsam.
- (2) Developing Bone—Intracartilaginous and Subperiosteal.—Remove the forearms and legs of a human or animal embryo by cutting through the elbow, and

knee-joints. (Fœtal pigs from five to six inches long are very satisfactory.) Treat as in technic (1). Block so that the two long bones will lie in such a plane that both will be cut at the same time. Cut thin longitudinal sections through the ossification centres, stain with hæmatoxylin-picro-acid-fuchsin, and mount in balsam. Cut away the ends of one or two of the embedded bones, leaving only the ossification centres. Block so as to cut transverse sections through the ossification centre. Stain and mount as the preceding.

In the picro-acid-fuchsin stained sections of developing bone the cartilage is stained blue; cells, including red blood cells, yellow; connective tissue from pale pink to red, according to density; bone a deep red.

# The Cartilages.

The costal cartilages are hyaline. They are covered by a closely adherent connective-tissue membrane, the perichondrium. Where cartilage joins bone there is a firm union between the two tissues and the perichondrium becomes continuous with the periosteum.

The articular cartilages are described below under articulations.

The other skeletal cartilages, such as those of the larynx, trachea, bronchi, and of the organs of special sense, are more conveniently considered with the organs in which they occur.

# Articulations.

Joints are immovable (synarthrosis) or movable (diarthrosis). In synarthrosis union may be cartilaginous (synchondrosis), or by means of fibrous connective tissue (syndesmosis).

SYNCHONDROSIS.—The cartilage is usually of the fibrous form except near the edge of the bone, where it is hyaline. The intervertebral discs consist of a ring of fibro-cartilage surrounding a central gelatinous substance, the nucleus pulposus, the latter representing the remains of the notochord.

Syndesmosis.—Union is by means of ligaments. These may consist wholly of fibrous tissue, the fibres and cells being arranged much as in tendon, or mainly of course elastic fibres separated by loose fibrous tissue. In such syndesmoses as the sutures of the cranial bones, the union is by means of short fibrous ligaments between the adjacent serrated edges.

DIARTHROSIS.—In diarthrosis must be considered (a) the articular cartilages, (b) the glenoid ligaments and interarticular cartilages, (c) the joint capsule.

(a) Articular cartilages cover the ends of the bones. They are

of the hyaline variety, being the remains of the original cartilaginous matrix in which the bones are formed. Next to the bone is a narrow strip of cartilage in which the matrix is calcified. This is separated from the remaining uncalcified portion of the cartilage by a narrow so-called "striated" zone. The most superficial of the cartilage cells are arranged in rows parallel to the surface; in the mid-region the grouping of cells is largely in twos and fours as in ordinary hyaline cartilage (page 90); while in the deepest zone of the uncalcified cartilage the cells are arranged in rows perpendicular to the surface.

- (b) The *glenoid ligaments* and interarticular cartilages conform more to the structure of dense fibrous tissue than to that of cartilage.
- (c) The joint capsule consists of two layers, an outer layer of dense fibrous tissue intimately blended with the ligamentous structures of the joint and known as the stratum fibrosum, and an inner layer, the stratum synoviale or synovial membrane, which forms the lining of the joint cavity. The outer part of the stratum synoviale consists of areolar tissue with its loosely arranged white and elastic fibres interlacing in all directions and scattered connective-tissue cells and fat cells. Nearer the free surface of the membrane the fibres run parallel to the surface and the cellular elements are more abundant. The cells are scattered among the fibres and are stellate branching cells like those usually found in fibrous connective tissue. On the free surface, however, the cells are closely packed and although in places often several layers deep, are probably of the nature of endothelium.

From the free surfaces of synovial membranes, processes (synovial villi—Haversian fringes) project into the joint cavity. Some of these are non-vascular and consist mainly of stellate cells similar to those of the synovial membrane. Others have a distinct core of fibrous tissue containing blood-vessels and covered with stellate connective-tissue cells. From the primary villi small secondary non-vascular villi are frequently given off.

#### TECHNIC.

(1) Joint Capsule and Articular Cartilage.—Remove one of the small joints—human or animal—cutting the bones through about one-half inch back from the joint. Treat as in technic 1, p. 171, making longitudinal sections through the entire joint.

<sup>&</sup>lt;sup>1</sup>In the acromio-clavicular, sterno-clavicular, costo-vertebral, and maxillary articulations the cartilage is of the fibrous form. The same is true of the cartilage covering the head of the ulna, while the surface of the radius, which enters into the wrist-joint, is covered not by cartilage, but by dense fibrous tissue.

(2) Synovial Villi.—Remove a piece of the capsular ligament from near the border of the patella and cut out a bit of the velvety tissue which lines its inner surface. Examine fresh in a drop of normal salt solution. Fix a second piece of the ligament in formalin-Müller's fluid (technic 5, p. 7), make sections perpendicular to the surface, stain with hæmatoxylin-eosin (technic 1, p. 18), and mount in balsam.

# General References for Further Study.

Kölliker: Handbuch der Gewebelehre, vol. i.

Stöhr: Text-book of Histology.

Schäfer: Histology and Microscopical Anatomy, in Quain's Elements of

Anatomy.

# CHAPTER IV

# THE MUSCULAR SYSTEM.1

The voluntary muscular system consists of a number of organs the muscles—and of certain accessory structures—the tendons, tendon sheaths, and bursæ.

A VOLUNTARY MUSCLE consists of striated muscle fibres arranged in bundles or fascicles and supported by connective tissue.

The entire muscle is enclosed by a rather firm connective-tissue sheath or capsule—the epimysium (Fig. 111). This sends trabeculæ

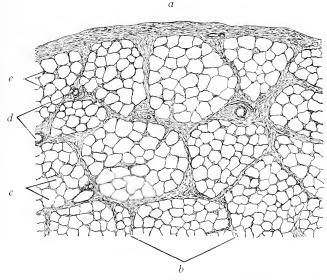


Fig. 111.—From a Transverse Section of a Small Human Muscle, showing relations of muscle fibres to connective tissue. a, Epimysium; b, perimysium; c, muscle fibres; d, arteries; e, endomysium.

of more loosely arranged connective tissue into the substance of the muscle. These divide the muscle fibres into bundles or *fascicles*. Around each fascicle the connective tissue forms a more or less definite

<sup>&</sup>lt;sup>1</sup> Definite arrangements of smooth muscle, such as are found in the stomach and intestines, also the muscle of the heart, are properly a part of the muscular system. They are, however, best considered under tissues and in connection with the organs in which they occur.

envelope, the perifascicular sheath or perimysium. From the latter delicate strands of connective tissue pass into the fascicles between the individual muscle fibres. This constitutes the intrafascicular connective tissue or endomysium, which everywhere completely separates the fibres from one another so that the sarcolemma of one fibre never comes in contact with the sarcolemma of any other fibre. It should

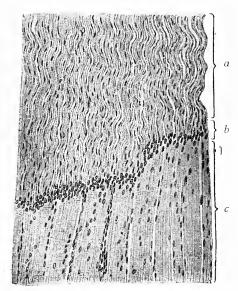


Fig. 112.—From a longitudinal Section through muscle fibres or parenchyma. Junction of Muscle and Tendon, X 150. (Böhm and Davidoff.) a, Tendon; b, line of union showing increase in number of muscle nuclei; c, muscle.

be noted that these terms indicate merely location; epi-, peri-, and endo-mysium all being connective tissue grading from coarse to fine, as it passes from without inward. The structure of the muscle as an organ is thus seen to conform to the structure of other organs, in that it is surrounded by a connective-tissue capsule, which sends septa into the organ, dividing it into a number of compartments and serving for the support of the essential tissue of the organ, the

The structure of tendon has been described (see page 78).

Tendon sheaths and bursæ are similar in structure, consisting of mixed white and elastic fibres. Their free surfaces are usually lined by flat cells, which are described by some as connective-tissues cells, by others as endothelium.

At the junction of muscle and tendon, the muscle fibre with its sarcolemma ends in a rounded or blunt extremity (Fig. 58, p. 106). Here the fibrils of the tendon fibres are in part cemented to the sarcolemma, and in part are continuous with the fibres of the endo- and peri-mysium. Along the line of union of muscle and tendon the muscle nuclei are more numerous than elsewhere (Fig. 112, b), and it has been suggested that there is here a zone of indifferent or formative tissue which is capable of developing on the one hand into muscle, on the other into the connective tissue of tendon.

Growth of Muscle takes place mainly at the ends of the fibres

where the nuclei are most numerous. In addition to the growth incident to increase in size of the individual or of the particular muscle, there is a constant wearing out of muscle fibres and their replacement by new fibres. This is accomplished as follows: The muscle fibre first breaks up into a number of segments (sarcostyles), some of which contain nuclei while others are non-nucleated. The sarcostyles next divide into smaller fragments, and finally completely disintegrate. This is followed by a process of absorption and complete disappearance of the fibre. From the free sarcoplasm new muscle fibres are formed. In the early stages of their development these are known as myoblasts. The latter develop into muscle fibres in the same manner as described under the histogenesis of muscle (p. 108).

Blood-vessels.—The larger arteries of muscle run in the perimy-sium, their general direction being parallel to the muscle bundles. From these, small branches are given off at right angles. These in turn give rise to an anastomosing capillary network with elongated meshes, which surrounds the individual muscle fibres on all sides. From these capillaries, veins arise which follow the arteries. Even the smallest branches of these veins are supplied with valves.

In tendons blood-vessels are few. They run mainly in the connective tissue which surrounds the fibre bundles. Tendon sheaths and bursæ, on the other hand, are well supplied with blood-vessels.

The **lymphatics** of muscle are not numerous. They accompany the blood-vessels. In tendon definite lymph vessels are found only on the surface.

**Nerves.**—The terminations of nerves in muscle and tendon are described under nerve endings (page 388).

## TECHNIC.

- (1) A Muscle.—Select a small muscle, human or animal, and, attaching a weight to the lower end to keep it stretched, fix in formalin-Müller's fluid (technic 5, p. 7), and harden in alcohol. Stain transverse sections with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) and mount in balsam.
- (2) Junction of Muscle and Tendon.—Any muscle-tendon junction may be selected. Fix in formalin-Müller's fluid, keeping stretched by means of a weight attached to the lower end. Cut longitudinal sections through the muscle-tendon junction, stain with hæmatoxylin-picro-acid-fuchsin, and mount in balsam. The gastrocnemius of a frog is convenient on account of its small size, and because by bending the knee over and tying there, the muscle can be easily put on the stretch and kept in that condition during fixation. Place the entire preparation in the fixative removing the muscle-tendon from the bone after fixation.

# CHAPTER V.

# GLANDS AND THE GENERAL STRUCTURE OF MUCOUS MEMBRANES.

# Glands-General Structure and Classification.

Attention was called in describing the functional activities of cells (page 46) to the fact that certain cells possess the power of not only carrying on the nutritive functions necessary to maintain their own existence, but also of elaborating certain products either necessary for the general body functions (secretions) or for the body to eliminate as waste (excretions). Such cells are known as gland cells or glandular epithelium, and an aggregation of these cells to form a definite structure for the purpose of carrying on secretion or excretion is known as a gland.

A gland may consist of a single cell, as, e.g., the mucous or goblet cell on the free surface of a mucous membrane or the unicellular glands of invertebrates. Such a cell undergoes certain changes by which a portion of its protoplasm is transformed into or replaced by a substance which is to be used outside the cell itself. The appearance which this cell presents depends upon the stage of secretion. It is thus possible to differentiate between a "resting" and an "active" cell or between an "empty" and a "loaded" cell. The mucous secreting cell of the intestine is one of the simple columnar cells which constitute the epithelium of the mucous membrane. It is distinguishable as a mucous or goblet cell only after secretion begins. The resting cell is granular and takes a rather dark cytoplasmic stain. As the cell becomes active, part of the cytoplasm is transformed into, or is replaced by, a clear substance which does not stain like cytoplasm, but reacts to hæmatoxylin. The mucus collects first in the free end of the cell, and gradually increases in amount until the entire cell is filled, with the exception of a small area at the base, where a little unchanged protoplasm surrounds a flattened nucleus. The cell at this stage is much larger than in the resting state, and finally ruptures on the free surface and pours out its Opinions differ as to the further behavior of this cell. According to some, its life history is now ended, and its place is taken by

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other cells which pass through the same process. This undoubtedly takes place in the sebaceous glands, the cells of which disintegrate to form the secretion. Others believe that in most cases the cell is reconstructed from the nucleus and unchanged cytoplasm, and again passes through the process of secretion. How many times a cell may repeat the secretory process is not known. In stratified epithelium secretion may begin while the cell is still deeply situated, but is completed only as the cell reaches the surface, where its mucus is to be discharged.

Most glands are composed of more than one cell, usually of a large number of cells, and these cells, instead of lying directly upon the surface, line more or less extensive invaginations into which they pour their secretions.

In the simplest form of glandular invagination all the cells lining the lumen are secreting cells. In more highly developed glands only the deeper cells secrete, the remainder of the gland serving merely to carry the secretion to the surface. This latter part is then known as the excretory duct, in contradistinction to the deeper secreting portion. In both the duct portion and secreting portion of a gland the epithelium usually rests upon a more or less definite basement membrane or membrana propria (page 63). Beneath the basement membrane, separating and supporting the glandular elements, is the connective tissue of the gland. This varies greatly in structure and quantity in different glands.

When the secreting portion of the gland is a tubule, the lumen of which is of fairly uniform diameter, the gland is known as a *tubular gland*. When the lumen of the secreting portion is dilated in the form of a *sac* or *alveolus*, the gland is known as a *saccular* or *alveolar gland*. Intermediate forms have been described as tubulo-alveolar glands.

A gland may consist of a single tubule or saccule, or of a single system of ducts leading to terminal tubules or saccules—simple gland. A gland may consist of a number of more or less elaborate duct systems with their terminal tubules or saccules—compound gland. A few glands. e.g., the thyreoid and thymus, have no ducts, and are known as ductless glands.

All compound glands are surrounded by connective tissue which forms a more or less definite *capsule*. From the capsule connective-tissue *septa* or *trabeculæ* extend into the gland. The broadest septa usually divide the gland into a number of macroscopic compartments

or *lobes*. Smaller septa from the capsule and from the interlobar septa divide the lobes into smaller compartments usually microscopic in size—the *lobules*. A lobule is not only a definite portion of the gland separated from the rest of the gland by connective tissue, but represents a definite grouping of tubules or alveoli with reference to one or more terminal ducts. The glandular (epithelial) tissue is known as the *parenchyma* of the gland, in contradistinction to the connective or *interstitial* tissue.

The relations of the glandular tissue proper to the connective tissue are best understood by reference to development. All glands, simple and compound, originate as simple evaginations from a surface lined with epithelium. The epithelial evagination grows down into the underlying connective tissue. In a compound gland this invagination tubule becomes the main excretory duct. As the tubule grows, it divides and subdivides to form the larger and smaller ducts and finally the secreting tubules or alveoli. During the development of the gland tubules, the connective tissue is also developing, but is being largely replaced by the more rapidly growing tubules. The gland tubules do not develop irregularly, but in definite groups, each group being dependent upon the tubule (duct) from which it originates. Thus the invagination tubule (main excretory duct) gives rise to a few large branches (lobar ducts), each one of which gives off the subdivisions which constitute a lobe. From each lobar duct there arise within the lobe a large number of smaller branches (lobular ducts) each one of which gives rise to the subdivisions included in a lobule. As the lobe groups and lobule groups of tubules develop, the largest strands of connective tissue are left between adjacent lobes (interlobar connective tissue), smaller strands between lobules (interlobular connective tissue), and the finest connective tissue between the tubules or alveoli within the lobule (intralobular connective tissue).

Glands may thus be classified according to their shape and arrangement as follows:

1. Tubular glands.

- (a) Simple tubular  $\begin{cases} \text{straight.} \\ \text{coiled.} \\ \text{branched.} \end{cases}$
- (b) Compound tubular.
- 2. Saccular or alveolar glands.
  - (a) Simple saccular.
  - (b) Compound saccular or racemose.
- 3. Ductless glands.
- 1. **Tubular Glands.**—(a) SIMPLE TUBULAR GLANDS are simple tubules which open on the surface, their lining epithelium being continuous with the surface epithelium. All the cells may be secreting cells or only the more deeply situated. In the latter case the upper

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portion of the tubule serves merely as a duct. In the more highly developed of the simple tubular glands we distinguish a *mouth*, opening upon the surface, a *neck*, usually somewhat constricted, and a *fundus*, or deep secreting portion of the gland.

Simple tubular glands are divided according to the behavior of the fundus, into (1) straight, (2) coiled, and (3) branched.

- (1) A straight tubular gland is one in which the entire tubule runs a straight unbranched course, e.g., the glands of the large intestine (Fig. 113, 1).
- (2) A coiled tubular gland is one in which the deeper portion of the tubule is coiled or convoluted, e.g., the sudoriferous glands of the skin (Fig. 113, 2).

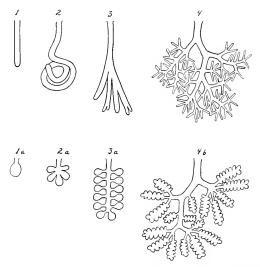


Fig. 113.—Diagram Illustrating Different Forms of Glands. Upper row, tubular glands; 1, 2, and 3, simple tubular glands; 4, compound tubular gland. Lower row, alveolar glands; 1a, 2a, and 3a, simple alveolar glands; 4a, compound alveolar gland. For description of 1a, 2a, and 3a, see simple alveolar glands in text.

(3) A forked or branched tubular gland is a simple tubular gland in which the deeper portion of the tubule branches, the several branches being lined with secreting cells and opening into a superficial portion, which serves as a duct. Examples of slightly forked glands are seen in the cardiac end of the stomach, and in the uterus. Other tubular glands show much more extensive branching, the main duct giving rise to a number of secondary ducts, from which are given off the terminal tubules. The mucous glands of the mouth, esophagus, trachea,

and bronchi are examples of these more elaborate simple tubular glands (Fig. 113, 3).

(b) Compound tubular glands consist of a number, often of a large number, of distinct duct systems. These open into a common or main excretory duct. The smaller ducts end in terminal tubules. Many of the largest glands of the body are of this type, e.g., the salivary glands, liver, kidney, and testis (Fig. 113, 4).

In certain compound tubular glands, as, e.g., the liver, extensive anastomoses of the terminal tubules occur. These are sometimes called *reticular glands*.

- 2. Alveolar Glands.—(a) SIMPLE ALVEOLAR GLANDS.—The simplest form of alveolar gland consists of a *single sac* connected with the surface by a constricted portion, the *neck*, the whole being shaped like a flask (Fig. 113, 1 a). Such glands are found in the skin of certain amphibians; they do not occur in man. Simple alveolar glands, in which there are several saccules (Fig. 113, 2 a), are represented by the smaller sebaceous glands. *Simple branched alveolar glands*, in which a common duct gives rise to a number of saccules (Fig. 113, 3 a), are seen in the larger sebaceous glands, and in the Meibomian glands.
- (b) Compound Alveolar Glands.—These resemble the compound tubular glands in general structure, consisting of a large number of duct systems, all emptying into a common excretory duct. The main duct of each system repeatedly branches, and the small terminal ducts, instead of ending in tubules of uniform lumen, as in a tubular gland, end in sac-like dilatations, the alveoli or acini (Fig. 113, 4 a). The best example of a compound alveolar gland is the mammary gland, although the lung is constructed on the principle of a compound alveolar gland.

Certain structures remain to be considered which are properly classified as glands, but in which during development the excretory duct has disappeared. Such glands are known as *ductless glands*.

The ovary is a ductless gland, the specific secretion of which, the ovum, is under normal conditions taken up by the oviduct and carried to the uterus. This is known as a *dehiscent gland*.

Other ductless glands, such as the thyreoid and adrenal, are known as glands of *internal secretion*, their specific secretions passing directly into the blood or lymph systems.

A few glands, e.g., the liver and pancreas, have both an internal secretion, and an external secretion.

# General Structure of Mucous Membranes.

The alimentary tract, the respiratory tubules, parts of the genitourinary system, and some of the organs of special sense are lined by mucous membranes. While differing as to details in different organs, the general structure of all mucous membranes is similar. The essential parts are (1) surface epithelium, (2) basement membrane, and (3) stroma or tunica propria. The epithelium may be simple columnar, as in the gastro-intestinal canal; ciliated, as in the bronchi; stratified squamous, as in the esophagus, etc. The epithelium rests upon a basement membrane or membrana propria which, like the same membrane in glands, is described by some as a product of the epithelium, by others as a modification of the underlying connective tissue. Beneath the basement membrane is a connective-tissue stroma, or tunica propria. This usually consists of loosely arranged fibrous tissue with some elastic fibres. It may contain smooth muscle cells and lymphoid tissue.

In addition to the three layers above described there is frequently a fourth layer between the stroma and the underlying connective tissue. This consists of one or more layers of smooth muscle, and is known as the *muscularis mucosa*.

A mucous membrane usually rests upon a layer of connective tissue rich in blood-vessels, lymphatics, and nerves—the *submucosa*.

# CHAPTER VI.

# THE DIGESTIVE SYSTEM.

THE *digestive system* consists of the alimentary tract and certain associated structures such as glands, teeth, etc.

The *alimentary tract* is a tube extending from lips to anus. Different parts of the tube present modifications both as to calibre and as to structure of wall.

The embryological subdivision of the canal into headgut, foregut, midgut, and endgut admits of further subdivision upon an anatomical basis as follows:

- I. Headgut: (a) Mouth, including the tongue and teeth.
  - (b) Pharynx.
- II. Foregut: (a) Œsophagus.
  - (b) Stomach.
- III. Midgut: Small intestine.
- IV. Endgut: (a) Large intestine.
  - (b) Rectum.

The entire canal is lined by *mucous membrane*, the modifications of which constitute the most essential difference in structure of its several subdivisions.

Beneath the mucosa is usually more or less connective tissue, which in a large portion of the canal forms a definite *submucosa*.

Muscular tissue is present beneath the submucosa throughout the greater part of the canal. In most regions it forms a definite, continuous, muscular tunic.

The upper and lower ends of the tube—mouth, pharynx, œsophagus, and rectum—are quite firmly attached by fibrous tissue to the surrounding structures. The remainder of the tube is less firmly attached, lying coiled in the abdominal cavity, its surface covered, except along its attached border, by a serous membrane, the visceral peritoneum.

#### I. THE HEADGUT.

#### The Mouth.

The Mucous Membrane of the Mouth.—This consists of stratified squamous epithelium lying upon a connective-tissue stroma or tunica propria. The latter is thrown up into papillæ, which do not, however, appear upon the free surface of the epithelium. The submucosa is a firm connective-tissue layer with few elastic fibres. The thickness of the epithelium, the character of the stroma, and the height of the papillæ vary in different parts of the mouth. There is no muscularis mucosæ.

At the junction of the skin and mucous membrane (red margin of the lips) the epithelial layer is much thickened, the stroma is thinned, and the papillæ are very high. At this point the stratum corneum of the skin passes over into the softer nucleated epithelium of the mouth, while the stratum lucidum and stratum granulosum of the skin terminate (see skin, page 354).

The mucous membrane of the gums has prominent, long, slender papillæ, the summits of which are covered by a very thin layer of epithelium. This nearness of the vascular stroma to the surface accounts for the ease with which the gums bleed. That portion of the gums which extends over the teeth is devoid of papillæ. The submucosa of the gums is firmly attached to the underlying periosteum.

The mucous membrane lining the cheeks has low, small papillæ, and the submucosa is closely adherent to the muscular fibres of the buccinator.

Covering the hard palate, the mucous membrane is thin and the short papillæ are obliquely placed, their apices being directed anteriorly. The submucosa is firmly attached to the periosteum.

Over the soft palate the papillæ of the mucous membrane are low or even absent. They are somewhat higher on the uvula, the posterior surface of which shows a transitional condition of its epithelium, areas of stratified squamous alternating with areas of stratified columnar ciliated epithelium. Throughout the mucous membrane of the soft palate, uvula, and fauces, the stroma and submucosa contain diffuse lymphatic tissue. In some places the lymphoid cells are so closely placed as to form distinct nodules.

GLANDS OF THE ORAL MUCOSA. 1—Distributed throughout the oral mucosa are small branched tubular glands. Only in those parts

<sup>&</sup>lt;sup>1</sup> For description of the larger salivary glands see page 242.

of the mucous membrane which are closely attached to underlying bone, as on the gums and hard palate, are mucous glands few or entirely absent. While the deeper portions of the glands are in the submucosa, some of the tubules usually lie in the stroma of the mucous membrane.

The *ducts* open upon the surface and are lined with a continuation of the surface stratified squamous epithelium as far as the first bifurcation. Here the epithelium becomes stratified columnar, and this, as the smaller branches are approached, passes over into the simple columnar type. Not infrequently ducts of small secondary glands empty into the main duct during its passage through the mucosa.

According to the character of their secretions, the oral glands are divided into:

- (a) Mucous glands, which secrete a mucin-containing fluid (mucus);
- (b) Serous glands, which secrete a serous (albuminous) fluid;
- (c) Mixed glands, the secretion of which is partly mucous and partly serous.

Morphologically, also, a similar distinction can be made in regard to the glandular epithelium which lines the terminal tubules, the tubules of mucous glands being lined with "mucous" cells, those of serous glands with "serous cells," while of the mixed glands the cells of some tubules are mucous, of others serous. In certain tubules both mucous and serous cells occur. The appearance which these cells present depends largely upon their secretory condition at the time of death.

Serous cells when resting have a slightly granular protoplasm, which in the fresh condition is highly refractive, giving the cells a transparent appearance. With the beginning of secretion the granules increase in number and the cells become darker. Stained with hæmatoxylin-eosin, serous tubules have a purplish color. The nuclei are spherical or oval, and are situated between the centre and base of the cell (Fig. 159, p. 245).

Mucous cells are in the quiescent state rather small cuboidal or pyramidal cells, with cloudy cytoplasm and nuclei situated at the base of the cell. When active the mucous cells are much larger, with clear cytoplasm and with nuclei flattened against the basement membrane. The protoplasm of the fresh unstained mucous cell is less highly refractive than that of the serous cell. It consequently appears darker and less transparent. Mucous tubules are larger and more irregular in shape than serous tubules, and when stained with hæmatoxylin-eosin

either remain almost wholly unstained or take a pale blue hæmatoxylin stain (Fig. 159, p. 245). Many mucous tubules have in addition to the mucous cells a peculiar, often crescentic-shaped group of cells on one side of the tubule, between the mucous cells and the basement membrane. These cells are granular and stain very much like serous cells with hæmatoxylin-eosin, thus resembling the latter in appearance. On account of the shape of the groups, they are known as the *crescents* of *Gianuzzi* or *demilunes* of *Heidenhain* (Fig. 159, p. 245). The cells of the crescents are connected with the lumen by means of *secretory canals*, which pass between the mucous cells and end in branches within the protoplasm of the crescent cells. It is quite possible that some of the crescents are not serous cells but mucous cells in the non-active condition which have been pushed away from the lumen by the more active cells. Such cell groups are not connected with the lumen of the gland by intercellular secretory canals.

Peculiar irregular branching cells have been described, extending from the basement membrane in between the mucous cells. They are known as "basket" cells and are supposed to be supportive in character.

The cells of both mucous and serous tubules rest upon a membrana propria, outside of which, separating the tubules, is a cellular connective-tissue stroma.

Of the small glands of the mouth, a group near the root of the tongue are of the mucous variety, some "lingual" glands in the region of the circumvallate papillæ are serous, while the remainder are of the mixed type.

Blood-vessels.—The larger vessels run mainly in the submucosa. The arteries of the submucosa give off one group of branches to the tunica propria, where they break up into a dense subepithelial capillary network, sending capillary loops into the papillæ. A second group of arterial branches pass to the submucosa, where they give rise to capillary networks among the tubules of the mucous glands. From the capillaries veins arise which accompany the arteries.

**Lymphatics.**—The larger lymph vessels lie in the submucosa. These send smaller branches into the tunica propria, where they open into small lymph capillaries and spaces.

Nerves.—Medullated nerve fibres form plexuses in the submucosa and deeper parts of the mucosa. From these plexuses, branches are given off which lose their medullary sheaths and form a second plexus of non-medullated fibres just beneath the epithelium. From

this subepithelial plexus, branches pass in between the epithelial cells to terminate in end brushes or in tactile corpuscles. The nerves belong to the cerebro-spinal system, and are dendrites of sensory ganglion cells. Axones of sympathetic neurones are also present in the oral mucosa, destined mainly for the muscle-tissue of the blood-vessels.

#### TECHNIC.

- (1) The superficial cells of the oral mucous membrane may be prepared for examination as in technic 1, page 57.
- (2) For the study of the mucous membrane of different parts of the mouth, fix small pieces in formalin-Müller's fluid (technic 5, p. 7), cut sections perpendicular to the surface, stain with hæmatoxylin-eosin (technic 1, p. 18), and mount in balsam.
- (3) Small mucous and serous glands of the mouth may be studied in the preceding sections.

#### THE TONGUE.

The tongue is composed mainly of striated muscle fibres, supported by connective tissue and covered by a mucous membrane. While the

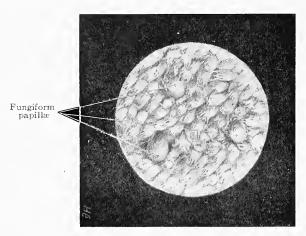


Fig. 114.—Surface View of Tongue showing filiform papillæ and three fungiform papillæ (Spaltcholz).

bundles of fibres interlace in all directions, three fairly distinct planes can be differentiated.

- (1) Vertical and somewhat radiating fibres—hyoglossus, genio-glossus, and vertical fibres of the lingualis.
  - (2) Transverse fibres—transverse fibres of the lingualis.

(3) Longitudinal fibres—the styloglossus and longitudinal (superior and inferior) fibres of the lingualis.

The connective tissue which supports the muscle fibres and separates them into bundles contains mucous glands and fat. A strong band of connective tissue, the *septum linguæ*, extends lengthwise through the middle of the tongue, dividing it into right and left halves.

The *submucosa* of the tongue is not well developed, the stroma of the mucosa resting directly upon the underlying muscle.

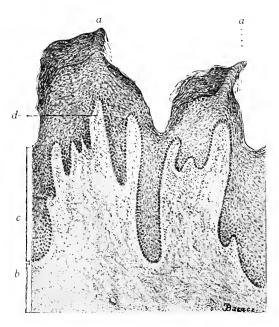


Fig. 115.—Vertical Section through Two Filiform Papillæ from Human Tongue.  $\times$  80. (Szymonowicz.) a, Horny epithelium; b, stroma; c, epithelium; d, secondary papilla.

The *mucous membrane* of the tongue resembles that of the mouth, but differs from the latter in that in addition to the low papillæ, such as are found in the oral mucosa, the upper surface of the tongue is studded with numerous and much larger papillæ or villi. These project from the surface and give to the tongue its characteristic roughness. Three forms of papillæ are distinguished. Filiform, fungiform, and circumvallate.

(1) FILIFORM PAPILLÆ (Fig. 115).—These are the most numerous and are distributed over the entire dorsum of the organ. Each consists of a central core of connective tissue containing elastic fibres,

which is long and slender, and is covered by stratified squamous epithelium. From the summit of each papilla are given off several secondary papillæ. The epithelium covering the papillæ is hornified and often extends from the surface as a long thread-like projection—hence the name, filiform.

(2) Fungiform Papillæ (Fig. 116).—Scattered irregularly over the entire dorsum among the filiform papillæ, but fewer in number, are larger papillæ of somewhat different structure known as fungiform papillæ. Their summits are rounded instead of pointed and their

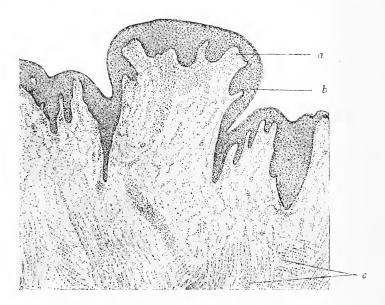


Fig. 116.—Vertical Section through Fungiform Papilla of Human Tongue.  $\times$  45. (Szymonowicz.) a, Secondary papilla; b, epithelium; c, muscle fibres.

bases are narrowed. Secondary papillæ are given off not only from the summit, but from the sides of the papilla. The epithelial covering is comparatively thin and is not hornified. The connectivetissue core of these papillæ contains but few elastic fibres.

(3) The Circumvallate Papillæ (Fig. 117).—These are from nine to fifteen in number, and are grouped on the posterior surface of the dorsum of the tongue. They resemble the fungiform papillæ, but are much larger. Each lies rather deep in the mucous membrane, surrounded by a groove or *trench* and *wall* (whence the name circumvallate). The wall is somewhat lower than the papilla, thus allowing the latter to project slightly above the surface. Secondary papillæ

are confined to the upper surface of the papilla, the sides being free from secondary papille. The surface of the papilla and the borders of the groove and wall are covered by stratified squamous epithelium. Lying in the epithelium of the side wall and sometimes of the opposite trench wall are oval bodies, the so-called *taste buds*, which serve as organs for the nerves of taste (see nervous system). Into the trench surrounding the circumvallate papilla open the ducts of serous glands (Ebner's glands).

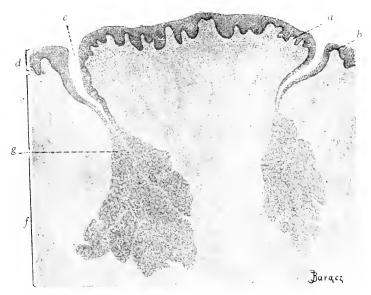


Fig. 117.—Vertical Section through a Circumvallate Papilla of Human Tongue.  $\times$  37. (Szymonowicz.) *a*, Secondary papilla; *b*, wall; *c*, trench; *d*, epithelium of tongue; *e*, stroma; *f*, submucosa; *g*, Ebner's glands.

The *lymph follicles* of the tongue have been already described (page 157) under the head of the lingual tonsils.

For glands of the tongue see page 195.

The larger blood-vessels run in the connective-tissue septa. These give off smaller branches, which break up into capillary networks surrounding the muscle fibres and forming a plexus just beneath the epithelium. From the latter are given off capillaries to the papillæ. The capillaries converge to form veins, which in general follow the course of the arteries.

Fine lymph spaces occur in the papillæ and open into a plexus of small lymph capillaries just beneath the papillæ. These communi-

cate with a deeper plexus of larger lymphatics, which increase in size and number as they pass backward and form an especially dense lymphatic network at the root of the tongue in the region of the lingual tonsils.

Nerves.—Sympathetic fibres pass mainly to the smooth muscle of the blood-vessels and to the glands. Medullated motor nerve fibres supply the lingual muscles. Medullated sensory nerves include those of the special sense of taste as well as those of ordinary sensation. They end freely among the epithelial cells or in connection with special end-organs—the *taste buds* mainly in the circumvallate papillæ, and the *end-bulbs of Krause* in the fungiform papillæ.

#### TECHNIC.

Remove pieces of the dorsum of the tongue, selecting parts that will include the different forms of papillæ and cutting well into the underlying muscular tissue. Treat as in technic 2, p. 196, or sections may be stained with hæmatoxylin-picroacid-fuchsin (technic 3, p. 19).

In sections from the back part of the tongue good examples of mucous and serous glands are usually found.

In small sections of the tongue the muscle fibres are seen arranged in bundles, surrounded by connective tissue and interlacing in all directions. For the study of the arrangement of the different planes of muscle, complete transverse sections should be made at intervals through the entire tongue. The muscle and connective-tissue relations are best brought out by the hæmatoxylin-picro-acid-fuchsin stain.

#### THE TEETH.

A tooth is a hard bone-like structure, part of which projects above the surface of the jaw as the *crown*, while the deeper portion, the *root* or *fang*, is buried in a socket of the alveolar margin (Fig. 118). The junction of the root and crown is known as the *neck*.

A tooth consists of a soft central core, the *pulp cavity*, surrounded by *dentine* (Figs. 118 and 119). The latter constitutes the main bulk of the tooth. The exposed portion of the dentine is covered by a thin layer of extremely hard substance, the *enamel* (Fig. 118, 1), while the alveolar portion of the dentine is covered with *cementum* (Fig. 118, 3). Of these the dentine and cementum are of connective-tissue origin, the enamel of epithelial.

The *pulp cavity* occupies the central axis of the tooth (Figs. 118 and 119). In the root it is known as the *root canal*. At the apex of the

root it communicates with the underlying tissue by means of a minute opening, through which blood-vessels and nerves enter the pulp cavity.

The *dentinal pulp* consists of loose connective tissue of an embryonal type, composed of many fusiform and stellate cells and comparatively delicate fibrils not joined to form bundles. The pulp is richly supplied

with blood-vessels and nerves which are found only in this part of the tooth. Along the dentinal surface of the pulp the connective tissue cells are arranged as a single laver of columnar cells, the odontoblasts. These cells are closely allied to osteoblasts. Their nuclei lie Each cell toward their inner ends. sends out an inner process, which is usually single and passes into the dentinal pulp, several lateral processes which interlace with and probably anastomose with similar processes from other cells, and one or more outer fibrelike processes which enter the dentine, where they form the dentinal fibres. These frequently extend entirely through the dentine.

DENTINE (Figs. 119 and 120, D) is somewhat harder than bone which it resembles in structure. According to Fig. 118.—Vertical Section of Tooth in von Bibra its chemical composition is:

situ. × 15. (Waldeyer.) c, Pulpe capity the letter being at about the

Organic matter,	28.01
Calcium phosphate and fluorid,	66.72
Calcium carbonate,	3.36
Magnesium phosphate,	1.18
Other salts,	0.73

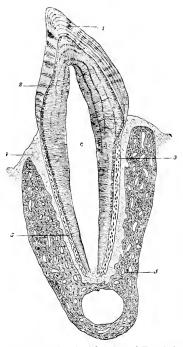


Fig. 118.—Vertical Section of Tooth in situ. × 15. (Waldeyer.) c, Pulp cavity, the letter being at about the junction of crown and root; 1, enamel showing radial and longitudinal markings; 2, dentine showing dental canals; 3, cementum (containing bone corpuscles); 4, dental periosteum; 5, bone of lower jaw.

Dentine constitutes the bulk of the tooth and is peculiar in that it contains canaliculi, *dental canals* (Figs. 119 and 120, Dk), but no lacunæ or bone cells. The latter are represented by the odontoblasts of the pulp, which, as already noted, lie at the inner side of the dentine, into the canaliculi of which they send the *dentinal fibres*. Dentine is non-vascular. The dental canals begin at the dental pulp, where they have a calibre of 2 to  $5\mu$ . They pass outward radially, taking a somewhat curved course, to the limit of the dentine, and, while taking

different directions in different parts of the dentine, are essentially parallel. In a longitudinal section of the dentine of the crown, lines are seen running parallel to the surface of the tooth. They are known as the *incremental lines of Schreger*. They are apparently due to regularity of curvature in the dental tubules. In their passage through the dentine the main canals gradually grow smaller until their diameter

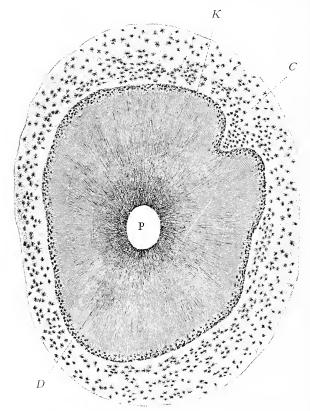


Fig. 119.—Cross Section through Root of Human Canine Tooth ( $\times$  25) (Sobotta), showing relations of pulp cavity, dentine, and cementum. P, Pulp cavity; D, dentine; C, cementum; K, Tomes' granular layer.

is from 0.5 to 1 $\mu$ . They give off minute side branches from 0.3 to 0.6 $\mu$  in diameter, which leave the main tubules at almost right angles, but soon turn slightly outward. They anastomose with similar branches from other canals. This anastomosis takes place not only between branches of adjacent canals, but also between branches of canals some distance apart. The main canals terminate either in blind extremities, or form loops by anastomosing with neighboring

tubules. Some of the tubules have quite extensive terminal branchings, other tubules have only two or three end branches. A few tubules run slightly beyond the limits of the dentine into the enamel. They do not pass into the cementum. The arrangement of the dental canals and their branches differs in different parts of the tooth. In the crown there are few large branches and the main canals are quite straight, most of them ending blindly in brush-like branchings just under the enamel, but some continuing over into the enamel for from 10 to 4.0%, where they lie in the cement between the prisms. In

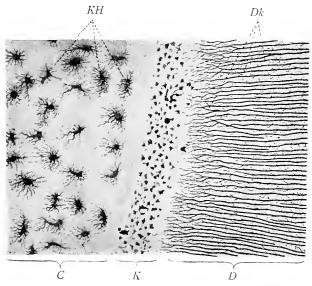


Fig. 120.—From Longitudinal Section through Root of Human Molar Tooth ( $\times$  200) (Sobotta), showing junction of dentine and cementum. C, Cementum; D, dentine; K, Tomes' granular layer; Dk, dental canals; KH, lacunæ of cementum.

the root the canals have more large branches and are more uneven. They do not pass over into the cementum, but end at the granular layer. The dentine immediately around a dental canal is more dense and hard than elsewhere and forms a sort of sheath for the canal—Neumann's dental sheath. Between the dental canals is a calcified ground substance, in which are connective-tissue fibres running in the long axis of the tooth.

Spaces which probably represent incomplete calcification of the dentine occur in the peripheral portion of the dentine of the crown. These are known as *interglobular spaces* (Fig. 121, Jg). They are filled with a substance resembling uncalcified dentine. The interglobular

spaces do not interrupt the dental canals which pass through them with no break in their continuity.

In the outer part of the dentine of the root are similar spaces which are smaller and more closely placed. These form the so-called Tomes' granular layer (Fig. 120, K). In the root of the tooth this layer is quite thick, separating the cementum from the dentine. Its spaces or lacunæ send off tiny canaliculi which run in all directions and anastomose with one another, with the dentinal tubules, and with the lacunæ of the cementum. This layer, with its small closely placed spaces and fine irregularly running canaliculi, contrasts sharply on the one side (Fig. 120) with the dentine and its straight parallel tubules; and on the other side, with the cementum and its large and more widely separated lacunæ. Over the crown of the tooth this layer is much thinner and as the apex is approached, becomes lost completely, the dental tubules extending to, and some of them entering slightly, (see above) the enamel.

The ENAMEL covers the exposed part or crown of the tooth and is the hardest substance in the body. It contains little more than a trace of organic substance, its chemical composition being, according to von Bibra:

Organic matter,	3.59
Calcium phosphate and fluorid,	89.82
Calcium carbonate,	4.37
Magnesium phosphate,	1.34
Other salts,	0.88

It consists of long six-sided prisms 3 to  $6\mu$  in diameter—enamel fibres or enamel prisms (Fig. 121, Sp)—which take a slightly wavy course through the entire thickness of the enamel. The prisms are attached to one another by a small amount of cement substance, and are grouped into bundles, the prisms of each bundle being parallel, but the bundles themselves frequently crossing one another at acute angles. In the human adult the prisms are homogeneous; in the embryo they show a longitudinal fibrillation. Rather indistinct parallel lines (the lines of Retzius) cross the enamel prisms. They probably represent the deposition in layers of the lime salts, although they are considered by some as artefacts. The enamel is covered by an apparently structureless membrane, the cuticula dentis.

The CEMENTUM (Fig. 120, C) covers the dentine of the root in a manner similar to that in which the enamel covers the dentine of the crown (Fig. 118, 1 and 3). It forms a thin layer at the neck, but in-

creases in thickness as the deeper part of the root is reached. Cementum is bone tissue. It contains lacunæ and bone cells. From the lacunæ radiate canaliculi, but there is no distinct lamellation and no Haversian systems or blood-vessels, excepting in the large teeth of the larger mammalia, and in the teeth of the aged, where they may be present. Channels, similar to Volkmann's canals in bone, not surrounded by concentric lamelæ, but serving for the passage of bloodvessels, are quite frequent in the thicker portions of the cementum.

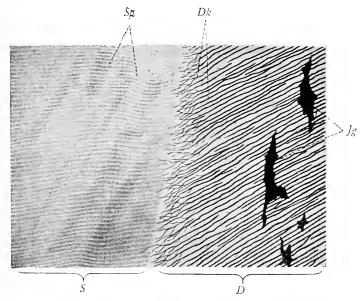


Fig. 121.—From Longitudinal Section of Crown of Human Premolar ( $\times$  200) (Sobotta), showing junction of enamel and dentine. S, Enamel; D, dentine: Sp, enamel prisms; Dk, dental canals; Jg, interglobular spaces. A few dentinal fibres are seen passing beyond the limits of the dentine into the enamel. The oblique dark bands in the enamel are the lines of Retzius.

The ground substance of the cementum is continuous with that of the dentine and many canaliculi of the former open into the interglobular spaces of the latter. Many uncalcified Sharpey's fibres penetrate the cementum.

The union between the root of the tooth and the alveolar periosteum is accomplished by a reflection of the latter over the root, where it forms the *dental periosteum*, or *peridental membrane* (Fig. 118, 4). This membrane consists of dense fibrous connective tissue. At the neck of the tooth it blends with the submucosa of the gum to form the so-called *circular dentoid ligament*, an annular band of dense

fibrous tissue, which extends around the tooth. The peridental membrane is formed of fibrillar connective tissue free from elastic fibres. Its fibres are directly continuous with Sharpey's fibres of the cementum.

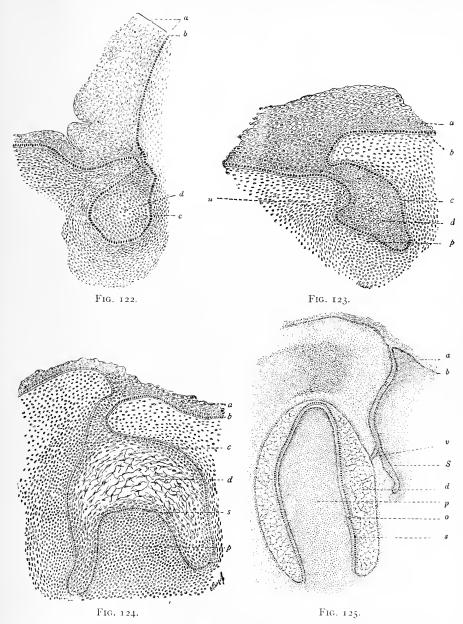
**Blood-vessels** of teeth are confined entirely to the pulp cavity. One or two small arteries reach the pulp cavity from the underlying connective tissue, through the foramen in the apex of the root. These break up into a capillary network in the dental pulp.

Lymphatics have as yet not been demonstrated in the dental pulp.

Nerves.—Medullated fibres accompany the blood-vessels through the apical canal. In the pulp they break up into a number of non-medullated branches, which form a plexus along the outer edge of the pulp, beneath the odontoblasts. From this plexus branches are given off which pass in between the odontoblasts, some terminating there, while others end between the odontoblasts and the dentine.

Development.—The enamel of the teeth is of ectodermic origin, the remainder of mesodermic. The earliest indication of tooth formation occurs about the seventh week of intra-uterine life (embryos 12 to 15 mm.). It consists in a dipping down of the epithelium covering the edge of the jaw into the underlying connective tissue (mesoderm) where it forms the dental shelf, or common dental germ. Soon after the formation of the dental shelf, a groove appears along the margin of the jaw where the ingrowth of epithelium occurred. This is known as the dental groove. The epithelium of the dental shelf is at first of uniform thickness. Soon, however, at intervals along the outer side of the dental shelf, the cells of the shelf undergo proliferation and form thickneings, ten in the upper and ten in the lower jaw, each one corresponding to the position of a future milk tooth. These are known as special dental germs, and remain for some time connected with one another and with the surface epithelium by means of the rest of the dental ridge.

Into the side of each special dental germ there occurs about the end of the third month (embryos of about 40 mm.) an invagination of the underlying connective tissue. In the upper jaw the invagination takes place on the upper and inner side, in the lower jaw on the lower and inner side, of each dental germ. Each invagination forms a dental papilla (Fig. 124), over which the tissue of the special dental germ forms a sort of cap, the latter being known from its subsequent function as the enamel organ, the papilla itself giving rise to the pulp and dentine. The dental germs are at this stage connected with each other by remaining portions of the dental shelf, and with the surface epithelium by remains



Figs. 122, 123, 124, 125.—Four Stages in the Development of a Tooth (from lower jaw of sheep embryo). (Bohm-Davidoff.) Fig. 122, Beginning of enamel organ showing connection with epithelium of mouth; Fig. 123, Later stage showing same with first trace of papilla; Fig. 124, Later stage showing papilla well formed, the differentiation of the enamel pulp and of the inner and outer enamel cells can be seen; odontoblast appearing along periphery of the papilla; Fig. 125 shows also beginning enamel organ of permanent tooth; Figs. 122, 123, 124, × 110, Fig. 125, × 40. a, Epithelium of mouth; b, its basal layer; c, superficial cells of enamel organ; d, enamel pulp; p, dental papilla; s, enamel cells; c, odontoblasts; S, enamel organ of permanent tooth just beginning to differentiate; v, remains of enamel ledge of milk tooth; u, surrounding connective tissue.

of the original invagination. The next step is the almost complete separation of the special dental germs and ridge from the surface epithelium (Fig. 125), and the formation around each special dental germ of a vascular membrane, the *dental sac*. The attenuated strand of epithelial cells, which still maintains a connection between the dental germs and the epithelium of the gums, is known as the *neck* of the *enamel organ* and it is from this that an extension soon occurs to the inner side of the

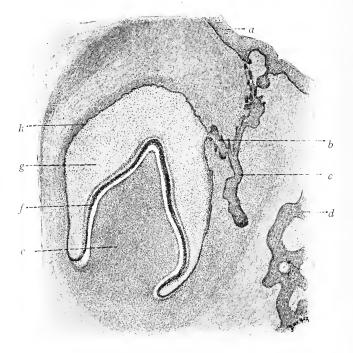


Fig. 126.—Developing Tooth from Three-and-one-half-months' Human Embryo.  $\times$  65. (Szymonowicz.) a, Epithelium of gums; b, neck of enamel organ; c, dental germ of permanent tooth; d, bone of lower jaw; e, dental papilla; f, inner enamel cells; g, enamel pulp; h, outer enamel cells.

dental germs of the milk teeth, to form the *dental germs* of the *permanent teeth* (Fig. 126,  $\epsilon$ ). Into the latter, connective-tissue papillæ extend as in the case of the milk teeth. There are thus present as early as the fifth month of feetal existence the germs of all milk and of some permanent teeth.

The ENAMEL is formed by the enamel organ. At the stage represented in Fig. 128, it consists of three layers: (1) The outer enamel cells, somewhat flattened; (2) the inner enamel cells, high columnar epithelium; (3) a layer of enamel pulp, situated between the other

layers, and consisting of stellate anastomosing cells with considerable intercellular substance (Figs. 128 and 129). A membrane, the cuticular membrane, is first laid down between the inner enamel cells and the dentine. Each of the inner enamel cells now sends out a process, Tomes' process, from its inner end. The processes are separated by a considerable amount of cement, and are the beginnings of the enamel prisms. Calcification now takes place both in the prisms and in the

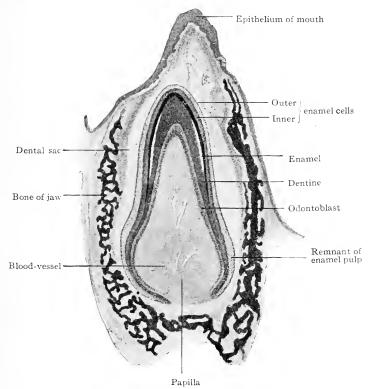


FIG. 127.—Longitudinal section of a developing tooth of a new-born puppy (Bonnett). late stage.

cement substance, beginning in the ends nearest the papilla. As this proceeds outward, the prisms become much elongated and the cement substance reduced in amount. Further growth in thickness of enamel occurs by lengthening of the enamel prisms. During the formation of the enamel, the enamel pulp and the external enamel cells disappear.

The formation of enamel in the milk teeth begins about the end of the fourth month and continues until the eruption of the teeth. The extent of the enamel organ is considerably greater than that of the enamel, the former covering the entire tooth, both root and crown, with the exception of the base of the papilla where the latter is connected with the underlying connective tissue. As the tooth develops, the enamel organ disappears over the root, remaining to form the enamel only over that part of the tooth which is to be subsequently exposed. The function of the enamel pulp is not known. It disappears as the tooth grows. It has been suggested that it may furnish nutrition or serve as an avenue through which nutrition reaches the non-vascular

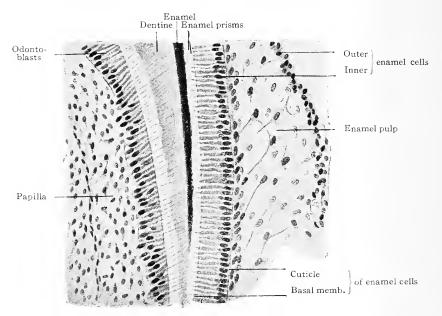


Fig. 128.—Section through border of a developing tooth of a new-born puppy. (Bonnett).

enamel organ. It may serve as an area of least resistance through which the tooth grows.

The DENTINE is the first of the dental tissues to become hard. Both dentine and pulp develop, as noted on p. 206, from the mesoderm of the dental papilla. When the latter is first formed it is of the same structure as the surrounding mesoderm with which it is continuous, except that it is somewhat more dense; later it assumes more the character of embryonal connective tissue, blood-vessels and nerves growing into it from the underlying connective tissue. The most peripheral cells of the pulp, those lying nearest the enamel organ, differentiate from the rest of the pulp to form a single layer of columnar or

pyramidal cells—the *odontoblasts*. The outer end of each cell is broad, while the inner end which contains the nucleus narrows to a point from which a delicate process extends into the pulp and probably anastomoses with other cell processes. These cells are analogous to the osteoblasts of developing bone and like them appear to determine the de-

position of lime salts. The lime salts are first laid down in a membrane-like structure—the membrana preformativa—which the odontoblasts apparently form between themselves and the enamel. From this membrane the transformation of the connective tissue into dentine progresses inward toward the pulp, additional dentine continuing to be laid down in layers, each new layer internal to the preceding. In this way the dental papilla is reduced in size to form the pulp cavity. In the outer part of the dentine spaces remain in which no lime salts are deposited. These are the interglobular spaces. As calcification proceeds the odontoblasts do not become enclosed within the dentine as do the osteoblasts within bone. They leave merely long slender processes, the dental fibres, lying in minute chan-

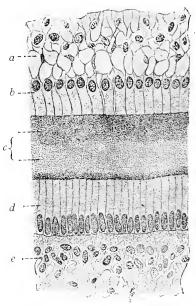


FIG. 129.—From Cross-section through a Developing Tooth.  $\times$  720. (Böhm and von Davidoff.) Note close relationship between odontoblasts and tissue of dental pulp. a, Dental pulp; b, odontoblasts; c, dentine; d, inner enamel cells; e, enamel pulp.

nels through the dentine, dental canals, while the bodies of the cells form a single layer along the inner margin of the dentine. There are thus no lacunæ and no cells within the dentine. This relation of odontoblasts to dentine, and probably the original odontoblasts, persist, not only throughout embryonic but through adult life.

While the tooth lies within the gum, the somewhat condensed connective tissue which surrounds it constitutes the *dental sac*.

As the germs of the milk teeth develop, the dental shelf broadens by extending inward toward the tongue. Along this inner margin appear the germs of the permanent teeth, the development of the various teeth structures from the germs being identical with the process described in the case of the milk teeth.

Twenty of the permanent teeth correspond in position to the twenty milk teeth, while twelve new molar germs, six in the upper and six in the lower jaw, represent the *true molars* of the adult. The first permanent tooth germ to appear is that of the first molar, about the beginning of the fifth month (embryos of about 180 mm.). It lies just behind the second molar of the milk dentition. The germs of the incisors and canines appear about the end of the sixth month, those of the premolars, which replace the milk molars, in the beginning of the eighth month. The germs of the second and third (wisdom teeth) molars do not appear until after birth, those of the former at about six months, of the latter during the fifth year.

The CEMENTUM is developed by ossification of that part of the dental sac which covers the root, its development being similar to subperiosteal bone formation (p. 177), without the formation of Haversian systems.

#### TECHNIC.

- (1) Teeth are extremely difficult organs from which to obtain satisfactory material for study. Sections of hard (undecalcified) and of decalcified teeth may be prepared in the same manner as sections of bone—technics 1, p. 171; 2, p. 172. The decalcified tooth should include if possible the alveolar margin of the jaw, so that in longitudinal sections the mode of implantation and the relation of the tooth to the surrounding structures can be seen.
- (2) For the study of developing teeth, embryo pigs, sheep, cats, dogs, etc., are suitable. For the early stages feetal pigs should be five to six inches long; for the intermediate, ten to twelve inches. The later stages are best obtained from a small new-born animal, e.g., kitten or small pup. The jaw—preferably the lower—or pieces of the jaw are fixed in formalin-Müller's fluid (technic 5, p. 7), hardened in alcohol, and decalcified (page 9). Subsequent treatment is the same as for developing bone (technic 1, p. 179).

## The Pharynx.

The wall of the pharynx consists of three coats—mucous, muscular, and fibrous.

1. The mucous membrane has a surface epithelium and an underlying stroma.

The EPITHELIUM is stratified squamous except in the region of the posterior nares, where it is stratified columnar ciliated, continuous with the similar epithelium of the nasal mucosa.

The STROMA, or tunica propria, consists of mixed fibrous and elastic tissue infiltrated with lymphoid cells. In certain regions these cells form distinct *lymph nodules* (see pharyngeal tonsils, page 157).

Beneath the stratified squamous epithelium the stroma is thrown up into numerous low papillæ. These are absent in regions covered by ciliated cells. Bounding the stroma externally is a strongly developed layer of longitudinal elastic fibres, the *elastic limiting layer*, which separates the stroma from the muscular coat and sends stout bands in between the muscle bundles of the latter.

- 2. The muscular coat lies beneath the elastic layer and is formed of very irregularly arranged muscle fibres belonging to the constrictor muscles of the pharynx.
- 3. The fibrous coat consists of a dense network of mixed fibrous and elastic tissue. It has no distinct external limit, and binds the pharynx to the surrounding structures.

The distribution of **blood-vessels**, **lymphatics**, and **nerves** is similar to that in the oral mucosa.

Small, branched, tubular, *mucous glands* are present in the stroma, and extend down into the intermuscular connective tissue. They are most numerous near the opening of the Eustachian tube.

#### TECHNIC.

For the study of the structure of the walls of the pharynx, material should be prepared as in technic 2, p. 196.

#### II. THE FOREGUT.

## The Esophagus.

The walls of the œsophagus are continuous with those of the pharynx and closely resemble the latter in structure. They consist of four layers, which from within outward are mucous, submucous, muscular, and fibrous (Fig. 130).

- 1. The mucous membrane resembles that of the pharynx except that beneath the stroma is a well-developed *muscularis mucosæ* composed of smooth muscle cells arranged longitudinally. The muscularis mucosæ forms a complete coat only in the lower part of the æsophagus. The epithelium is stratified squamous and rests upon a papillated stroma.
- 2. The submucosa is composed of loosely arranged fibrous and elastic tissue. It contains mucous glands, the larger blood-vessels, lymphatics, and nerves.
- 3. **The Muscular Coat.**—In the upper portion of the esophagus this coat is composed of striated muscle fibres; in the middle portion.

of mixed striated and smooth muscle. In the lower portion there are two distinct layers of smooth muscle, an inner circular and an outer longitudinal. The latter is not continuous.

4. The fibrous coat consists of bundles of white fibrous tissue with many elastic fibres. It serves to connect the œsophagus with the surrounding structures.

Two kinds of glands occur in the œsophagus.

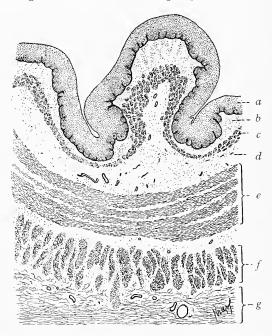


Fig. 130.—Transverse Section through Wall of Dog's Œsophagus.  $\times$  18. (Böhm and von Davidoff.) a, Epithelium; b, stroma; c, muscularis mucosæ; d, submucosa; e, circular muscle layer; f, longitudinal muscle layer; g, fibrous layer.

- (1) Mucous Glands.—These are of the same structure as those of the tongue, but much smaller. They lie in the submucosa and are distributed throughout the entire œsophagus, though most numerous in its upper third. The ducts pass obliquely downward on their way to the surface. Just before entering the muscularis mucosæ the duct widens out to form a sort of ampulla. Beyond this it again becomes narrow and enters the epithelium in the depression between two adjacent papillæ. A small lymph nodule is usually attached to the duct as it passes through the tunica propria.
- (2) SIMPLE BRANCHED TUBULAR GLANDS.—These resemble the glands of the cardiac end of the stomach, but branch much more

profusely. Some contain both chief and acid cells, others only chief cells (see stomach, page 219). They lie in the tunica propria, and are for the most part confined to a narrow zone at the lower end of the œsophagus and to the level of the fifth tracheal ring. Scattered groups also occur in other regions.

The distribution of blood-vessels, lymphatics, and nerves in the œsophagus is similar to their distribution in the mouth (p. 195). Between the two muscular coats the nerve fibres form plexuses in which are many sympathetic nerve cells. These plexuses are analogous to the plexuses of Meissner in the stomach and intestine.

#### TECHNIC.

Remove a portion of the wall of the œsophagus, wash carefully in normal salt solution, and pin out, mucous-membrane side up, on a piece of cork. Fix in formalin-Müller's fluid and harden in alcohol (technic 5, p. 7). Transverse or longitudinal sections should be cut through the entire thickness of the wall. If the details of the muscular coat are to be studied, sections from at least three different levels should be taken: one near the upper end, one at about the middle, and the other in the lower third. Stain with hæmatoxylin-eosin or hæmatoxylin-picroacid-fuchsin (technic 1, p. 18; 3, p. 19) and mount in balsam.

# GENERAL STRUCTURE OF THE WALLS OF THE GASTRO-INTESTINAL CANAL.

The walls of the stomach and intestines are made up of four coats (Fig. 131). These from the lumen outward are mucous, submucous, muscular, and serous.

1. The mucous membrane (Fig. 131) consists of surface epithelium, glands, stroma, and muscularis mucosæ. The surface epithelium is simple columnar and rests upon a distinct basement membrane. The arrangement of the glands and the nature of the gland cells differ in different parts of the tract. The stroma is a loosely arranged, richly cellular connective tissue, which in many places is so infiltrated with lymphoid cells as to constitute diffuse lymphatic tissue. In other places it contains circumscribed masses of lymphatic tissue, lymph nodules. The amount of stroma depends upon the closeness with which the glands are packed. The muscularis mucosæ consists of smooth muscle cells, which have a generally longitudinal arrangement. Where, however, the muscularis mucosæ is thick there are usually two distinct layers—an inner circular and an outer longitudinal. Folds of considerable extent occur in the mucous membrane. Those of the

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stomach are known as rugæ, and are not constant, depending upon the degree of distention of the organ. Those of the small intestine are much more definite, and are known as valvulæ conniventes.

2. **The submucosa** (Fig. 131) is a loose connective-tissue structure. It contains the larger blood-vessels, lymphatics, and nerves.

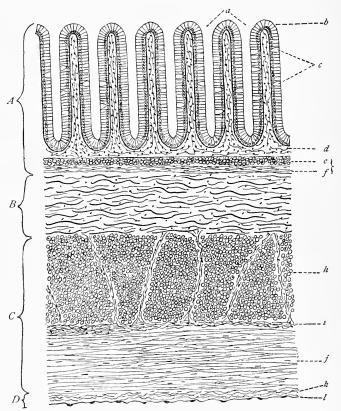


Fig. 131.—Diagram of Structure of Wall of Gastro-intestinal Canal. A, Mucous membrane; a, glands; b, epithelium; c, goblet cells; d, stroma; e, inner circular; f, outer longitudinal layers of g, muscularis mucosae. B, Submucosa. C, Muscular coat; h, its inner circular layer; g, its outer longitudinal layer; g, intermuscular connective-tissue septum. D, serous coat; g, its connective-tissue layer; g, its endothelial layer.

3. The muscular coat (Fig. 131) consists of two layers of smooth muscle, which in the intestine are sharply differentiated into an *inner circular* and an *outer longitudinal*. In the stomach the direction of the layers of the muscular coat is less definite. A narrow layer of connective tissue separates the two layers of muscle. From this, septa extend into the muscle tissue, separating it into bundles.

4. The serous coat (Fig. 131) is the visceral layer of the peritoneum. It consists of a thin layer of connective tissue covered by a single layer of mesothelium. Along the attachment of the mesentery the serous coat is wanting.

The subdivisions of the gastro-intestinal canal differ from one another mainly in regard to the structure of their mucous membranes, and especially in regard to the structure of the glands of the mucous membrane and submucosa.

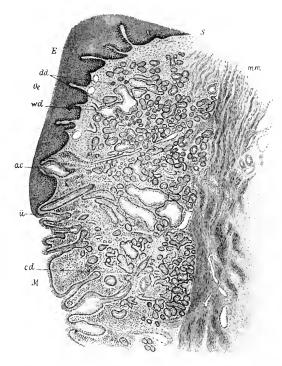


FIG. 132.—Section through Junction of Œsophagus and Stomach of Man.  $\times$  121 (Schäfer.) Oe, Œsophagus; M, stomach; ed, cardiac glands; vd, dilated ducts of cardiac glands; S, stroma; E, stratified squamous epithelium of œsophagus; mm, muscularis mucosæ; ed, irregularly cut tubules of cardiac glands; dd, cardiac glands in lower end of the œsophagus: ii, limit of stratified œsophageal epithelium.

### The Stomach.

At the junction of œsophagus and stomach there is an abrupt transition from the stratified squamous epithelium of the former with its smooth surface to the simple columnar epithelium of the latter with its elevations and depressions. In the deeper structures the line of demarcation is not so abrupt, the muscularis mucosæ of the œsophagus

being continuous with that of the stomach, and glands of the stomach type extending up under the stratified epithelium of the œsophagus (Fig. 132).

1. The mucous membrane of the stomach is folded into ridges or  $rug\omega$ , the height and number of which depend, as already noted, upon the degree of distention of the organ. The rugw are most prominent in the collapsed organ, almost absent when the organ is fully distended. In addition to the rugw the entire mucous membrane is studded with minute depressions barely visible to the naked eye, the so-called gastric pits (Fig. 134, Mg). These mark the openings of the gastric glands. In the fundus they are comparatively shallow, extending

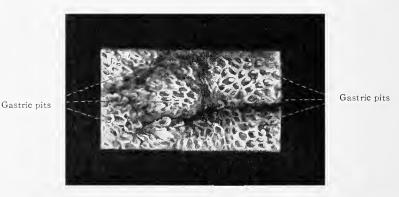


Fig. 133.—Surface View of Mucous Membrane of Stomach showing gastrick pits (Spalteholz).

through about one-fifth the thickness of the mucosa; in the pylorus the pits are much deeper, extending through half or more of the thickness of the mucous membrane (compare Figs. 134 and 137).

The Epithelium.—This is of the simple columnar type, covers the entire surface of the gastric mucosa and extends down into the pits (Fig. 134). The cells are of the high, clear, mucous type (Fig. 135, M and M'). The end of the cell toward the lumen is clear, usually consists mostly of mucous, and consequently stains lightly. There is no such distinct cuticle as in the intestine. The basal end of the cell contains the spheroidal, oval, or sometimes flattened nucleus, is granular, and takes a darker stain. The amount of mucus in the cell depends upon its functional condition. The cells rest upon a distinct basement membrane.

THE GASTRIC GLANDS.—Extending from the bottoms of the pits, their epithelium continuous with that of the pits themselves, are the

gastric glands. These are of two kinds, *peptic* or *fundus glands*, distributed throughout the greater part of the gastric mucosa, and *pyloric glands*, confined to the immediate region of the pylorus.

The *peptic glands* (Fig. 134) are simple, sometimes branched, tubular glands, of which from three to seven open into each gastric pit. They extend through the entire thickness of the stroma, to the muscularis mucosæ.

Each gland consists of (1) a mouth opening into the pit; (2) a constricted portion, the neck; (3) the body or main portion of the tubule; and (4) a slightly dilated and bent blind extremity, the fundus (Fig. 134). The mouth marks the transition from the higher epithelium of the pit to the low cuboidal of the neck (Fig. 135, h). In the body and fundus of the gland two types of cells are found: (a) chief cells (central, peptic, or adelomorphous), and (b) parietal cells (acid, oxyntic, or delomorphous).

The chief cells (Fig. 135, a) are the more numerous. They are of the low columnar type, often pyramidal with apices directed toward the lumen. Their bases rest either on the basement membrane or against the parietal cells. The appearance which these cells present depends upon their functional condition (p. 239). They usually appear clear and granular and take a light stain.

The parietal cells (Fig. 135, b) are oval or polygonal in shape, and

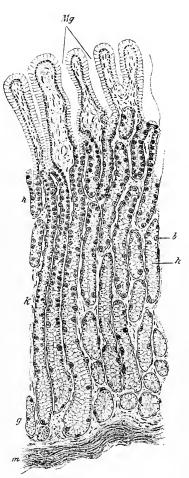


Fig. 134.—Vertical Section through the Mucous Membrane of the Fundus of the Stomach. ×85. (Kölliker.) Mg, Gastric pits; h, neck; k, body; g, fundus of peptic glands; h, chief cells; b, parietal cells; m, muscularis mucosæ.

lie here and there against the basement membrane. The nucleus is spherical, somewhat larger than that of the chief cell, and is usually situated at the center of the cell. The protoplasm is finely granular and in the fresh unstained condition appears clearer than that of the chief

cells. The parietal cells stain intensely with the aniline dyes with the result that in stained specimens the two kinds of cells are in marked contrast, the parietal cells being much darker than the chief cells. Although lying against the basement membrane and frequently pushing it out so as to form little protuberances beyond the even line of the

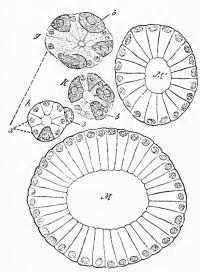


Fig. 135.—Cross-sections at Various Levels of Peptic Glands of Stomach.  $\times$  400. (Kölliker.) M, Section through gastric pit near surface; M', section through gastric pit near bottom; h, mouth of gland; k, neck; g, body near fundus; a, chief cells; b, parietal cells.

gland tubule, the parietal cells always maintain a connection with the lumen. This is accomplished by means of little clefts between the chief cells, intercellular secretory tubules, which extend down to the parietal cells. By means of the method of Golgi may be demonstrated not only the intercellular secretory tubules, but also the fact that upon reaching the cells these are continuous with a network of minute spaces within the cell—the intracellular secretory tubules (Fig. 136). Parietal cells are not distributed uniformly throughout the gland, but are most numerous in the body, where they frequently almost obscure the chief cells. In the fundus of the gland parietal cells are less numerous. For this

reason and because of the wider lumen of the fundus, transverse and longitudinal sections of this part of the tubule are most satisfactory for the study of the relations of the two kinds of cells (Figs. 134 and 135).

Lying near the basement membrane among the bases of the columnar epithelial cells are small spherical or irregular cells with dark nuclei. These are young epithelial cells which from their function are known as "replacing cells" (see page 65).

The PYLORIC GLANDS (Figs. 137 and 138) are simple branched tubular glands, several of which open into each of the *deep pyloric pits*. The glands, though short, are quite tortuous, so that in sections the tubules are seen cut mainly transversely or obliquely. In most of the pyloric glands but one type of cell is found. These resemble the chief cells of the fundus, but present a more uniform appearance, probably due to the absence of parietal cells. As in the fundus, "replacing cells"

lie between the bases of the columnar epithelial cells. Parietal cells are not always entirely absent, but occur here and there in the pyloric tubules, especially near the fundus.

The transition from fundus to pylorus is not abrupt, but is marked by a "transitional border zone," in which fundus and pyloric glands are intermingled.

In the transition zone between œsophagus and stomach are found glands which resemble the peptic glands, but acontain no parietal cells.

The STROMA (Figs. 134 and 137) or TUNICA PROPRIA, in which the glands are embedded, consists of mixed fibrillar and reticular connective tissue infiltrated with lymphoid cells. In the fundus of the stomach the glands are so closely packed that the stroma is reduced to thin strands, which pass up between the glands and also separate them from the muscularis mucosæ. In the pylorus the glands are more widely separated and the stroma is correspondingly greater in amount. In both fundus and pylorus thicker strands of stroma surround a number of gland tubules, thus separating them into

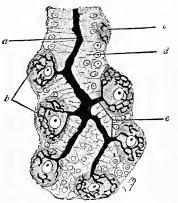


Fig. 136.—Longitudinal Section of Fundus of Gland from Pyloric End of Dog's Stomach. (Golgi method. See 4, p. 26.) *a*, Lumen of gland; *b*, intracellular canals in parietal cells; *e*, cut-off portion of parietal cell; *d*, chief cells; *e*, intercellular canals leading from lumen of gland to canals in parietal cells.

more or less well-defined groups. In addition to the diffuse lymphatic tissue of the stroma, closely packed aggregations of lymphoid cells are found in the shape of distinct nodules, known as "solitary follicles." These occur throughout the entire gastric mucosa, but are most numerous in the pylorus. The nodules are usually egg-shaped, their apices lying just beneath the epithelium, their bases resting upon the muscularis mucosæ. Less commonly they lie partly in the submucosa. Over the nodules the epithelium is more or less infiltrated with migratory leucocytes. Most of the nodules contain germinal centres, around which the lymphoid cells are more closely packed than elsewhere (see page 148).

The MUSCULARIS MUCOSÆ (Figs. 134 and 137, m) may consist of a single layer of smooth muscle with cells arranged longitudinally or obliquely, or there may be two distinct layers, an inner circular and an outer longitudinal. From the muscularis mucosæ

single cells and groups of cells extend into the stroma between the gland tubules.

2. The submucosa consists of connective tissue, loosely arranged, many elastic fibres, and some fat. It contains the larger blood-vessels and nerves, including the plexus of Meissner (p. 238).

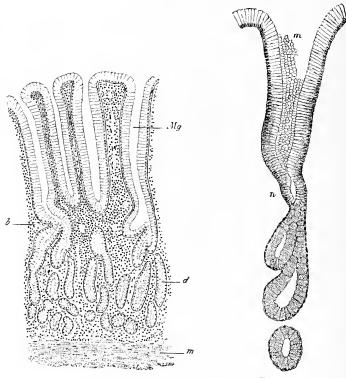


FIG. 137. FIG. 138.

Fig. 137.—Vertical Section through Mucous Membrane of Pyloric End of Stomach.  $\times$  85. (Kölliker.) Mg, Gastric pit; b, blood-vessel in stroma; d, longitudinal section of body of gland; m, muscularis mucosæ.

Fig. 138.—Pyloric Gland from Vertical Section through Wall of Dog's Stomach. (Ebstein.) m, Gastric pit in which are seen some transversely cut cells; n, neck of gland; f, fundus cut transversely.

3. The muscular coat is usually described as consisting of three layers, an *inner oblique*, a *middle circular*, and an *outer longitudinal*.

In the fundus the muscle bundles run in various directions so that the division of the muscular coat into layers having definite directions can be made out only in the pylorus. Here the inner and middle layers are thickened to form the sphincter pylori. In the connective tissue which separates the groups of muscle cells are collections of sympathetic nerve cells and fibres which while much less distinct are analogous to Auerbach's plexus of the intestine.

4. The serous coat consists of a layer of loosely arranged connective tissue covered by a single layer of mesothelium.

#### TECHNIC.

- (1) Remove a human stomach (not more than two or three hours after death) or that of a recently killed dog. Open along the lesser curvature, and carefully remove the excess of mucus by washing with normal saline. Cut pieces through the entire thickness of the wall, one from the fundus and one from the pylorus; pin out, mucus membrane side up, on pieces of cork, fix in formalin-Müller's fluid (technic 5, p. 7) or in Zenker's fluid (technic 9, p. 8), and harden in alcohol. Sections are cut as thin as possible, care being taken that the plane is such that the glands are cut longitudinally, stained with hæmatoxylin-eosin (technic 1, p. 18), and mounted in balsam.
- (2) Instead of removing pieces of stomach and pinning them out on cork, as suggested in the preceding technic, the entire stomach may be filled with the fixative, the ends being tied, and then placed in a large quantity of the fixing fluid. After fixation, pieces are removed and hardened in graded alcohols. If this method is used, great care must be taken not to overdistend the organ, only very moderate distention being desirable. Further treatment is the same as in the preceding technic (1).
- (3) For comparison of resting with active gastric cells, preparations should be made from the stomach of an animal that has been for from twenty-four to forty-eight hours without food, and from a stomach during active digestion. Fix in Zenker's fluid as in technic (1), above. Examine unstained sections and sections stained with hæmatoxylin-eosin.
- (4) Sections through the junction of œsophagus and stomach and through the junction of stomach and duodenum furnish instructive pictures. They should be prepared as in technic (1).
- (5) For the study of the distribution of the blood-vessels sections of an injected stomach should be made. This is best accomplished by selecting a small animal, such as a rat or guinea-pig, and injecting in toto through the ascending aorta, or by injecting only the hind part of the animal through the abdominal aorta. Technic, p. 22.

#### III. THE MIDGUT.

#### The Small Intestine.

On passing from stomach to small intestine the rugæ of the former disappear, but are replaced by much more definite foldings of the mucosa, the *valvulæ conniventes* (Fig. 140). These folds involve the entire thickness of the mucous membrane and part of the submucosa. They are in general parallel to one another, and pass in a circular or

oblique manner, partly around the lumen of the gut. The entire surface of the intestine, including the valvulæ, is studded with minute projections just visible to the naked eye, and known as *villi* (Figs. 141 and 142). These involve only the epithelium and stroma, although they also contain some muscular elements derived from the muscularis mucosæ. The villi differ in shape in the different parts of the small intestine, being leaf-shaped in the duodenum, rounded in the jejunum, club-shaped in the ileum. The valvulæ conniventes and the villi are characteristic of the small intestine. It is important to note that

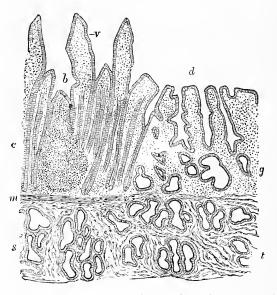


Fig. 139.—Section through Junction of Pylorus and Duodenum. (Klein.) v, Villi of duodenum; d, stomach, showing gastric pits; b, apex of a solitary lymph nodule; c, crypt of Lieberkühn; s, secreting tubules of Brunner's glands; g, pyloric glands; t, tubules of Brunner's glands in submucosa of stomach; m, muscularis mucosæ.

while the pits of the stomach are depressions in the mucous membrane, the intestinal villi are definite projections above its general surface (Fig. 139).

The wall of the intestine consists of the same four coats described as constituting the wall of the stomach, *mucosa*, *submucosa*, *muscularis*, and *serosa*.

1. **The mucosa,** as in the stomach, is composed of a lining *epithe-lium*, *stroma*, *glands*, and *muscularis mucosa*. Of these the epithelium, the stroma, and cells from the muscularis mucosæ are concerned in the formation of the villi.

The VILLUS consists of a central core—a fold of the stroma—of

mixed fibrous and reticular tissue infiltrated with lymphoid cells, and of a covering *epithelium*.

The epithelium is of the simple columnar type. The cells are high and have thickened striated free borders (Figs. 143 and 144). These contiguous thickened free borders unite to form a distinct membrane, the cuticular membrane (Fig. 144, c). Scattered among the columnar cells are numerous mucous or goblet cells (Figs. 143 and 144, b). The goblet cells are derived from the columnar cells, and

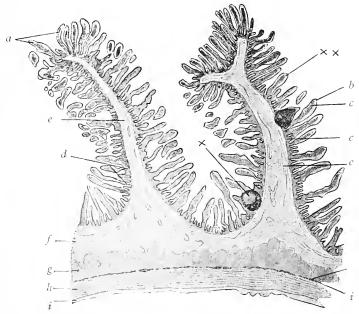
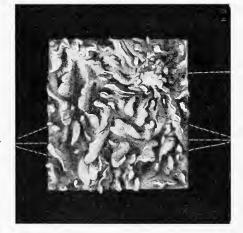


FIG. 140.—Vertical Longitudinal Section of Human Jejunum ( $\times$  16) (Stöhr), including two valvulæ conniventes. a, Villi, in many of which the stroma has shrunken away from the epithelium leaving a clear space,  $\times$   $\times$ . Lying free in the lumen of the gut are seen sections of villi cut in various directions. b, Epithelium; c, stroma: d, crypts of Lieberkühn;  $\times$ , solitary lymph nodule with germinal centre: c, tissue of submucosa forming centre of one of the valvulæ conniventes; f, submucosa; g, inner circular layer of muscle; h, outer longitudinal layer of muscle; h, Auerbach's plexus; g, serous coat.

vary in appearance according to the amount of secretion which they contain. A cell at the beginning of secretion contains only a small amount of mucus near its free border. As secretion increases the mucus gradually replaces the cytoplasm until the latter is represented only by a crescentic mass containing a flattened nucleus and pressed against the basement membrane. The cell now discharges its mucus upon the free surface. The goblet cells possess no thickened border, appearing, when seen from the surface, as openings surrounded on all

sides by the cuticulæ of the adjacent columnar cells. Small spherical cells with deeply staining nuclei are found in varying numbers among the epithelial cells. These are so-called wandering cells, migratory



Lymph nodules

Mouths of crypts.

Villi.

Fig. 141.—Surface View of Small Intestine near upper end, showing villi and one solitary lymph nodule. × 12. (Spalteholz).

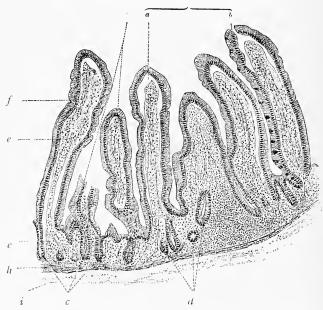


Fig. 142.—Vertical Section through Mucous Membrane of Human Jejunum.  $\times$  80. (Stöhr.) u and b, Artifacts due to shrinkage; c, intestinal crypts (Lieberkühn); d, oblique and transverse sections of crypts; e, stroma; f, epithelium; g, tangentially cut villi; h, muscularis mucosae; i, submucosa.

leucocytes, from the underlying stroma (Figs. 143, h, and 144, l). Other cells with dark-staining nuclei, "replacing cells," are found between the bases of the columnar cells (pages 65 and 220).

In addition to the connective-tissue and lymphoid cells, which constitute the main bulk of the villus core (Figs. 143 and 144), isolated smooth muscle cells derived from the muscularis mucosæ occur, run-

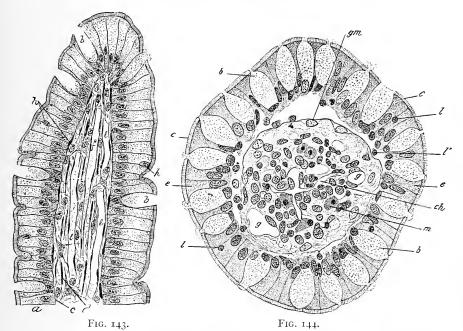


Fig. 143.—Longitudinal Section of Villus from Small Intestine of Dog. (Piersol.) a, Columnar epithelium; b, goblet cells; h, leucocytes; c, basement membrane; d, core of villus; e, blood-vessels; f, lacteal.

Fig. 144.—Cross-section of a Villus of Human Small Intestine.  $\times$  530. (Kölliker.) The stroma of the villus has shrunken away from the epithelium. b, Goblet cell;  $\epsilon$ , cuticula showing striations; e, columnar epithelial cell: gm, basement membrane with nuclei; l, leucocyte in epithelium; l', leucocyte just beneath epithelium; m, large leucocyte in stroma; ch, central chyle vessel; g, blood-vessel.

ning in the long axis of the villus. A single lymph or chyle vessel (Fig. 143, f; 144, ch) with distinct endothelial walls traverses the centre of each villus, ending at its tip in a slightly dilated blind extremity. As it is usually seen collapsed, it appears as two closely approximated rows of flat cells with bulging nuclei. The capillaries of the villus lie for the most part away from the chyle vessel, just beneath the basement membrane (Fig. 143, e; 144, g).

From the depths of the depressions between the villi, simple tubular

glands—glands or crypts of Lieberkühn (Figs. 142 and 145)—extend down through the stroma as far as the muscularis mucosæ. These crypts are lined with an epithelium similar to and continuous with that covering the villi. The cells are, however, lower, and there are fewer goblet cells. In addition to these cells there are also found in the depths of the crypts of Lieberkühn peculiar coarsely granular cells, the cells

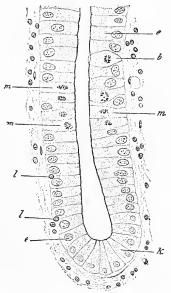


Fig. 145.—Longitudinal Section of Fundus of Crypt of Lieberkühn. ×530. (Kölliker.) b, Goblet cell showing mitosis; e, epithelial cell; k, cell of Paneth; l, leucocyte in epithelium; m, mitosis in epithelial cell. Surrounding the crypt is seen the stroma of the mucous membrane.

of Paneth (Fig. 145, k). They are found in man and in rodents, but do not occur in the carnivora. They probably produce a specific secretion, the nature of which is unknown.

The *stroma*, besides forming the centres of the villi, fills in the spaces between the crypts of Lieberkühn and between the latter and the muscularis mucosæ. In places the lymphoid cells are closely packed to form distinct nodules or "solitary follicles," such as are found in the stomach (see page 221).

Pever's Patches (agminated follicles) (Fig. 146).—These are groups of lymph nodules found mainly in the ileum, especially near its junction with the jejunum. They always occur on the side of the gut opposite to the attachment of the mesentery. Each patch consists of from ten to seventy nodules, so arranged that the entire patch has a generally oval shape, its long diameter lying lengthwise of the intestine. The nodules of which

a patch is composed lie side by side. Their apices are directed toward the lumen and project almost through the mucosa, being uncovered by villi, a single layer of columnar epithelium alone separating their surfaces from the lumen of the gut. The bases of the nodules are not confined to the stroma, but usually spread out in the submucosa. The relation of the patch to the stroma and submucosa can be best appreciated by following the course of the muscularis mucosæ. This is seen to stop abruptly at the circumference of the patch, appearing throughout the patch as isolated groups of smooth muscle cells. The nodules rarely remain distinct, but are confluent

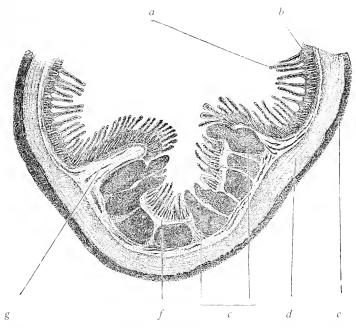


Fig. 146.—Transverse Section of Cat's Small Intestine through a Peyer's Patch. (Stöhr.) a, Villi; b, crypts; c, longitudinal muscle layer; d, circular muscle layer; e, lymph nodules; f, muscularis mucosæ; g, submucosa.

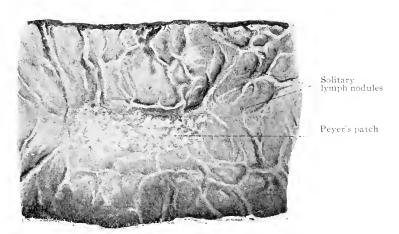


Fig. 147.—Surface View of Mucous Membrane of Small Intestine (Ileum), showing Peyer's patch (Spalteholz).

with the exception of their apices and bases. It should be noted that both solitary nodules and Peyer's patches are structures of the mucosa, and that their presence in the submucosa is secondary.

THE MUSCULARIS MUCOS. E (Figs. 142 and 148) consists of an inner circular and an outer longitudinal layer of smooth muscle.

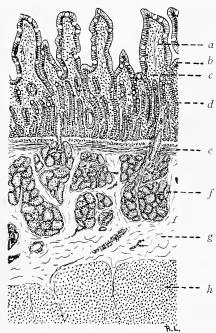


FIG. 148.—From Vertical Longitudinal Section of Cat's Duodenum to show Brunner's Glands. (Larrabee.) a, Villus; b, epithelium; c, stroma; d, glands; e, muscularis mucosæ; f, Brunner's glands; g, submucosa; h, circular muscle layer.

2. The submucosa (Figs. 140, 142, 148) consists, as in the stomach, of loosely arranged connective tissue and contains the larger blood-vessels. It is free from glands except in the duodenum, where it contains the glands of Brunner (Fig. 148). These are branched tubular glands lined with a granular columnar epithelium similar to that of the pyloric The ducts are also glands. lined with simple columnar epithelium. They pass through the muscularis mucosæ and empty either into a crypt of Lieberkühn or on the surface between the villi. Brunner's glands frequently occur in the pylorus, and it is not uncommon for the pyloric glands to extend downward somewhat into the duodenum. Meissner's

plexus of nerve fibres, mingled with groups of sympathetic ganglion cells, lies in the submucosa (see page 238).

- 3. The muscular coat (Figs. 140 and 148) consists of two well-defined layers of smooth muscle, an inner circular and an outer longitudinal. Connective-tissue septa divide the muscle cells into groups or bundles, while between the two layers of muscle is a connective-tissue septum which varies greatly in thickness at different places and contains a plexus of nerve fibres and sympathetic ganglion cells known as the plexus of Auerbach (see page 238).
- 4. The serous coat consists as in the stomach of loose connective tissue covered by a single layer of mesothelium.

## IV. THE ENDGUT.

## The Large Intestine.

The wall of the large intestine consists of the same four coats which have been described as constituting the walls of the stomach and small intestine, *mucous*, *submucous*, *muscular*, and *serous*.

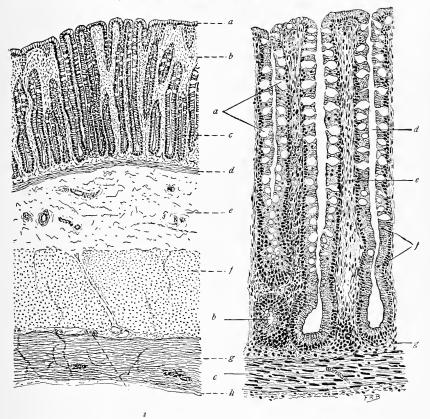


Fig. 149. Fig. 150. Fig. 149.—From Vertical Longitudinal Section of Cat's Large Intestine. (Larrabee.) a, Epithelium; b, stroma; c, fundus of gland; d, muscularis mucosæ; e, submucosa; f, cir-

cular muscle layer; g, longitudinal muscle layer; h, serous coat; i, Auerbach's plexus. Fig. 150.—From Vertical Longitudinal Section of the Mucous Membrane of the Human Large Intestine. (Technic 1, p. 241.) a, Mucous (goblet) cells; b, fundus of a gland cut obliquely; c, muscularis mucosæ; d, lumen of a gland cut longitudinally; c, stroma between the glands; f, leucocytes in the epithelium; g, stroma between fundi of glands and muscularis mucosæ.

1. The mucous membrane has a comparatively smooth surface, there being neither pits as in the stomach nor villi as in the small intestine (Fig. 149). The glands are of the simple tubular variety,

are considerably longer than those of the small intestine, are almost straight, and extend through the entire thickness of the stroma. Owing to the closeness with which the gland tubules are packed, the amount of stroma is usually small. The surface cells (Fig. 149, a) are very high and narrow, with small, deeply placed nuclei, and are not usually intermingled with goblet cells. Passing from the surface down into the glands, the cells become somewhat lower and goblet cells become numerous (Fig. 150, a and d). Both superficial and deep cells rest upon a basement membrane similar to that in the small intestine. The stroma also, though less in amount, is similar in structure to the stroma of the small intestine.

The MUSCULARIS MUCOS. $\pm$  (Fig. 150, c) consists of an inner circular and an outer longitudinal layer of smooth muscle.

- 2. The submucosa (Fig. 149, e) consists of loosely arranged connective tissue. It contains large blood-vessels and the nerve plexus of Meissner (see page 238). Solitary lymph follicles occur throughout the mucous membrane of the large intestine. While properly considered as structures of the stroma from which they originate, the follicles lie mainly in the submucosa. (For details of structure see page 148.)
- 3. Of the muscularis (Fig. 149) the inner circular layer only is complete, the muscle tissue of the external longitudinal coat being arranged mainly as three strong, flat, longitudinal bands, the lineæ coli. Between these bands the longitudinal muscular coat is either very thin or entirely absent. In the connective tissue, lying to the outer side of the circular muscle coat, is the nerve plexus of Auerbach. (For details see page 238.)
- 4. The serous coat consists, as in the stomach and small intestine, of loose connective tissue covered by a single layer of mesothelium.

## THE VERMIFORM APPENDIX.

The vermiform appendix is a diverticulum from the large intestine. Its walls are continuous with those of the latter, and closely resemble them in general structure. There are the same four coats, *mucous*, *submucous*, *muscular*, and *serous*.

1. The mucous membrane (Fig. 151) consists of epithelium, glands, stroma, and muscularis mucosæ. The *epithelium* resembles that of the large intestine. The glands vary in number, but are usually much less closely packed than in the large intestine. They are most

numerous in the appendices of infants and children. The *gland tubules* (Fig. 151, *j*) are usually rudimentary, but in most cases have the same structure as the intestinal glands, and are evidently functional as they contain mucous cells in all stages of secretion. In consequence of the wider separation of the tubules the *stroma* is more abundant than in the large intestine, but has the same structure. The *muscularis* 

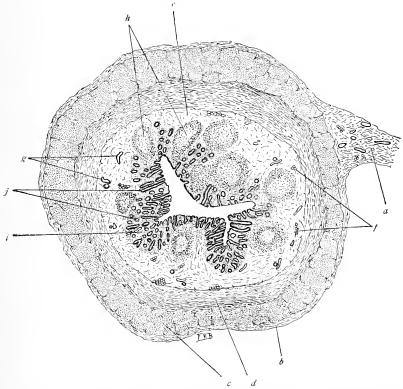


Fig. 151.—Transverse Section of Human Vermiform Appendix. (Technic 2, p. 241.) a, Mesoappendix; b, serous membrane (serosa); c, outer longitudinal muscle layer; d, inner circular muscle layer; e, submucosa; f, groups of fat cells in submucosa; g, blood-vessels in submucosa; g, lymph nodules; g, stroma; g, glands opening into lumen and cut in various planes; muscularis mucosæ not present.

mucosæ is usually fairly distinct as a thin circularly disposed band of smooth muscle cells just beneath the stroma. It is not always present. In some cases the mucosa as such is practically absent, being replaced by fibrous tissue. This condition is especially common after middle age, and may or may not be associated with obliteration of the lumen.

2. The submucosa (Fig. 151, e) is similar to that of the intestine.

- 3. The muscular coat varies greatly, both as to thickness and as to the amount of admixture of fibrous tissue. The inner circular layer (Fig. 151, d) is usually thick and well developed. The outer longitudinal layer (Fig. 151, c) differs from that of the large intestine in having no arrangement into lineæ, the muscle tissue forming a continuous layer. Less commonly a more or less marked tendency to an arrangement of the cells of the longitudinal coat into bundles, between which the outer coat is thin or wanting, is observed.
  - 4. The serosa has the usual structure of peritoneum.

The lymph nodules (Fig. 151, h) constitute the most conspicuous feature of the appendix. They lie mainly in the submucosa. In children and young adults the nodules are oval or spherical; in later life somewhat flattened. The nodules may be entirely distinct, or may be arranged as in a Peyer's patch with distinct apices and bases, but with their central portions confluent. The muscularis mucosæ either passes through the superficial portions of the nodules, or, where they are separated from the lumen, passes over them.

The distribution of **blood-vessels**, **lymphatics**, and **nerves** is similar to that in the large intestine.

## The Rectum.

- 1. The mucous membrane of the rectum has a structure similar to that of the large intestine. The glands are longer and the mucosa is consequently somewhat thicker. In the lower part of the rectum definite longitudinal foldings of the mucosa occur, the so-called columnæ rectales. A change in the character of the mucous membrane begins at the upper end of the columnæ rectales. Here the simple columnar epithelium of the gut passes over into a stratified squamous epithelium, beneath which is a papillated stroma. The glands continue for a short distance beyond the change in the epithelium, but soon completely disappear. At the anus there is a transition from mucous membrane to skin similar to that described as occurring at the margin of the lips (page 193).
- 2. The submucosa is similar in structure to that of the large intestine.

The muscularis of the rectum differs from that of the large intestine in that the longitudinal layer is continuous and thick.

The serous coat is absent in the lower part of the rectum, being replaced by a fibrous connective-tissue layer, which connects the rectum with the surrounding structures.

## The Peritoneum, Mesentery, and Omentum.

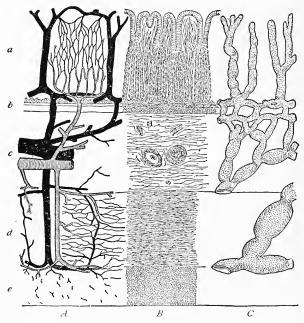
The peritoneum (see also p. 144) is a serous membrane which lines the walls of the abdomen (parietal peritoneum) and is reflected over the contained viscera (visceral peritoneum). It consists of two layers, a connective-tissue stroma and mesothelium. The stroma consists of loosely arranged connective-tissue bundles, which interlace in a plane parallel to the surface. There are numerous elastic fibres, especially in the deeper layer of the parietal peritoneum. There are comparatively few connective-tissue cells. The mesothelium consists of a single layer of flat polygonal cells with bulging nuclei. The cells have irregular wavy outlines, which are easily demonstrated with silver nitrate (Fig. 26). The shape of the cells varies considerably according to the direction in which the tissues are stretched. Over some parts, e.g., the liver and intestine, the peritoneum or serosa is thin and very closely attached. In places where the peritoneum is freely movable, a considerable amount of loose connective tissue, rich in elastic fibres and containing varying numbers of fat cells, connects the peritoneum with the underlying tissue. This is known as the "subserous tissue." The peritoneum is well supplied with blood-vessels and lymphatics. The former give rise to a rich capillary network.

The *mesentery* is a sheet of loosely arranged connective tissue covered with peritoneum. It is reflected from the post-abdominal wall to the viscera, and serves to carry to these organs their blood-vessels, lymphatics, and nerves. In the case of the stomach, duodenum, and large intestine, the mesentery is comparatively short, and the organs are therefore quite firmly fixed to the abdominal wall. In the case of the small intestine the mesentery is long and the intestine, therefore, freely movable. The mesentery is richly supplied with lymph nodes and there is usually a considerable amount of fat. From the mesentery, the peritoneum passes over to and envelops the viscera.

The *omentum* (Fig. 26) is a sheet of tissue which passes from the liver to the lesser curvature of the stomach (gastro-hepatic omentum) to which it is attached, and from the greater curvature of the stomach to the transverse colon (greater omentum). It is similar in structure to the mesentery, and contains usually much fat and many lymph nodes. Its connective-tissue bundles are arranged in networks, the strand and meshes of which vary greatly in size and shape. The strands are covered by a single layer of mesothelium.

## BLOOD-VESSELS OF THE STOMACH AND INFESTINES.

The arteries reach the gastro-intestinal canal through the mesentery and pass through the muscular coats to the submucosa, where they form an extensive plexus of large vessels (Heller's plexus) (Fig. 152, c). Within the muscular coats the main arteries give off small branches to the muscle tissue. From the plexus of the submucosa two main sets of vessels arise, one passing outward to supply the mus-



F16. 152.—Scheme of Blood-vessels and Lymphatics of Stomach.  $\times$  70. (Szymonowicz, after Mall.) a, Mucous membrane; b, muscularis mucosæ; c, submucosæ; d, inner circular muscle layer; e, outer longitudinal muscle layer; A, blood-vessels; B, structure of coats; C, lymphatics.

cular coats, the other inward to supply the mucous membrane (Fig. 152). Of the former the larger vessels pass directly to the intermuscular septum, where they form a plexus from which branches are given off to the two muscular tunics. A few small branches from the larger recurrent vessels also supply the inner muscular layer. Of the branches of the submucosa plexus which pass to the mucous membrane, the shorter supply the muscularis mucosæ, while the longer branches pierce the latter to form a capillary plexus among the glands of the stroma. From the capillaries small veins take origin which pierce the muscularis

mucosæ and form a close-meshed venous plexus in the submucosa (Fig. 152). These in turn give rise to larger veins, which accompany the arteries into the mesentery.

In the small intestine the distribution of the blood-vessels is modified by the presence of the villi (Fig. 153). Each villus receives one small artery, or, in the case of the larger villi, two or three small arteries.

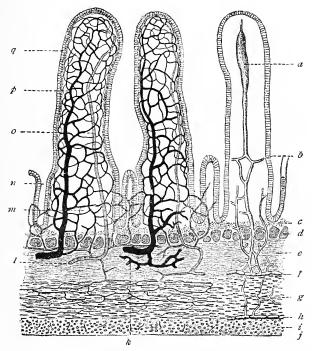


Fig. 153.—Scheme of Blood-vessels and Lymphatics of Human Small Intestine. (From Böhm and von Davidoff, after Mall.) a, Central lacteal of villus; b, lacteal: c, stroma; d, muscularis mucosa; e, submucosa; f, plexus of lymph vessels; g, circular muscle layer; h, plexus of lymph vessels; i, longitudinal muscle layer; j, serous coat; k, vein; l, artery; m, base of villus; n, crypt; o, artery of villus; p, vein of villus; q, epithelium.

The artery passes through the long axis of the villus close under the epithelium to its summit, giving off a network of fine capillaries, which for the most part lie just beneath the epithelium. From these, one or two small veins arise which lie on the oposite side of the villus from the artery.

### Lymphatics of the Stomach and Intestine.

Small lymph or chyle capillaries begin as blind canals in the stroma of the mucous membrane among the tubular glands (Fig. 152).

In the small intestine a lymph (chyle) capillary occupies the centre of the long axis of each villus, ending in a blind extremity beneath the epithelium of its summit (Fig. 153). These vessels unite to form a narrow-meshed plexus of lymph capillaries in the deeper part of the stroma, lying parallel to the muscularis mucosæ. Vessels from this plexus pass through the muscularis mucosæ and form a wider meshed plexus of larger lymph vessels in the submucosa. A third lymphatic plexus lies in the connective tissue which separates the two layers of muscle. From the plexus in the submucosa, branches pass through the inner muscular layer, receive vessels from the intermuscular plexus, and then pierce the outer muscular layer to pass into the mesentery in company with the arteries and veins.

## NERVES OF THE STOMACH AND INTESTINES.

The nerves which supply the stomach and intestines are mainly non-medullated sympathetic fibres. They reach the intestinal walls through the mesentery. In the connective tissue between the two

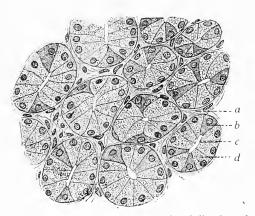


Fig. 154.—Section through Glands of Fundus of Human Stomach in Condition of Hunger. × 500.
(Böhm and von Davidoff.) a, Stroma; b, parietal cell; c, lumen; d, chief cell.

layers of muscle, these fibres are associated with groups of sympathetic ganglion cells to form the plexus myentericus or plexus of Auerbach. The dendrites of the ganglion cells interlace, forming a large part of the plexus. The axones are grouped together in small bundles of non-medullated fibres, which pass into the muscular coats, where they form intricate plexuses, from which are given off club-shaped termi-

nals to the smooth muscle cells. From Auerbach's plexus fibres pass to the submucosa, where they form a similar but finer-meshed, more delicate plexus, also associated with groups of sympathetic ganglion cells, the *plexus of Meissner*. Both fibres and cells are smaller than those of Auerbach's plexus. From Meissner's plexus delicate fibrils pass to their terminations in submucosa, muscularis mucosæ, and mucous membrane.

## SECRETION AND ABSORPTION.

The secretory activities of epithelial cells have already been mentioned (page 186). The epithelium of the gastro-intestinal tract must be considered as having two main functions: (1) The secretion of substances necessary to digestion; and (2) the absorption of the products of digestion.

(1) Secretion.—The production of mucus takes place in the mucous or goblet cell, which, as already mentioned, probably represents a differentiation of the ordinary columnar epithelial cell. The chief

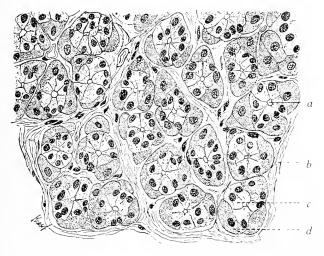


Fig. 155.—Section through Glands of Fundus of Human Stomach during Digestion  $\times$  500. (Böhm and von Davidoff.) a, Lumen; b, stroma; c, chief cell; d, parietal cell

cells, "peptic cells," of the stomach glands are large and clear during fasting, become granular and cloudy with the onset of digestion, and smaller with loss of granules during the digestive process. As activity of the chief cells (Fig. 155) is coincident with an increase in the pepsin found in the gastric mucosa, it is probable that these cells produce pepsin, and that the granules represent some stage in the elaboration of the ferment. As their name of "acid cells" would indicate, the parietal cells were considered the source of the hydrochloric acid of the stomach. While doubt still exists as to the function of these cells, recent investigations make it probable that it is not the secretion of hydrochloric acid. The cells of Brunner's glands undergo changes during digestion, which are quite similar to those described as occurring in the chief cells of the stomach glands, and are probably also con-

cerned in the production of pepsin. The only function of the intestinal crypts which has yet been determined is the secretion of mucus. The possibility that certain cells of the crypts of the small intestine produce a specific secretion has been mentioned (page 228).

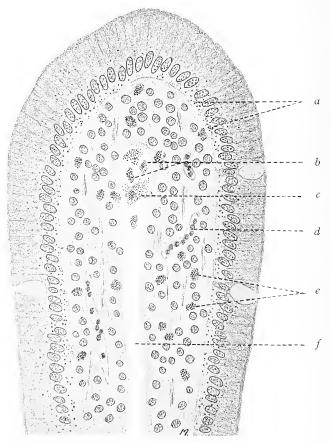


Fig. 156.—Fat Absorption. Longitudinal section of villus of cat's small intestine, three hours after feeding.  $\times$  350. Osmic acid. a, Fat droplets in epithelial cells; b, fat droplets in leucocytes in stroma; c, fat droplets in leucocytes within lacteal; d, fat droplets free in lacteal; e, capillary containing blood cells; f, central lacteal of villus.

(2) ABSORPTION OF FAT.—While various other products of digestion are absorbed by the intestine, the absorption of fat is the one most casily observed. After feeding fat, fatty acids, or soaps, fat globules are found to have penetrated the intestinal mucosa, and may be seen in (a) the epithelial cells, (b) the leucocytes, and (c) the lacteals of the villi (Fig. 156). Fat globules are never seen in the thickened free borders of the cells. Hence it seems probable that the fat before passing through

this part of the cell becomes split up into glycerin and fatty acids which are united again to form fat within the protoplasm of the cell. Leucocytes containing fat globules are seen throughout the stroma. Within the lacteals are found fat-containing leucocytes and free fat droplets of various size. It would thus seem probable that the process of fat absorption consists in: (1) The passage of glycerin and fatty acids through the cell borders; (2) their reunion in the cell to form fat; (3) the transference of these fat globules to leucocytes; which (4) carry them to the lacteals. In the lacteals the fat is probably set free by disintegration of the leucocytes.

#### TECHNIC.

(1) The technic for the small and large intestines and rectum is the same as for the stomach. Accurate fixation of the villi is difficult, there being usually some shrinkage of the connective tissue of the core away from the epithelium.

A longitudinal section should be made through the junction of small and large intestine, showing the transition from the villus-covered surface of the former to the comparatively smooth surface of the latter.

To show Brunner's glands a section of the duodenum is required.

To show the varying shapes of the villi in the different regions, sections should also be made of the jejunum and ileum.

Solitary follicles may usually be seen in any of the above sections.

A small Peyer's patch, together with the entire thickness of the intestinal wall, should be removed, treated as above, stained with hæmatoxylin-eosin (technic 1, p. 18), or with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19), and mounted in balsam.

- (2) A vermiform appendix, as fresh as possible, should be cut transversely into small pieces, fixed in formalin-Müller's fluid (technic 5, p. 7), and hardened in alcohol. Thin transverse sections are made through the entire wall, stained with hæmatoxylin-eosin or hæmatoxylin-picro-acid-fuchsin, and mounted in balsam.
- (3) Fat Absorption.—For the purpose of studying the process by which fat passes from the lumen of the gut into the chyle vessels, an animal should be killed at the height of fat absorption. A frog fed with fat bacon and killed two days later, a dog fed with fat meat, or a cat with cream and killed after from four to eight hours, furnishes good material. Usually if the preparation is to be successful, the lumen of the intestine will be found to contain emulsified fat and the lacteals of the mesentery are seen distended with chyle. Extremely thin slices of the mucous membrane of the small intestine are fixed in 1-per-cent. osmic acid or in osmium bichromate solution (5-per-cent. aqueous solution potassium bichromate and 2-percent. aqueous solution osmic acid—equal parts) for twelve to twenty-four hours, after which they are passed rather quickly through graded alcohols. Sections should be thin and mounted, either unstained or after a slight cosin stain, in glycerin.
- (4) The blood-vessels of the stomach are best studied in injected specimens. (See page 22.)

# The Larger Glands of the Digestive System.

The smaller tubular glands which form a part of the mucous membrane and submucosa of the alimentary tract have been already described. Certain larger glandular structures, the development of which is similar to that of the smaller tubules but which come to lie wholly without the alimentary tract, connected with it only by their main excretory ducts, and which are yet functionally an important part of the digestive system, remain to be considered.

These are:

- 1. The salivary glands  $\begin{cases} (a) & \text{The parotid.} \\ (b) & \text{The sublingual.} \\ (c) & \text{The submaxillary.} \end{cases}$
- 2. The pancreas.
- 3. The liver.

# The Salivary Glands.

The salivary glands are all compound tubular glands. In man the parotid is serous; the sublingual and submaxillary, mixed serous and mucous (page 194). Only the general structure of these glands is here described, the minute structure of mucous and serous glands having been described on page 194.

Each gland consists of gland tissue proper and of a supporting connective-tissue framework. The framework consists of a connective-tissue capsule which encloses the gland, but blends externally with and attaches the gland to the surrounding structures. From the capsule trabeculæ pass into the gland, subdividing it into lobes and lobules. The gland tissue proper consists of systems of excretory ducts opening into secretory tubules, all being lined with one or more layers of epithelial cells. Each gland has one main excretory duct. This divides into branches—interlobar ducts—which run to the lobes in the connective tissue which separates them. The interlobar ducts give rise to branches which, as they pass to the lobules in the interlobular connective tissue, are known as interlobular ducts. From the latter, branches enter the lobules-intralobular ducts-and split up into terminal secreting tubules which constitute the bulk of the lobule. As the smaller intralobular ducts are lined with cells of a secretory type, and probably take part in the elaboration of the secretion of the gland, they have been called salivary or secreting tubules. These, in the submaxillary and parotid glands, open into tubules which have a narrow lumen and are lined with low or flat epithelium; lying between the secreting tubules and the terminal tubules, they are known as *intercalated or intermediate tubules*. From the interlobular connective tissue delicate extensions pass into the lobules, separating the gland tubules. The glandular tissue is known as the *parenchyma* of the gland in contradistinction to the connective or *interstitial tissue*.

The parotid gland in man, dog, cat, and rabbit is a purely serous gland. Its duct system is complex. The main excretory duct (Stenoni) is lined by two layers of columnar epithelium resting upon a

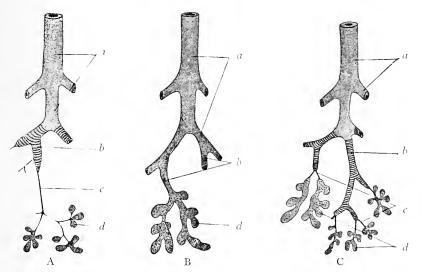
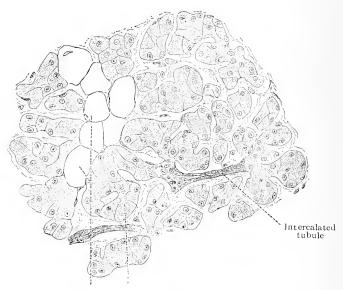


Fig. 157.—Diagrams to illustrate the Structure of the Salivary Glands. (Stöhr.) A, Parotid; B, sublingual; C, submaxillary. a, Excretory duct; b, secreting tubule; c, intermediate tubule; d, terminal tubule.

distinct basement membrane. The main duct divides into numerous branches, which in turn give rise to the *secreting* or *salivary* tubules. These are continuous with the long narrow *intermediate tubules*, from each of which are given off a number of short *terminal tubules* (Figs. 157, A and 158). The two-layered epithelium of the main duct becomes reduced in the smaller ducts to a single layer of columnar cells. The salivary tubules are lined with high columnar epithelium, the bases of the cells showing distinct longitudinal striations. In the intermediate tubule the epithelium is flat, sometimes spindle-shaped. The terminal tubules are lined with serous cells (page 194). The connective tissue usually contains a considerable number of fat cells.

The sublingual gland is a mixed gland in man, dog. cat, and

rabbit. The duct system is less complex than in the parotid. The main duct (Bartholini) sends off branches which are continuous with tubules, showing a few secretory mucous cells. These open directly into the *terminal tubules* which are convoluted and vary greatly in diameter (Fig. 157, B). The excretory duct is like that of the parotid gland, lined with a two-layered columnar epithelium resting upon a basement membrane. In the smaller ducts the epithelium is reduced to a single layer of columnar cells. There are no intermediate tubules.



Fat cells Terminal tubule

Fig. 158.—Section of Human Parotid Gland. × 252 (Stöhr). The narrow lumina of the terminal tubules do not show in this figure.

The terminal tubules are lined with both serous and mucous cells (page 194). The crescents of Gianuzzi (page 195) are numerous and large. The connective tissue of the gland contains many lymphoid cells (Fig 159).

Near the sublingual gland is a group of some 5 to 20 simple tubular glands. Their terminal tubules are lined almost wholly with mucous cells. This group of tubules has been designated the "sublingualis minor."

The submaxillary gland is also a mixed gland in man, dog, cat, and rabbit. In complexity of its duct system it stands between the parotid and the sublingual (Fig. 157). The main duct (Wharton's) has not only a two-layered epithelial lining resting upon a basement

membrane, but is distinguished by a richly cellular stroma and a thin layer of longitudinally disposed smooth muscle. Branches of the main duct open into long secreting tubules which communicate with the terminal tubules by means of short narrow intermediate tubules (Fig. 157, C). The secretory tubules are lined as in the parotid with columnar cells whose bases are longitudinally striated. These cells usually contain more or less yellow pigment. The intermediate tubules have a low cuboidal or flat epithelium. Most of the end tubules contain

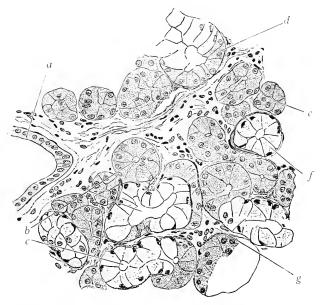


FIG. 159.—Section of Human Sublingual Gland.  $\times$  252. (Stöhr). a, Excretory duct; b, lumina of serous and mucous tubules; c, mucous tubule; d, demilune; e, serous tubule; f, cross section mucous tubule; g, interstitial connective tissue.

serous cells only (page 194). The crescents of the mucous tubules (page 195) are less numerous and smaller than those in the sublingual, consisting as a rule of only from one to three cells (Fig. 160).

**Blood-vessels.**—The larger arteries run in the connective-tissue septa with the ducts, giving off branches which accompany the divisions of the ducts to the lobules, where they break up into capillary networks among the tubules. These give rise to veins which accompany the arteries.

The **lymphatics** begin as minute capillaries in the connective tissue separating the terminal tubules. These empty into larger lymph vessels which accompany the arteries in the septa.

The nerves of the salivary glands are derived from both cerebrospinal and sympathetic systems, and consist of both medullated and non-medullated fibres. The medullated fibres are afferent, probably the dendrites of cells located in the geniculate ganglion. Small bundles of these fibres accompany the ducts. Single fibres leave the bundles, lose their medullary sheaths, and form a non-medullated subepithelial plexus, from which delicate fibrils pass to end freely among the epithelial cells. Efferent impulses reach the gland through the sympathetic. The fibres are axones of cells situated in small

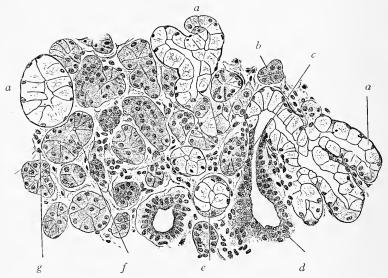


Fig. 160.—Section of Human Submaxillary Gland.  $\times$  252. (Stöhr.) a, Mucous tubule; b, serous tubule; c, intermediate tubule; d, "secretory" tubule; e, demilune; f, lumen; g, interstitial connective tissue.

peripheral ganglia; the cells sending axones to the submaxillary lying upon the main excretory duct and some of its larger branches; those sending axones to the sublingual being situated in a small ganglion—the sublingual—lying in the triangular area bounded by the chorda tympani, the lingual nerve, and Wharton's duct; those supplying the parotid probably being in the otic ganglion. Axones from these cells enter the glands with the excretory duct and follow its branchings to the terminal tubules, where they form plexuses beneath the epithelium. From these, terminals pass to the secreting cells. It is probable that the salivary glands also receive sympathetic fibres from cells of the superior cervical ganglia.

#### TECHNIC.

- (1) The salivary glands should be fixed in Flemming's fluid (technic 7, p. 7), or in formalin-Müller's fluid (technic 5, p. 7). Sections are cut as thin as possible, stained with hæmatoxylin-eosin (technic 1, p. 18), and mounted in balsam.
- (2) For the study of the secretory activities of the gland cells, glands from a fasting animal should first be examined and then compared with those of a gland the secretion of which has been stimulated by the subcutaneous injection of pilocarpine. Fix in Flemming's or in Zenker's fluid (technic 9, p. 8). Examine some sections unstained and mounted in glycerin, others stained with hæmatoxylin-eosin and mounted in balsam.
- (3) The finer intercellular and intracellular secretory tubules are demonstrated by Golgi's method. Small pieces of absolutely fresh gland are placed for three days in osmium-bichromate solution (3-per-cent. potassium bichromate solution, 4 volumes; 1-per-cent. osmic acid, 1 volume), and then transferred without washing to a 0.75-per-cent. aqueous solution of silver nitrate. Here they remain for from two to four days, the solution being frequently changed. The processes of dehydrating and embedding should be rapidly done, and sections mounted in glycerin, or, after clearing in xylol, in hard balsam.

## Pancreas.

The pancreas is a compound tubular gland. While in general similar to the salivary glands, it has a somewhat more complicated structure. A connective-tissue capsule surrounds the gland and gives off trabeculæ which pass into the organ and divide it into *lobules*.

In some of the lower animals, as for example the cat, these lobules are well defined, being completely separated from one another by connective tissue. In this respect they resemble the lobules of the pig's liver. A number of these *primary lobules* are grouped together and surrounded by connective tissue, which is considerably broader and looser in structure than that separating the primary lobules. These constitute a *lobule group* or *secondary lobule*.

In the human pancreas the division into lobules and lobule groups is much less distinct, although it can usually be made out. This is due to the incompleteness of the connective-tissue septa, the human pancreas in this respect resembling the human liver. Rarely the human pancreas is distinctly lobulated.

The gland has a main excretory duct, the pancreatic duct or duct of Wirsung. In many cases there is also a secondary excretory duct, the accessory pancreatic duct or duct of Santorini. Both open into the duodenum. The main duct extends almost the entire length of the gland, giving off short lateral branches, one of which enters the centre of each lobule group. Here it splits up into branches which pass to the

primary lobules. From these *intralobular ducts* are given off long, narrow, *intermediate tubules*, which in turn give rise to the *terminal secreting tubules* (Fig. 161).

The *excretory ducts* are lined with a simple high columnar epithelium which rests upon a basement membrane. Outside of this is a connect-

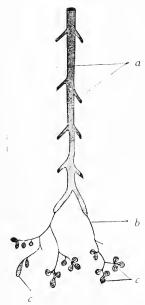


FIG. 161.—Diagram to illustrate Structure of Pancreas. (Stöhr.) a, Excretory duct; b, intermediate tubule; c, c, terminal tubules.

ive-tissue coat, the thickness of which is directly proportionate to the size of the duct. In the pancreatic duct goblet cells are present, and the accompanying connective tissue of the main duct and of its larger branches contains small *mucous glands*. As the ducts decrease in size, the epithelium becomes lower until the intermediate tubule is reached where it becomes flat.

The terminal tubules themselves are most of them very short, frequently almost spherical. This and the fact that several terminal tubules are given off from the end of each intermediate tubule have led to the description of these tubules as alveoli, and of the pancreas as a tubulo-alveolar gland, although there is no dilatation of the lumen. The terminal tubules are lined with an irregularly conical epithelium resting upon a basement membrane (Figs. 162 and 163). The appearance of these cells depends upon their functional condition. Each cell consists of a central zone bordering the

lumen, which contains numerous granules known as zymogen granules, and of a peripheral zone next to the basement membrane, which is homogeneous and contains the nucleus (Fig. 163). The zymogen granules are quite large granules and as they are highly refractive stand out distinctly even in the fresh, unstained condition and under low magnification. The relative size of these zones depends upon whether the cell is in the active or resting state (compare Fig. 164, A and B). During rest (fasting) the two zones are of about equal size. During the early stages of activity (intestinal digestion) the granules largely disappear and the clear zone occupies almost the entire cell. During the height of digestion the granules are increased in number to such an extent that they almost fill the cell, while after prolonged secretion they are again almost absent. The cell

now returns to the resting state in which the two zones are about equal. The increase and disappearance of the granules are marked by the appearance of the fluid secretion of the gland in the lumen.

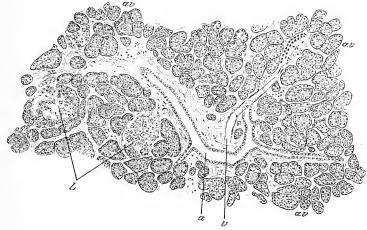
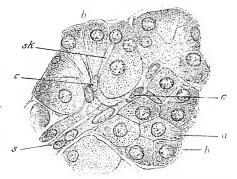


Fig. 162.—Section of Human Pancreas. X 112. (Kölliker.) av, Alveoli; a, interlobular duct surrounded by interlobular connective tissue; L, islands of Langerhans; v, small vein.

It would thus seem probable that the zymogen granules are the intracellular representatives of the secretion of the gland.

In sections of the gland there are seen within the lumina of many of the secreting tubules one or more small cells of which little but the

nucleus can usually be made out. These cells lie in contact. with the secreting cells, and resemble the flat cells which line the intermediate tubule. They are known as the centroacinar (centro-tubular) cells of Langerhans (Fig. 163,  $\epsilon$ ). Their significance is not definitely known. Langerhans believed that they were derived from Fig. 163.-From Section of Human Pancreas. the intermediate tubule, the epithelium of which, instead of directly joining that of the



 $\times$  700. (Kölliker.) a, Gland cell; b, basement membrane; s, intermediate tubule; c, centroacinar cells; sk, intracellular secretory tubule.

terminal tubule as in the submaxillary gland, was continued over into the lumen of the terminal tubule (Fig. 163). This interpretation has been quite generally accepted.

Cells which differ from the secreting cells are frequently found wedged in between the latter. They extend from the lumen to the basement membrane and are probably *sustentacular*.

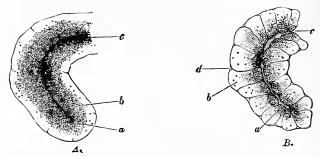


Fig. 164.—Sections of Alveoli from Rabbit's Pancreas. (Foster, after Kühne and Lea.) A, Resting alveolus, the inner zone (a), containing zymogen granules, occupying a little more of the cell than the outer clear zone (b); c, indistinct lumen. B, Active alveolus, granules coarser, fewer, and confined to inner ends of the cell (a), the outer clear zone (b) being much larger; outlines of cells and of lumen much more distinct.

Passing from the lumen of the terminal tubule, sometimes between the centro-tubular cells, directly into the cytoplasm of the secreting cells are minute *intracellular secretory tubules*. These are demonstrable only by special methods (Golgi) (Fig. 165).

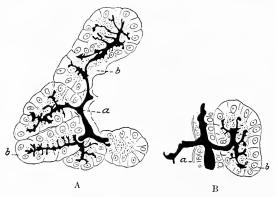


Fig. 165.—Sections through Alveoli of Human Pancreas—Golgi Method—(Dogiel), to show intracellular secretory tubules. a, Intermediate tubule giving off several terminal tubules, from which pass off minute intracellular secretory tubules; b, gland cells lining terminal tubules.

The pancreas also contains peculiar groups of cells, the *cell-islands* of Langerhans, having a diameter from 200 to  $300\mu$  (Figs. 162, 166, and 167). The "island" cells differ quite markedly both in arrangement and structure from those which line the terminal tubules (Fig. 166).

They contain no zymogen granules. They are arranged in anastomosing cords or strands which are separated from one another by capillaries. There are no ducts and the method of Golgi shows no inter- or intra-cellular secretory tubules. Their protoplasm is unstained by basic dyes, but stains homogeneously with acid dyes. Their nuclei vary greatly in size, some, especially where the cells are closely

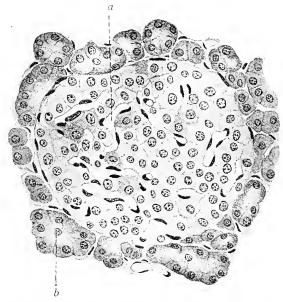


Fig. 166.—Island of Langerhans and few surrounding Pancreatic Tubules. (Böhm and von Davidoff.) *a*, Capillary; *b*, tubule.

packed, being small, others being large and vesicular. Some of the islands are quite sharply outlined by delicate fibrils of connective tissue containing a few elastic fibres (Fig. 166). Others blend with the surrounding tissues.

The origin, structure, and function of these islands have been subjects of much controversy. For some time they were considered of lymphoid origin. They are now believed to be epithelial cells having a developmental history similar to the cells lining the secreting tubules. Each cell-island consists of, in addition to the cells, a tuft or glomerulus of broad tortuous anastomosing capillaries, which arise from the network of capillaries which surround the secreting tubules. The close relation of cells and capillaries and the absence of any ducts have led to the hypothesis that these cells furnish a secretion—internal secretion—which passes directly into the blood-vessels.

In a recent publication Opic reviews previous work upon the histology of the pancreas and adds the results of his own careful researches. He concludes that the

cell-islands of Langerhans are definite structures "formed in embryological life," that "they possess an anatomical identity as definite as the glomeruli of the kidney or the Malpighian body of the spleen, and that they subserve some special function." He calls attention to the similarity which Schäfer noted between these cell-islands and such small ductless structures as the carotid and coccygeal glands and the parathyreoid bodies. From his study of the pancreas in diabetes, Opie concludes that the islands of Langerhans are concerned in carbohydrate metabolism.

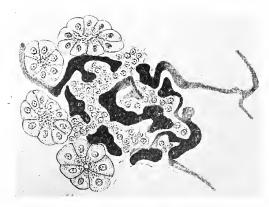


Fig. 167.—From Section of Pancreas, the blood-vessels of which had been injected (Kühne and Lea), showing island of Langerhans with injected blood-vessels, surrounded by sections of tubules. Zymogen granules are distinct in inner ends of cells.

Blood-vessels.—The arteries enter the pancreas with the main duct and break up into smaller arteries which accompany the smaller ducts. These end in a capillary network among the secreting tubules. From this, venous radicles arise which converge to form larger veins. These pass out of the gland in company with the arteries.

Lymphatics.—Of the lymphatics little is known.

Nerves.—The nerves 'are almost wholly from the sympathetic system, and are non-medullated. Some of them are axones of cells in sympathetic ganglia, outside the pancreas; others, of cells situated in small ganglia within the substance of the gland. They pass to plexuses among the secreting tubules, to which and to the walls of the vessels they send delicate terminal fibrils.

#### TECHNIC.

- (1) The general technic for the pancreas is the same as for the salivary glands (page 247).
- (2) Zymogen granules may be demonstrated by fixation in formalin-Müller's fluid (technic 5, p. 7), and staining with picro-acid-fuchsin (technic 2, p. 18), or with Heidenhain's iron hæmatoxylin (technic 3, p. 16).
- (3) The arrangement of the blood-vessels in the islands of Langerhans may be studied in specimens in which the vascular system has been injected (page 22).

#### The Liver.

The liver is a compound tubular gland, the secreting tubules of which anastomose. There are thus, strictly speaking, no "terminal tubules" in the liver, the lumina and walls of neighboring tubules anastomosing without any distinct line of demarcation.

The liver is surrounded by a connective-tissue *capsule*, the *capsule* of *Glisson*. At the *hilum* this capsule extends deep into the substance of the liver, giving off broad connective-tissue *septa*, which divide the

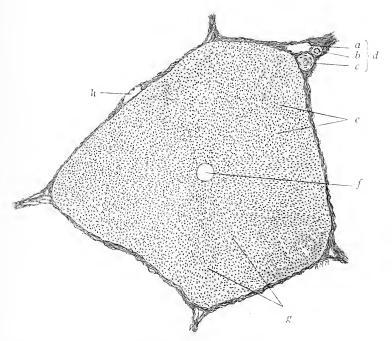


Fig. 168—Section of Lobule of Pig's Liver  $\times$  60 (technic 1, p. 261), showing lobule completely surrounded by connective tissue. a, Portal vein: b, bile duct; c, hepatic artery; d, portal canal; e, capillaries; f, central vein: g, cords of liver cells; h, hepatic vein.

organ into *lobes*. From the capsule and from these interlobar septa, trabeculæ pass into the lobes, subdividing them into *lobules*. In some animals, as for example the pig, each lobule is completely invested by connective tissue (Fig. 168). In man, only islands of connective tissue are found, usually at points where three or more lobules meet (Fig. 169). The lobules are cylindrical or irregularly polyhedral in shape, about 1 mm. in breadth and 2 mm. in length. Excepting just beneath the capsule, where they are frequently arranged with their

apices toward the surface, the liver lobules have an irregular arrangement.

The lobule (Fig. 168) which may be considered the anatomic unit of structure of the liver, consists of secreting tubules arranged in a definite manner relatively to the blood-vessels. The blood-vessels of the liver must therefore be first considered.

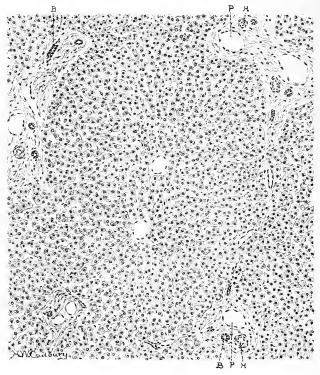


FIG. 169.—Section of Human Liver.  $\times$  80. (Hendrickson.) P, Portal vein; H, hepatic artery; B, bile duct. P, H, B constitute the portal canal and lie in the connective tissue between the lobules.

The BLOOD SUPPLY of the liver is peculiar in that in addition to the ordinary arterial supply and venous return, which all organs possess, the liver receives venous blood in large quantities through the portal vein. There are thus two afferent vessels, the hepatic artery and the portal vein, the former carrying arterial blood, the latter venous blood from the intestine. Both vessels enter the liver at the hilum and divide into large interlobar branches, which follow the connective-tissue septa between the lobes. From these are given off interlobular branches, which run in the smaller connective-tissue septa between the

lobules. From the interlobular branches of the portal vein arise veins which are still interlobular and encircle the lobules. These send off short branches which pass to the surface of the lobule, where they break up into a rich *intralobular capillary network*. These intralobular capillaries all converge toward the centre of the lobule, where they empty into the *central vein* (Fig. 168). The central veins are the

smallest radicles of the hepatic veins, which are the efferent vessels of the liver. Each central vein begins at the apex of the lobule as a small vessel little larger than a capillary. As it passes through the centre of the long axis of the lobule the central vein constantly receives capillaries from all sides, and, increasing in size, leaves the lobule at its base. Here it unites with the central veins of other lobules to form the *sublobular vein* which is a branch of the hepatic (Fig. 176).

The hepatic artery accompanies the portal vein, following the branchings of the latter through the interlobar and interlobular connective tissue, where its finer twigs break up into *capillary networks*. Some of these capillaries empty into the smaller branches of the portal vein; others enter the lobules and anastomose with the intralobular portal capillaries.

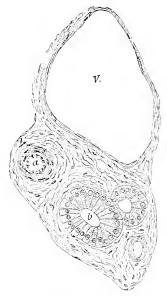


Fig. 170.—Portal Canal. X315. (Klein and Smith.) a, Hepatic artery; V, portal vein; b, bile duct.

The MAIN EXCRETORY DUCT—hepatic duct—leaves the liver at the hilum near the entrance of the portal vein and hepatic artery. Within the liver the duct divides and subdivides, giving off interlobar, and these in turn interlobular branches. These ramify in the connective tissue, where they always accompany the branches of the portal vein and hepatic artery. These three structures—the hepatic artery, the portal vein, and the bile duct, which always occur together in the connective tissue which marks the point of separation of three or more lobules—together constitute the portal canal (Fig. 170). From the interlobular ducts short branches pass to the surfaces of the lobules. From these are given off extremely narrow tubules, which enter the lobule as intralobular secreting tubules.

The walls of the ducts consist of a single layer of epithelial cells

resting upon a basement membrane and surrounded by connective tissue (Fig. 170). The height of the epithelium and the amount of connective tissue are directly proportionate to the size of the duct. In the largest ducts there are usually a few scattered smooth muscle cells. The walls of the secreting tubules are formed by the liver cells.

The LIVER CELLS (Fig. 171) are irregularly polyhedral in shape. They have a granular protoplasm which frequently contains glycogen, pigment granules, and droplets of fat and bile. Each cell contains

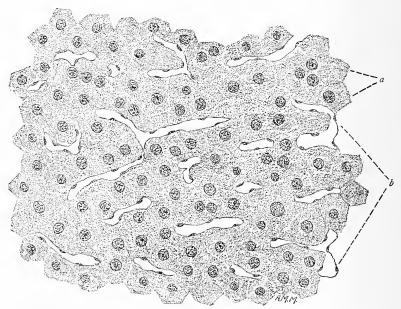


Fig. 171.—Part of Lobule of Human Liver, showing capillaries and anastomosing cords of liver cells.  $\times$  350. a, Liver cells; b, capillaries.

one or more spherical nuclei. Like other gland cells, the granularity of the protoplasm depends upon its functional condition. Within the cells are minute irregular canals, some of which can be injected through the blood-vessels, while others are apparently continuous with the secreting tubules (Fig. 173,  $\Lambda$  and B).

The capillaries of the portal vein, as they anastomose and converge from the periphery to the centre of the lobule, form long-meshed capillary networks. In the meshes of this network lie the anastomosing secreting tubules. On account of the shape of the capillary network, the liver cells, which form the walls of these tubules, are arranged in anastomosing rows or cords, known as hepatic cords or cords of liver cells (Fig. 171).

The secreting tubules (Fig. 172) are extremely minute channels, the walls of which are the liver cells. A secretory tubule always runs

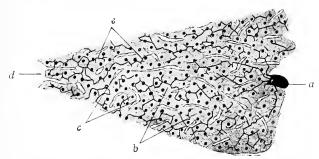


FIG. 172.—Part of Lobule of Human Liver, Golgi Method (technic 3, p. 261), to show relations of bile duct to intralobular secretory tubules and of the latter to the liver cells. a, Bile duct; b, cords of liver cells; e, blood capillaries; d, central vein; e, secretory tubules.

between two contiguous liver cells, in each of which a groove is formed. The *blood capillaries*, on the other hand, are found at the corners where three or more liver cells come in contact. It thus results that bile tubules and blood capillaries rarely lie in contact, but are regularly

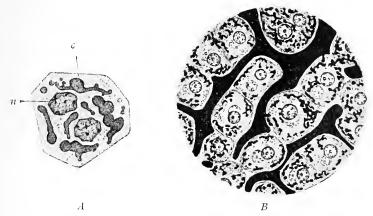


Fig. 173.—A, Cell from human liver showing intracellular canals (Browicz);  $\epsilon$ , intracellular canal; n, nucleus. B, From section of rabbit's liver injected through portal vein, showing intracellular canals (continuous with intercellular blood capillaries). (Schäfer.)

separated by part of a liver cell. Exceptions to this rule sometimes occur. While most of the secretory tubules anastomose, some of them end blindly either between the liver cells or, in some instances, after extending a short distance within the cell protoplasm (Fig. 173, A).

At the surface of the lobule there is a modification of some of the liver cells to a low cuboidal type, and these become continuous with the lining cells of the smallest bile ducts, the secretory tubule being continuous with the duct lumen.

Special methods of technic have demonstrated a connective-tissue framework within the lobule. This consists of a *reticulum* of extremely delicate fibrils which envelop the capillary blood-vessels, and of a smaller number of coarser fibres which radiate from the region of the central vein—*radiate fibres* (Fig. 174).

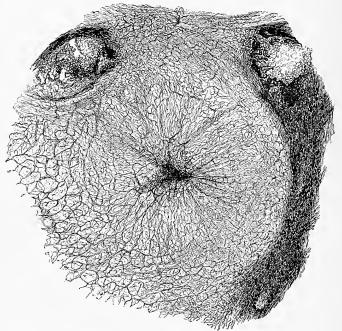


Fig. 174.—Liver Lobule, to show Connective-tissue Framework. (Mall.)

Special technical methods also show the presence of stellate cells —cells of Kupffer—within the lobule. These are interpreted by Kupffer as belonging to the endothelium of the intralobular capillaries.

Comparing the liver with other compound tubular glands, it is seen to present certain marked peculiarities which distinguish it and which make its structure as a compound tubular gland difficult to understand. The most important of these are the following: (Figs. 175 and 176).

The extremely small amount of connective tissue; in the human liver not enough interlobular connective tissue to outline the lobules,

while intralobular connective tissue demonstrable by ordinary staining methods is wholly absent. There is thus no connective tissue seen separating the cells of one tubule from those of another as, for example, in such a gland as the submaxillary. The result is that cells of neighboring tubules lie side by side, and back to back as it were, with no intervening connective tissue.

The fact that unlike the tubules of other glands, the liver tubule consists of only two rows of cells, between which lies the lumen. The latter is thus never in touch with more than two cells.

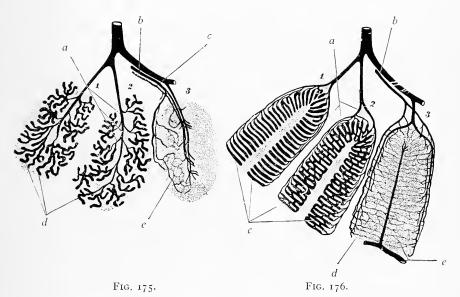


Fig. 175.—Scheme of an Ordinary Compound Tubular Gland. In lobule 3 only the ramifications of the excretory duct, without endpieces, are shown. (Stöhr). a, Branches of excretory duct; b, artery; c, vein; d, terminal tubules; e, capillaries. Fig. 176.—Scheme of Liver. In lobule 1, only the direction of the endpieces is shown;

Fig. 176.—Scheme of Liver. In lobule 1, only the direction of the endpieces is shown; in lobule 2 only their branching; in 3 only the excretory ducts. (Stöhr.) a, Branches of excretory duct; b, portal vein; c, terminal tubules (hepatic cords); d, capillaries; e, vein (central and sublobular).

The end-to-end anastomosis of the secreting tubules, there being no true terminal tubules; anastomosis of neighboring tubules by means of side branches; the arrangement of the bile capillaries in such a manner that a single liver cell abuts upon more than one capillary.

The more intimate relation of the liver cell to the blood capillaries. Thus most gland cells have one side on the lumen, one side only in contact with a capillary blood-vessel, the remaining sides being in contact with other cells of the same tubule. A liver cell, on the

other hand, may and usually does come in contact with several blood capillaries.

The arrangement of both blood-vessels and tubules within the lobule. In the submaxillary, for example, the terminal tubules are convoluted and run in all directions. In the liver the terminal tubules are straight and run in a definite direction from the periphery of the lobule toward the center. Again, while in other glands both intralobular arteries and ducts are distributed outward from the centre of the lobule, and the blood is returned through veins which pass to the periphery of the lobule, in the liver the interlobular ducts pass to the periphery of the lobule and give off secreting tubules which pass in toward the centre of the lobule. The afferent vessels also (portal veins) take the blood to the periphery of the lobule and distribute it to a capillary network which converges to an efferent vessel (hepatic vein) at the centre of the lobule. The veins are also peculiar in that they do not follow the arteries in leaving the liver but pursue an entirely independent course.

Blood-vessels.—These have been already described.

Lymph vessels form a network in the liver capsule. These communicate with deep lymphatics in the substance of the organ. The latter accompany the portal vein and follow the ramifications of its capillaries within the lobule as far as the central vein.

The nerves of the liver are mainly non-medullated axones of sympathetic neurones. The nerves accompany the blood-vessels and bile ducts, around which they form plexuses. These plexuses give off fibrils which end on the blood-vessels, bile ducts, and liver cells.

Three main ducts, all parts of a single excretory duct system, are concerned in the transportation of the bile to the intestine, the hepatic, the cystic, and the common. Their walls consist of a mucous membrane, a submucosa, and a layer of smooth muscle. The mucosa is composed of a simple columnar epithelium resting upon a basement membrane and a stroma which contains smooth muscle cells and small mucous glands. The submucosa is a thin layer of connective tissue. Hendrickson describes the muscular coat as consisting of three layers, an inner circular, a middle longitudinal, and an external oblique. At the entrance of the common bile duct into the intestine, and at the junction of the duct of Wirsung with the common duct, there are thickenings of the circular fibres to form sphincters. In the cystic duct occur folds of the mucosa—the Heisterian valve—into which the muscularis extends.

## The Gall-Bladder.

The wall of the gall-bladder consists of three coats—mucous, muscular, and serous.

The mucous membrane is thrown up into small folds or  $rug \alpha$ , which anastomose and give the mucous surface a reticular appearance. The epithelium is of the simple columnar variety with nuclei situated at the basal ends of the cells. A few mucous glands are usually found in the stroma.

The muscular coat consists of bundles of smooth muscle cells which are disposed in a very irregular manner, and are separated by considerable fibrous tissue. A richly vascular layer just beneath the stroma is almost free from muscle and corresponds to a submucosa. It frequently contains small lymph nodules.

The serous coat is a reflection of the peritoneum.

### TECHNIC.

- (1) Before taking up the study of the human liver, the liver from one of the lower animals in which each lobule is completely surrounded by connective tissue should be studied. Fix small pieces of a pig's liver in formalin-Müller's fluid (technic 5, p. 7.) Cut sections near and parallel to the surface. Stain with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) and mount in balsam. In the pig's liver the lobules are completely outlined by connective tissue and the yellow picric-acid-stained lobules are in sharp contrast with the red fuchsin-stained connective tissue.
- (2) For the study of the human liver treat small pieces of perfectly fresh tissue in the same manner as the preceding, but stain with hæmatoxylin-eosin (technic 1, p. 18).
- (3) The secretory tubules and smaller bile ducts may be demonstrated by technic 4, p. 26. A light eosin stain brings out the liver cells
- (4) For the study of the blood-vessels of the liver, inject the vessels through the inferior vena cava or portal vein. If the vena cava is used, it is convenient to inject from the heart directly through the right auricle into the vena cava. Sections should be rather thick and may be stained with eosin, or even lightly with hæmatoxylin-eosin (technic 1, p. 18), and mounted in balsam.
- (5) For demonstrating the intralobular connective tissue, Oppel recommends fixing fresh tissue in alcohol, placing for twenty-four hours in a 0.5-per-cent. aqueous solution of yellow chromate of potassium, washing in very dilute silver nitrate solution (a few drops of 0.75-per-cent. solution to 50 c.c. of water) and then transferring to 0.75-per-cent. silver nitrate solution, where it remains for twenty-four hours. Embed quickly in celloidin. The best tissue is usually found near the surfaces of the blocks. A similar result is obtained by fixing fresh tissue in 0.5-per-cent. chromic-acid solution for three days, then transferring to 0.5-per-cent. silver nitrate solution for two days.

## DEVELOPMENT OF THE DIGESTIVE SYSTEM.

In the development of the digestive system all the layers of the blastoderm are involved. Mesoderm and entoderm are, however, the lavers most concerned, as the ectoderm is used only in the formation of the oral and anal orifices. The primitive alimentary canal is formed by two folds which grow out from the ventral surface of the embryo and unite to form a canal, in a manner that is quite similar to the formation of the neural canal. In this way the primitive gut is lined with cells which previously formed the ventral surface of the embryo, i.e., entoderm. A portion of the mesoderm accompanies the entoderm in the formation of the folds. This is known as the visceral layer of the mesoderm. The primary gut is thus a closed sac or tube. It is connected with the umbilical vesicle, but has no connection with the exterior. These connections are formed later by oral and anal invaginations of ectoderm which extend inward and open up into the ends of the hitherto imperforate gut. The ends of the alimentary tract, including the oral cavity and all of the glands and other structures connected with it, are of ectodermic origin. The epithelial lining of the gut and the parenchyma of all glands connected with it are derived from entoderm. The muscle, the connective tissue, and the mesothelium of the serosa are developed from mesoderm.

The mesodermic elements show little variation throughout the gut, the peculiarities of the several anatomical divisions of the latter being dependent mainly on special differentiation of the entoderm (epithelium). Beneath the entodermic cells is a narrow layer of loosely arranged tissue which later separates into stroma, muscularis mucosæ, and submucosa. Outside of this a broader mesodermic band of firmer structure represents the future muscularis.

The *stomach* first appears as a spindle-shaped dilatation about the end of the first month. Its entodermic cells, which had consisted of a single layer, increase in number and arrange themselves in short cylindrical groups. These are the first traces of tubular glands. They increase in length and extend downward into the mesodermic tissue. For a time the cells lining the peptic glands are all apparently alike, but at about the fourth month the differentiation into chief cells and parietal cells takes place.

In the *intestines* a proliferation of the epithelium and of the underlying stroma results in the formation of *villi*. These appear about the tenth week, in both small and large intestines. In the former

they increase in size, while in the latter they atrophy and ultimately disappear. The simple tubular glands of the intestines develop in a manner similar to those of the stomach.

The mesothelium of the serosa is derived from the mesodermic cells of the primitive body cavity.

The development of the larger glands, connected with the digestive tract, takes place in a manner similar to the formation of the simple tubular glands. All originate in extensions downward of entodermic cords into the underlying mesodermic tissue. From the lower ends of these cords, branches extend in all directions to form the complex systems of tubules found in the compound glands.

The salivary glands being developed from the oral cavity, originate in similar invaginations of ectodermic tissue.

In the case of the *pancreas* a portion of the gland has an independent origin in the epithelium of the ductus choledochus. This portion ultimately unites with the main mass of the gland and its duct. The duct of Santorini sometimes remains patent, but in many cases atrophies so that the entire pancreatic secretion usually reaches the intestine through the pancreatic duct.

The *liver* begins as a ventral downgrowth of the intestinal epithelium into the mesoderm of the transverse septum. This almost immediately divides into two hepatic diverticula. About the ends of these diverticula active proliferation of entodermic cells takes place, and this represents the first appearance of liver tissue.

# General References for Further Study.

Oppel: Lehrbuch der vergleichenden mikroskopischen Anatomie.

Kölliker: Handbuch der Gewebelehre des Menschen.

Opie: The Pancreas.

Stöhr: Salivary Glands, in Text-book of Histology.

## CHAPTER VII.

## THE RESPIRATORY SYSTEM.

THE respiratory apparatus consists of a system of passages—nares, larynx, trachea, and bronchi, which serve for the transmission of air to and from the essential organ of respiration, the lungs.

## The Nares.

The nares, or nasal passages, are divided into vestibular, respiratory, and olfactory regions, the differentiation depending mainly upon the structure of their mucous membranes.

The VESTIBULAR REGION marks the transition between skin and mucous membrane (page 193). Its epithelium is of the stratified squamous variety and rests upon a basement membrane, which is thrown into folds by papillæ of the underlying stroma. The latter is richly cellular and contains sebaceous glands (page 362) and the follicles of the nasal hairs.

The RESPIRATORY REGION is much larger than both the vestibular and olfactory regions. Its epithelium is of the stratified columnar variety. The cells of the surface layer are ciliated and are interspersed with goblet cells. The stroma is distinguished by its thickness (3 to 5 mm. over the inferior turbinates) and by the presence of networks of such large veins that the tissue closely resembles erectile tissue. It contains considerable diffuse lymphoid tissue and here and there small lymph nodules. In the stroma are small simple tubular glands lined with both serous and mucous cells. There is no submucosa, the stroma being connected directly with the periosteum and perichondrium of the nasal bones and cartilages.

The mucous membrane of the accessory nasal sinuses is similar in structure to that of the respiratory region of the nares, but is thinner and contains fewer glands.

The OLFACTORY REGION can be distinguished with the naked eye by its brownish-yellow color, in contrast with the reddish tint of the

surrounding respiratory mucosa. The epithelium is of the stratified columnar type, and is considerably thicker than that of the respiratory region. The surface cells are of two kinds: (1) sustentacular cells, and (2) olfactory cells.

- (1) The sustentacular cells are the more numerous. Each cell consists of three parts: (a) A superficial portion, which is broad and cylindrical, and contains pigment, and granules arranged in longitudinal rows. The cells have well-marked, striated, thickened free borders, which unite to form the so-called membrana limitans olfactoria. (b) A middle portion which contains an oval nucleus. As the nuclei of these cells all lie in the same plane, they form a distinct narrow band, which is known as the zone of oval nuclei. (c) A thin filamentous process which extends from the nuclear portion down between the cells of the deeper layers. This process is irregular and pitted by pressure of surrounding cells. It usually forks and apparently anastomoses with processes of other cells to form a sort of protoplasmic reticulum.
- (2) The *olfactory cells* lie between the sustentacular cells. Their nuclei are spherical, lie at different levels, and are most of them more deeply placed than those of the sustentacular cells. They thus form a broad band, the *zone of round nuclei*. From the nuclear portion of the cell a delicate process extends to the surface, where it ends in several minute hair-like processes. From the opposite pole of the cell a longer process extends centrally as a centripetal nerve fibre. The olfactory cell is thus seen to be of the nature of a ganglion cell (see also page 382).

Between the nuclear parts of the olfactory cells and the basement membrane are the *basal cells*. These are small nucleated elements, the irregular branching protoplasm of which anastomoses with that of neighboring basal cells and of the sustentacular cells to form the peculiar protoplasmic reticulum already mentioned.

The basement membrane is not well developed.

The *stroma* consists of loosely arranged white fibres, delicate elastic fibres, and connective-tissue cells. Embedded in the stroma are large numbers of simple branched tubular glands, the glands of Bowman. Each tubule consists of a duct, a body, and a fundus. The secreting cells are large and irregular and contain a yellowish pigment, which with that of the sustentacular cells is responsible for the peculiar color of the olfactory mucosa. These glands were long described as serous, but are now believed to be mucous in character. They frequently extend beyond the limits of the olfactory region.

## The Larynx.

The larynx consists essentially of a group of cartilages united by strong fibrous bands and lined by mucous membrane.

The *epithelium* covering the true vocal cords, the laryngeal surface of the epiglottis, and the anterior surface of the arytenoid cartilages is of the stratified squamous variety with underlying papillæ. With these exceptions the mucous membrane of the larynx is lined with stratified columnar ciliated epithelium similar to that of the respiratory portion of the nares. Numerous goblet cells are usually present, and the epithelium rests upon a broad basement membrane. On the posterior surface of the epiglottis many taste buds (see Fig. 268 and page 532) are embedded in the epithelium.

The *stroma* is especially rich in elastic fibres. The true vocal cords consist almost wholly of longitudinal elastic fibres covered by stratified squamous epithelium. Lymphoid cells are present in varying numbers. In some places they are so numerous that the tissue assumes the character of diffuse lymphoid tissue. Distinct nodules sometimes occur.

Owing to the absence of a muscularis mucosæ the stroma passes over with no distinct line of demarcation into the submucosa. This is a more loosely arranged, less cellular connective tissue, and contains simple tubular glands lined with both serous and mucous cells.

Externally the submucosa merges into a layer of more dense fibrous tissue which connects it with the laryngeal cartilages and with the surrounding structures. Immediately surrounding the cartilages the connective tissue forms an extremely dense layer, the perichondrium.

Of the *cartilages* of the larynx, the epiglottis, the middle part of the thyreoid, the apex and vocal process of the arytenoid, the cartilages of Santorini and of Wrisburg are of the yellow elastic variety. The main body of the arytenoid, the rest of the thyreoid and the cricoid cartilages are hyaline. After the twentieth year, more or less ossification is usually found in the cricoid and thyreoid cartilages.

### The Trachea.

The walls of the trachea consist of three layers—mucosa, submucosa, and fibrosa (Fig. 177).

The mucosa is continuous with that of the larynx, which it closely resembles in structure. It consists of a stratified columnar ciliated epithelium, with numerous goblet cells, resting upon a broad base-

ment membrane, and of a stroma of mixed fibrous and elastic tissue containing many lymphoid cells.

The submucosa is not distinctly marked off from the stroma on account of the absence of a muscularis mucosæ. It is distinguished from the stroma by its looser, less cellular structure, by its numerous large blood-vessels, and by the presence of glands. These are of the simple branched tubular variety and are lined with both serous and mucous cells. Some of the mucous tubules have well-marked cres-

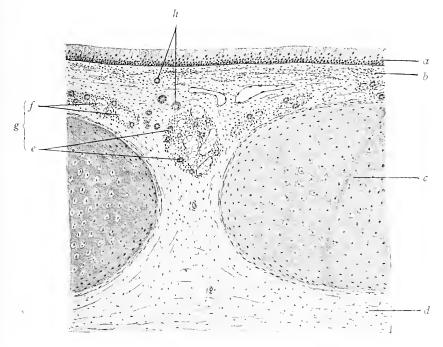


Fig. 177.—From Longitudinal Section of Human Trachea.  $\times$  40. (Technic 3, p. 269.) a, Epithelium; b, stroma; c, cartilage; d, fibrous coat; e, serous tubules; f, mucous tubules; g, glands in submucosa; h, ducts.

cents of Gianuzzi. The glands are most numerous between the ends of the cartilaginous rings, where they frequently penetrate the muscle and extend into the fibrosa.

The fibrosa is composed of coarse, rather loosely woven connective-tissue fibres embedded in which are the *tracheal cartilages*. These are incomplete rings of hyaline cartilage shaped like the letter C (Fig. 178). They are from sixteen to twenty in number and encircle about four-fifths of the tube, being open posteriorly. The openings between the ends of the cartilaginous rings are bridged over by a

thickened continuation of the fibrous coat, strengthened by a layer of smooth muscle (Fig. 178, m). The bundles of muscle cells run mainly in a transverse direction, and extend across the intervals between adjacent rings as well as between their open ends. There are frequently a few bundles of obliquely disposed cells and, most external, some few that run longitudinally.

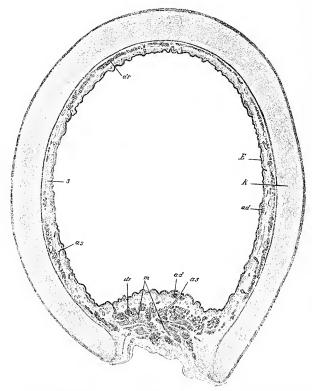


Fig. 178.—Transverse Section of Human Trachea through One of the Cartilage Rings.  $\times$  8. (Kölliker.) E, Epithelium of (s) mucous membrane; dr, glands; as, gland duct; ad, adenoid tissue; K, cartilage; m, smooth muscle cut longitudinally, extending across between ends of cartilage ring.

Outside the fibrous coat proper is a looser, more irregular connective tissue, which serves to attach the trachea to the surrounding structures.

**Blood-vessels,** lymphatics, and nerves have a similar distribution in larynx and trachea. The larger vessels pass directly to the submucosa. From these, smaller branches pass to the different coats, where they break up into capillary networks.

Lymphatics form plexuses in the submucosa and mucosa, the most superficial lying just beneath the subepithelial capillary plexus.

The nerves of the larynx and trachea are derived from both cerebro-spinal and sympathetic systems. The cerebro-spinal nerves are afferent, the dendrites of spinal ganglion cells. They form a sub-epithelial plexus from which are given off fibrils which pass into the epithelium and terminate freely among the epithelial cells. Other afferent fibres of cerebro-spinal nerves pass to the muscular coat of the trachea. Sympathetic nerve fibres form plexuses which are interspersed with minute groups of ganglion cells. Axones from these ganglion cells have been traced to the smooth muscle cells of the trachea. Sympathetic axones also pass to the glands of the trachea and larynx. On the under surface of the epiglottis small taste buds are found.

#### TECHNIC.

- (1) For the study of the details of structure of the walls of the nares and larynx, fix small pieces of perfectly fresh material from different regions in formalin-Müller's fluid (technic 5, p. 7), harden in alcohol, stain sections with hæmatoxylineosin (technic 1, p. 18), and mount in balsam.
- (2) The general relations of the parts can be studied by removing the larynx, upper part of the trachea, and corresponding portion of the œsophagus of an animal or of a new-born child, fixing and hardening as above, and cutting longitudinal sections through the entire specimen.
- (3) Trachea.—Remove a portion of the trachea and treat as in technic (1). Both longitudinal and transverse sections should be made; the longitudinal including at least two of the cartilaginous rings; the transverse being through one of the rings.

#### The Bronchi.

The primary bronchi and their largest branches have essentially the same structure as the trachea except that the cartilaginous rings are not as complete. Bronchi branch at acute angles and also give off small side branches.

As they decrease in calibre, the following changes take place in their walls (Figs. 179 to 182).

(1) The epithelium gradually becomes thinner. In a bronchus of medium size (Fig. 179) it has become reduced to three layers of cells, which Kölliker describes as an outer "basal" layer, a middle "replacing" layer, and a surface layer of ciliated and goblet cells. In the smaller bronchi (Figs. 181, 182) the epithelium is reduced to a single layer

of ciliated cells. These are at first high, but become gradually lower as the bronchi become smaller, until in the terminal branches the epithelium is simple cuboidal and non-ciliated. Among the ciliated cells are varying numbers of mucous or goblet cells.

(2) The stroma decreases in thickness as the bronchi become smaller. It consists of loosely arranged white and elastic fibres. This layer with the epithelium is folded longitudinally (Fig. 182.) There is considerable diffuse lymphatic tissue, and in some places small

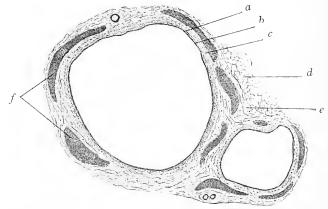


Fig. 179.—Transverse Section through two Medium-size Bronchi of the Human Lung.  $\times$  15. (Technic 2, p. 280.) In the fibrous coat are seen the bronchial arteries and veins. a, Epithelium; b, stroma; c, muscularis mucosæ; d, lung tissue; e, fibrous coat; f, plates of cartilage.

nodules occur, over which there may be lymphoid infiltration of the epithelium (see Tonsil, page 157). Near the root of the lung many small lymph nodules are found, which show different degrees of pigmentation.

- (3) With decrease in thickness of the epithelium and of the stroma, the thickness of the mucosa is maintained by the appearance of a layer of smooth muscle. In the larger bronchi this is a continuous layer of circularly disposed smooth muscle, and lies just external to the stroma, forming a muscularis mucosæ (Fig. 180). It reaches its greatest thickness relative to the size of the bronchus in the bronchi of medium size. As the bronchi become smaller it becomes thinner, then discontinuous, and in the smallest bronchi consists of only a few scattered muscle cells. These continue into the walls of the alveolar ducts, but are absent beyond this point.
  - (4) The submucosa decreases in thickness with decrease in the

calibre of the bronchi. It consists of loosely arranged connective tissue. Mixed glands (Fig. 180) are present until a diameter of about 1 mm. is reached, when they disappear. They lie in the submucosa and frequently extend through between the cartilage plates into the fibrous coat. The ducts pass through the muscular coat and open into pit-like depressions lined with a continuation of the surface ciliated epithelium.

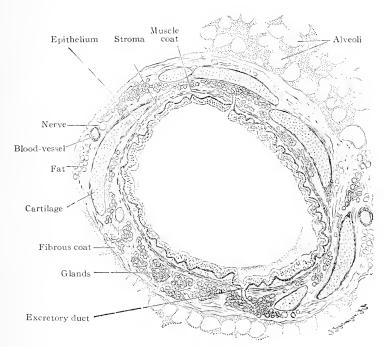


Fig. 180.—Cross Section of Human Bronchus (of a child) of 2 mm. diameter.  $\times$  30. (Stöhr.).

(5) The cartilages, which in the trachea and primary bronchi form nearly complete rings, become gradually smaller, and finally break up into short disconnected plates (Figs. 179 and 180). They are frequently fibrocartilage rather than hyaline. These plates decrease in size and number, and are absent after a diameter of 1 mm. is reached. Cartilage and mucous glands thus disappear at about the same time, although it is common for glands to extend over into smaller bronchi than do the cartilage plates.

The bronchi down to a diameter of from 1.5 to 1 mm. are interlobular, and belong to the duct system down to a diameter of about o.5 mm. From the small interlobular bronchi are given off the terminal bronchi. These are respiratory in character and are described with the lungs.

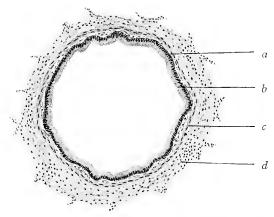


Fig. 181.—Transverse Section of Small Bronchus from Human Lung.  $\times$  115. (Technic 2, p. 280.) a, Stroma; b, epithelium; c, muscularis mucosæ; d, fibrous coat.

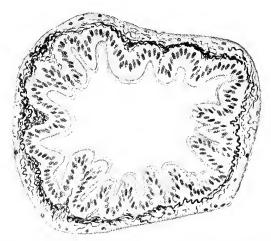


Fig. 182.—Transverse Section through small Bronchus of Human Lung. (Sobotta.) Simple columnar ciliated epithelium; no cartilage; no glands; mucosa folded longitudinally; elastic tissue stained with Weigert's elastic tissue stain.

In studying the bronchi it is convenient to arbitrarily divide them into large, medium-sized, and small bronchi.

Large bronchi have essentially the same structure as the trachea except for somewhat thinner walls.

Medium-sized bronchi (Fig. 179) have an epithelium about three layers deep,

disconnected plates of cartilage, a continuous layer of smooth muscle disposed circularly as a muscularis mucosæ, tubular glands.

Small bronchi have a single layer of ciliated epithelium, a thinner muscular coat, no glands, and no cartilage. (Figs. 181, 182.)

## The Lungs.

The lung is built upon the plan of a compound alveolar gland, the trachea and bronchial ramifications corresponding to duct systems, the air vesicles to gland alveoli.

The surface of the lung is covered by a serous membrane—the *pulmonary pleura*—which forms its *capsule*, and which at the root of the lung, or hilum, is reflected upon the inner surface of the chest wall as the *parietal pleura*. It consists of fibrillar connective tissue containing

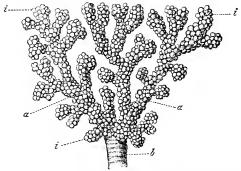


Fig. 183.—From Lung of an Ape. The bronchi and their dependent ducts and alveoli have been filled with quicksilver.  $\times$  15. (Kölliker, after Schulze.) b, Terminal bronchus; a, alveolar duct; i, alveoli.

fine elastic fibres which are more numerous in the visceral than in the parietal layer. From the capsule broad connective-tissue *septa* pass into the organ, dividing it into *lobes*. From the capsule and interlobar septa are given off smaller septa, which subdivide the lobes into *lobules*.

The human pulmonary lobule (Fig. 184) is irregularly pyramidal, and has a diameter of from 1 to 3 cm. The amount of interlobular connective tissue is so small that no distinct separation into lobules can usually be made out. The pulmonary lobule constitutes the anatomic unit of lung structure in the same sense that the liver lobule constitutes the anatomic unit of that organ. The most superficial lobules are arranged with their bases against the pleura. Elsewhere in the lung the lobules have an irregular arrangement.

The apex of each lobule is the point of entrance of a *terminal* or *respiratory bronchus* (Figs. 183 and 184) which is about 0.5 mm. in diameter. From each terminal bronchus open from three to six narrow passages—alveolar passages or alveolar ducts (Figs. 183, 184 and 185). The alveolar passages open into wider chambers—alveolar sacs or infundibula. The latter are irregularly pyramidal, their bases being directed away from the alveolar ducts. From the sides of the terminal bronchi, the alveolar ducts, and the alveolar sacs, are given off the alveoli—air vesicles or air cells (Figs. 183 and 185).

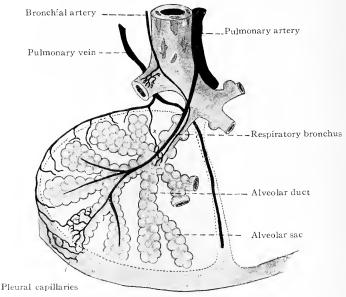


Fig. 184.—Scheme of a Pulmonary Lobule and its Blood Supply (Stöhr). The two main branches of the pulmonary vein are seen lying in the interlobular connective tissue.

According to Miller a further subdivision of the alveolar duct can be made. He describes the terminal bronchus as about 0.5 mm. in diameter, and as opening into from three to six narrow tubules, the *vestibula*. Each vestibulum is about 0.2 mm. in diameter, and opens into several larger, nearly spherical chambers, the *atria*. Each atrium communicates with a number of very narrow—0.14 mm.—*air-sac passages* from which open the *air sacs*. From the latter are given off on all sides the *air cells* or *alveoli*. Alveoli are not, however, confined to the periphery of the air sacs, but are given off in small numbers from the terminal bronchus, and in constantly increasing numbers from the alveolar ducts and infundibula.

The terminal bronchus. The proximal portion of the terminal or respiratory bronchus is lined by a simple columnar ciliated epithelium,

resting upon a basement membrane. Beneath this is a richly elastic stroma containing bundles of circularly disposed smooth muscle cells. The epithelium becomes gradually lower and non-ciliated, and near the distal end of the terminal bronchus there appear small groups or islands of flat, non-nucleated epithelial cells—respiratory epithelium.

The alveolar duct. Here the cuboidal epithelium is almost completely replaced by the respiratory. Beneath the epithelium the walls

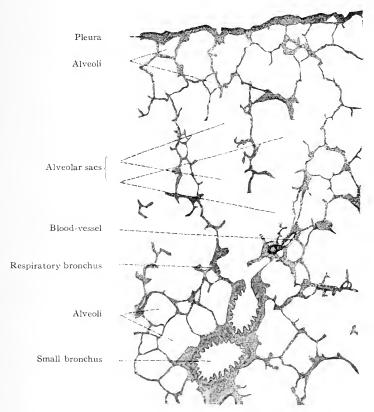


Fig. 185.—Section of Cat's Lung (Szymonowicz) surface lobule; respiratory bronchus opening into alveolar duct from which are given off two alveolar sacs.

have a structure similar to those of the distal end of the terminal bronchus, consisting of delicate fibro-elastic tissue with scattered smooth muscle cells. The basement membrane is extremely thin.

The alveolar sac. The epithelium of the alveolar sac consists of two kinds of cells, respiratory cells and so-called "fatal" cells (see Development, page 279).

The respiratory cells (Fig. 186) are some of them large. flat, non-nucleated plates, while others are much smaller, non-nucleated elements. The absence of nuclei and the extremely small amount of intercellular substance render these cells quite invisible in sections stained by the more common methods. The cell boundaries are best demonstrated by means of silver nitrate (technic 1, p. 71).

The "fætal" cells are granular, nucleated cells which are scattered among the respiratory cells. Their position appears to be less superficial than that of the respiratory cells, the fætal cells lying in the meshes

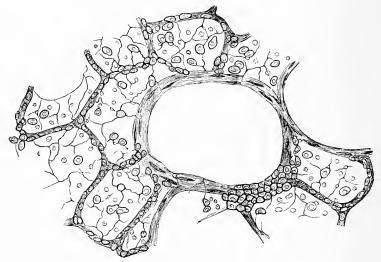


Fig. 186.—From Section of Cat's Lung Stained with Silver Nitrate. (Klein.) (Technic 1, p. 71.) Small bronchus surrounded by alveoli, in which are seen both flat cells (respiratory epithelium) and cuboidal cells (fœtal cells).

of the capillary network, the respiratory cells covering the capillaries. In the embryonic lung and in the lungs of a still-born child the air passages and alveoli contain only this type of cells, the small flat plates apparently resulting from a flattening out of the cuboidal cells due to pressure from inspiration, and the large flat plates to union of a number of small plates.

The alveolus is similar in structure to the alveolar duct, its walls consisting mainly of delicate elastic fibrils supporting respiratory and fœtal cells. Around the opening of the alveolus the elastic fibres are more numerous, forming a more or less definite ring. The disposition of elastic tissue in the wall of the alveoli is undoubtedly of importance in determining the contraction and expansion of the

alveoli under varying conditions of pressure. It has been estimated that on forced inspiration an alveolus can expand to three times its resting capacity. Each alveolus communicates not only with its alveolar sac, alveolar duct, or respiratory bronchus, by means of a broad opening, but alveoli are connected with one another by minute openings in their walls.

The interalveolar connective tissue, while extremely small in amount, serves to separate the alveoli from one another. Somewhat thicker

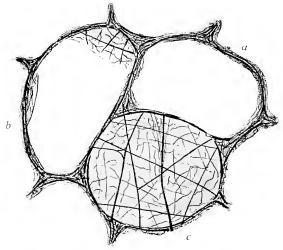


Fig. 187.—Section Through Three Alveoli of Human Lung.  $\times$  235. Weigert's elastic-tissue stain (technic 3, p. 26) to show arrangement of elastic tissue. a, Alveolus cut through side walls only; b, alveolus cut through side walls and portion of bottom or top; c, alveolus in which either the bottom or top is included in section.

connective tissue separates the alveoli of one alveolar passage from those of another. Still stronger connective-tissue bands separate adjacent lobules.

**Blood-vessels.**—Two systems of vessels distribute blood to the lungs. One, the *bronchial system*, carries blood for the nutrition of the lung tissue. The other, the much larger *pulmonary system*, carries blood for the respiratory function (Fig. 184).

The bronchial artery and the pulmonary artery enter the lung at its hilum. Within the lung the vessels branch, following the branchings of the bronchi, which they accompany (Fig. 184). The pulmonary vessels are much the larger and run in the connective tissue outside the bronchial walls. The bronchial vessels lie within the fibrous coat of the bronchus. A section of a bronchus thus usually shows the large

pulmonary vessels, one on either side of the bronchus, and two or more small bronchial vessels in the walls of the bronchus (Fig. 179).

The pulmonary lobule forms a distinct "blood-vascular unit." A branch of the pulmonary artery enters the apex of each lobule close to the lobular bronchus, and almost immediately breaks up into branches, one of which passes to each alveolar passage (Fig. 184).

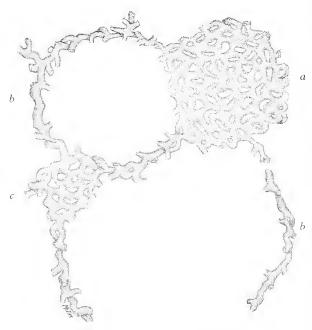


Fig. 188.—Parts of Four Alveoli from Section of Injected Human Lung.  $\times$  200. (Technic 5, p. 280.) *a*, Wall of alveolus seen on flat; *c*, same, but only small part of alveolar wall in plane of section; *b*, alveoli in which plane of section includes only side walls; alveolar wall seen on edge.

From these are given off minute terminal arterioles which pass to the central sides of the alveolar passages and alveoli, where they give rise to a rich capillary network. This capillary network is extremely closemeshed, and invests the alveoli on all sides (Fig. 188). Similar networks invest the walls of the respiratory bronchi, the alveolar ducts, and their alveoli. All of these capillary networks freely anastomose.

There are thus interposed between the blood in the capillaries and the air in the alveoli only three extremely thin layers: (1) The thin endothelium of the capillary wall; (2) the single layer of flat respiratory epithelial plates; and (3) the delicate basement membrane upon which

the respiratory epithelium rests together with an extremely small amount of fibrous and elastic tissues (see diagram, Fig. 189).

The *veins* begin as small radicles, one from the base of each alveolus (Fig. 184). These empty into small veins at the periphery of the lobule. These veins at first run in the interlobular connective tissue away from the artery and bronchus. Later they empty into the large pulmonary trunks which accompany the bronchi.

The *bronchial arteries* break up into capillary networks in the walls of the bronchi, supplying them as far as their respiratory divisions, beyond which point the capillaries belong to the pulmonary system.



Fig. 189.—Diagram of Tissues Interposed Between Blood and Air in Alveolus. a Respiratory epithelium; b, basement membrane and small amount of fibro-elastic tissue c, endothelium of capillary.

The bronchial arteries supply the walls of the bronchi, the bronchial lymph nodes, the walls of the pulmonary vessels, and the pulmonary pleura. Of the bronchial capillaries some empty into the bronchial veins, others into the pulmonary veins.

Lymphatics.—The lymphatics of the lung begin as small lymph spaces in the interalveolar connective tissue. These communicate with larger lymph channels in the interlobular septa. Some of these empty into the deep pulmonary lymphatics, which follow the pulmonary vessels to the lymph glands at the root of the lung. Others empty into the superficial pulmonary lymphatics, which form an extensive subpleural plexus connected with small subpleural lymph nodes, whence by means of several larger vessels the lymph is carried to the lymph nodes at the hilum.

Nerves.—Bundles of medullated and non-medullated fibres accompany the bronchial arteries and veins. Small sympathetic ganglia are distributed along these nerves. The fibres form plexuses in the fibrous layer of the bronchi, from which terminals pass to the muscle of the bronchi and of the vessel walls and to the mucosa. Free endings upon the epithelium of bronchi, air passages, and alveoli have been described.

#### DEVELOPMENT OF THE RESPIRATORY SYSTEM.

The epithelium of the respiratory system develops from entoderm, the connective-tissue elements from mesoderm. The first differentiation of respiratory system appears as a dipping down of the entoderm of the floor of the primitive pharynx. The tubule thus formed divides into a larger and longer right branch, which subdivides into three branches corresponding to the three lobes of the future right lung, and a smaller and shorter left branch, which subdivides into two branches corresponding to the two lobes of the future left lung. By repeated subdivisions of these tubules the entire bronchial system is formed. The last to develop are the respiratory divisions of the bronchi with their alveolar ducts, alveolar sacs and alveoli. The epithelium of the alveolar sacs and alveoli is at first entirely of the fœtal-cell type, the large flat respiratory plates appearing only after the lungs have become inflated. The fœtal and respiratory cells of the adult lung have therefore the same embryonic origin. During the early stages of lung development the mesodermic tissue predominates, but with the rapid growth of the tubules the proportion of the two changes until in the adult lung the mesodermic tissue becomes restricted to the inconspicuous pulmonary framework and the blood-vessels.

#### TECHNIC.

(1) The technic for the largest bronchi is the same as for the trachea (technic 3, p. 269). The medium size and small bronchi are studied in sections of the lung.

- (2) Lung and Bronchi.—Carefully remove the lungs and trachea (human, dog, or cat) and tie into the trachea a cannula to which a funnel is attached. Distend the lungs moderately (pressure of two to four inches) by pouring in formalin-Müller's fluid (technic 5, p. 7), and then immerse the whole in the same fixative for twenty-four hours. Cut into small blocks, using a very sharp razor so as not to squeeze the tissue, harden in alcohol, stain thin sections with hæmatoxylin-eosin (technic 1, p. 18), and mount in balsam or in eosin-glycerin. The larger bronchi are found in sections near the root of the lung. The arrangement of the pulmonary lobules is best seen in sections near and horizontal to the surface. Sections perpendicular to and including the surface show the pulmonary pleura.
  - (3) Respiratory Epithelium (technic 1, p. 71).

(4) Elastic Tissue of the Lung (technic 3, p. 26).

(5) Blood-vessels.—For the study of the blood-vessels, especially of the capillary networks of the alveoli, sections of injected lung should be made. A fresh lung is injected (page 22) with blue gelatin, through the pulmonary artery. It is then hardened in alcohol, embedded in celloidin, and thick sections are stained with eosin and mounted in balsam.

## The Thyreoid.

The thyreoid (Fig. 190) is a ductless structure built upon the general principle of a compound alveolar gland. There are usually two

lateral lobes connected by a narrow band of glandular tissue. the "isthmus." Each lobe is surrounded by a connective-tissue capsule, from which septa pass into the lobe, subdividing it into lobules. From the perilobular connective tissue finer strands extend into the lobules, separating the alveoli. The latter are spherical, oval, or irregular in shape. They vary greatly in diameter (40 to 120µ) and are as a rule non-communicating. At birth most of the alveoli are empty, but soon become more or less filled with a peculiar substance known as "colloid." The alveoli are lined with a single or double layer of cuboidal epithelial cells. Two types of cells are recognized.

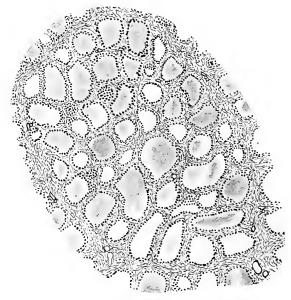


Fig. 190.—Section of Human Thyreoid. Most of the alveoli contain colloid.

One of these is actively secreting colloid and is known as a *secreting* or *colloid* cell. The other contains no colloid and is known as a *resting* or *reserve* cell. It is probable that their names indicate the relation of these cells to each other and that the reserve cell ultimately becomes a colloid-secreting cell.

The colloid cell appears in some cases simply to pour out its colloid secretion into the lumen, after which it may assume the character of a resting cell; in other cases the cell appears to be completely transformed into colloid, its place being taken by proliferation of the resting cells. In certain alveoli which are much distended with colloid the lining epithelium is flattened.

That the thyreoid exerts a decided influence upon general body metabolism is shown by the symptoms resulting from congenital absence of the gland (congenital myxcedema or cretinism) and by the effects of complete removal, the latter giving rise to a train of symptoms known as the "cachexia strumipriva."

The **blood supply** of the thyreoid is extremely rich, the vessels branching and anastomosing in the connective tissue and forming dense capillary networks around the alveoli.

Lymphatics accompany the blood-vessels in the connective tissue. Nerves are mainly non-medullated fibres which form plexuses around the blood-vessels and in the connective tissue surrounding the alveoli. Terminals to the secreting cells end in club-like dilatations

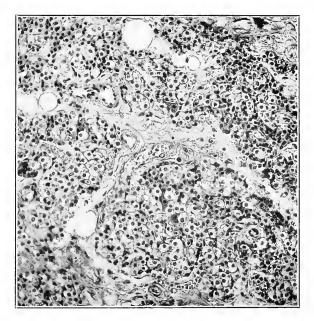


Fig. 191.—Section of Human Parathyreoid; showing mainly "clear," "principal", or "chief" cells. (Pool.)

against the bases or between the epithelial cells. A few afferent medullated fibres are found in the plexuses surrounding the blood-vessels.

DEVELOPMENT.—The thyreoid originates as a diverticulum from the entoderm of the primitive pharynx. It first appears in embryos of 3 to 5 mm. and grows ventrally into the mesoderm of the ventral wall of the neck. Here it forms a mass which lies transversely across the neck. It is composed of solid cords of cells which become hollow to form the alveoli of the gland. At first the gland is connected with the surface by the thyreo-glossal duct. This either disappears entirely or is represented in the adult by such rudimentary structures as the so-called prehyoid, suprahyoid, and accessory thyreoid glands. The gland at first consists of solid cords of cells. Ingrowth of connective tissue divides these into groups or lobules, and at the same time breaks up the long tubules into short segments. Dilatation of the alveoli occurs with the formation of colloid.

### The Parathyreoids.

These are small ductless glands which usually lie upon the posterior surface of the lateral lobes of the thyreoid. There are commonly two

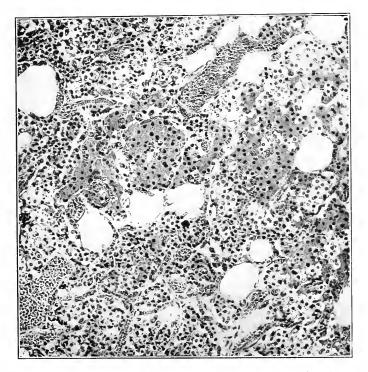


Fig. 192.—Section of Human Parathyreoid showing groups of oxyphile cells. (Pool.)

pairs, a superior and an inferior, on each side. The number is, however, subject to variation. Each gland is from 6 to 8 mm. long, about half that in breadth, and 2 mm. thick. Small groups of cells having the structure of the parathyreoids have been found below the thyreoid and within the thyreoid and thymus.

The parathyreoid is surrounded by a thin connective-tissue capsule which sends a variable amount of connective tissue into the gland as septa. When the amount is considerable the gland shows a subdivision into lobules. The stroma consists largely of reticular tissue and is very vascular. The number and arrangement of the cells vary. The gland may be almost wholly cellular with very little connective tissue, the groups of cells may be widely separated by interstitial tissue,

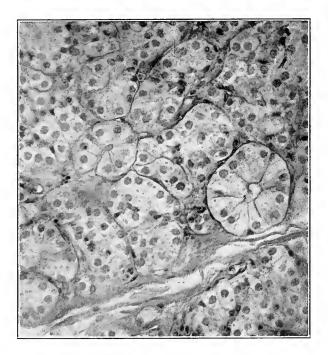


Fig. 193.—Section of Human Parathyreoid, showing lumina indicating tubular or tubulo-alveolar structure. (Pool.)

or there may be any intermediate condition. The cells are arranged in irregular groups or cords (Figs. 191, 192) sometimes around tubules, sometimes having a distinctly alveolar structure (Fig. 193); in the latter case colloid may be present in the lumen. Colloid has also been found between, and colloid and glycogen within, the cells.

The cells themselves are spheroidal, cuboidal or pyramidal, with basal nuclei. The appearance of the cells varies sufficiently to have caused two or three types to be distinguished. All, however, probably represent different functional conditions of the same cell. (1) *Chief* or *clear cells* (Fig. 191). These are the more numerous. Their bodies are

small and clear, and the cytoplasm does not stain readily. The nuclei are large in proportion to the cell and are clear and vesicular with loosely arranged pale chromatin network. (2) Oxyphile cells (Fig. 192). These are larger, their cytoplasm is more granular and takes a strong eosin stain. The nucleus is small, its chromatin network closely arranged and takes a dark stain. Compact groups of these cells occur especially just beneath the capsule. They are also found throughout the gland, arranged as cords, as single cells, or as small groups among the clear cells. Intermediate types have been described. It is probable that the clear cells represent the resting, the granular cells the active secreting condition of the same cell.

The parathyreoids originate as epithelial evaginations from the third and fourth branchial grooves, and develop wholly independently of the thyreoid.

The powerful influence which these minute organs exert is shown both clinically and experimentally. Fatal tetany, resulting from the earlier operations for complete removal of the thyreoids, has been shown by animal experimentation to be due not to the removal of the thyreoids, but to coincident removal of the parathyreoids, the removal of the latter only, in animals, giving the same results.\*

#### TECHNIC.

The thyreoid and parathyreoid glands are best fixed in formalin-Müller's fluid. Sections may be stained with hæmatoxylin-eosin or hæmatoxylin-picro-acid-fuchsin and mounted in balsam.

### General References for Further Study.

Miller, W. S.: Das Lungenläppchen, seine Blut- und Lymphgefässe.

Councilman: The Lobule of the Lung and its Relations to the Lymphatics.

Kölliker: Handbuch der Gewebelehre des Menschen.

Pool: Tetany Parathyreopriva. Annals of Surgery, October, 1907.

\* For much of the description of the parathyreoids and for the photograph the writer is indebted to Dr. Eugene H. Pool.

### CHAPTER VIII.

#### THE URINARY SYSTEM.

## The Kidney.

THE kidney is a compound tubular gland. It is enclosed by a firm connective-tissue capsule, the inner layer of which contains smooth muscle cells. In many of the lower animals and in the human

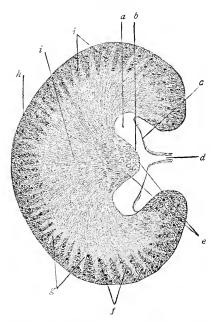


Fig. 194.—Longitudinal Section Through Kidney of Guinea-pig, including hilum and beginning of ureter. × 5. (Technic 1, p. 302.) a, Pelvis; b, papilla; e, wall of pelvis; d, ureter; e, ducts of Bellini; f, cortical pyramids; g, medullary rays; h, cortex; i, medulla; j, renal corpuscles.

fœtus septa extend from the capsule into the gland, dividing it into a number of lobes or *renculi*. In some animals, *e.g.*, the guineapig and rabbit, the entire kidney consists of a single *lobe* (Fig. 194). In the adult human kidney the division into lobes is not complete, the peripheral parts of the different lobes blending. Rarely the fœtal division into lobes persists in adult life, such as kidney being known as a "lobulated kidney."

On the mesially directed side of the kidney is a depression known as the *hilum* (Fig. 194). This serves as the point of entrance of the *renal artery* and of exit for the *renal vein* and *ureter*.

On section, a division of the organ into two zones is apparent to the naked eye (Figs. 194 and 195). The outer zone or *cortex* 

has a granular appearance, while the inner zone or *medulla* shows radial striations. This difference in appearance between cortex and medulla is mainly due, as will be seen subsequently, to the fact that in the cortex the kidney tubules are convoluted, while in the medulla

they run in parallel radial lines alternating with straight tl.od-vessels. The medullary portion of the kidney projects into the gettic, or upper expanded beginning of the ureter Figs. 162 and 163 in the firm of

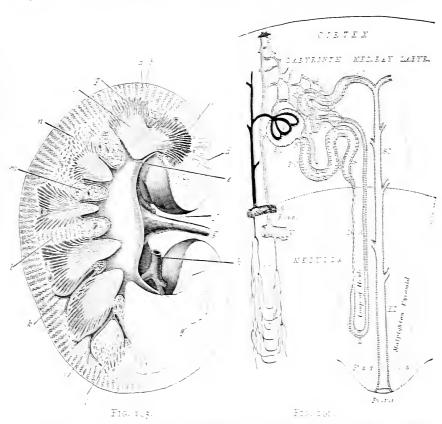


Fig. 105.—Longitudinul Secti n (d. Kl.) tney Thr. ugh Hilum. (a. C. mica, pyramica), medullary ray: c. medulla: b, ocriex: c renai cu yx: f, bilum: g, ureter, b, rena, artery. f, obliquely cut tubules of medulla. cand h, renaj arches. f, cylumn. f Bengni; m. c. mrentice tissue and fat surrounding renal vessels: n. medulia out it liquely, n. papilla g. medullary

pyramid. Merkel-Henle.

pyramid. Merke-frene.

Fig. 100.—Scheme of Uriniferous Tubule and of the Blood-vesses of the Kliney showing their relation to each other and to the different parts of the kliney. G. G. merulus: BC. Bowman's capsule: N. neck: PC. proximal convoluted tubule: S. spiral tubule. D. descending arm of Henle's loop: L. Henle's loop: A. ascending arm of Henle's loop: L. Henle's loop: A. ascending arm of Henle's loop: L. door of School convoluted tubule: BC. arched tubule: SC. straight convolute fibries. ED. duct of Bellini: A. arcuate arrey, and V. arcuate vein, giving of fine it are vesses of contex and vesses are to produce the produce of the second vesses of the Kliney. cortex and vasa recta to medulla: a. afferent vessel of glomerulus le efferent vessel of glomerulus) c. capillary network in cortical labyrinth; c. stellate veins—tr. vasa recta and capillary network of medulia. Pears l.

papilla. The number of papilla varies from ten to fifteen corresponding to the number of lobes in the foetal kidney. The pyramidal segment of medulla, the apex of which is a papilla—in other words, the medullary portion of a fætal lobe—is known as a medullary or Malpighian pyramid. The extensions downward of cortical substance between the Malpighian pyramids constitute the columns of Bertini or septa renis. Radiating lines—medullary rays or pyramids of Ferrein—extend outward from the base of each Malpighian pyramid into the cortex (Fig. 195). As the rays extend outward in groups they outline pyramidal cortical areas. These are known as the cortical pyramids or cortical labyrinths.

The secreting portion of the kidney is composed of a large number of long tortuous tubules, the *uriniferous tubules*.

Each URINIFEROUS TUBULE begins in an expansion known as  $Bowman's\ capsule$  (Figs. 196, BC, and 197, 3, 4, 5). This encloses a

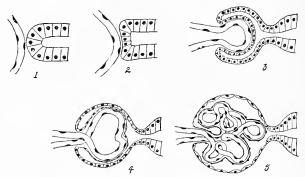


Fig. 107.—Diagrams Illustrating Successive Stages in Development of the Renal Corpuscle, 1 and 2, Approach of blood-vessel and blind end of tubule; 3, invagination of tubule by blood-vessels; 4 and 5, later stages, showing development of glomerulus and of the two-layered capsule of the renal corpuscle, the outer layer being the capsule of Bowman continuous with the epithelium of the first convoluted tubule.

tuft of blood capillaries, the *glomerulus*. Bowman's capsule and the glomerulus together constitute the *Malpighian body* or *renal corpuscle*. (Fig. 198). As it leaves the Malpighian body the uriniferous tubule becomes constricted to form the neck (Figs. 196, N, 197, and 198 b). It next broadens out into a greatly convoluted portion, the *first convoluted tubule* (Fig. 196, PC, and Fig. 199). The Malpighian body, the neck, and the first convoluted tubule are situated in the cortical pyramid (Fig. 196). The tubule next takes a quite straight course downward into the medulla—descending arm of Henle's loop (Fig. 196, D)—turns sharply upon itself—Henle's loop (Fig. 196, L)—and passes again toward the surface—ascending arm of Henle's loop (Fig. 196, L)—through the medulla and medullary ray. Leaving the medullary ray, it enters the same cortical pyramid from which it took origin to

become the second convoluted tubule (Fig. 196, DC). This tubule is in close proximity to the Malpighian body from which it started, lying, however, on the side of the afferent and efferent blood-vessels, i.e., on the side opposite its point of origin. The second convoluted tubule passes into the arched tubule (AC) which enters a medullary ray and continues straight down through the medullary ray and medulla as the straight or collecting tubule (SC). During its course the collecting tubule receives other arched tubules. As it descends it becomes broader, enters the papilla, where it is known as the duct of Bellin (ED), and opens on the surface of the papilla into the kidney pelvis About twenty ducts of Bellini open upon the surface of each papilla their openings being known as the foramina papillaria.

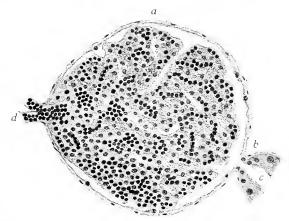


Fig. 198.—Malpighian Body from Human Kidney.  $\times$  280. (Technic 2, p. z02.) a, Bowman's capsule; b, neck; c, first convoluted tubule; d, afferent and efferent vessels.

Each tubule consists of a delicate homogeneous *membrana propria* upon which rests a *single layer* of *epithelial cells*. The shape and structure of the epithelium differ in different portions of the tubule.

1. The *Malpighian body* is spheroidal, and has a diameter of from 120 to 200 $\mu$ . The structure of the Malpighian body can be best understood by reference to its development (Fig. 197). During the development of the uriniferous tubules and of the blood-vessels of the kidney, the growing end of a vessel meets the growing end of a tubule in such a way that there is an invagination of the tubule by the blood-vessel (see Fig. 197). The result is that the end of the vessel which develops a tuft-like network of capillaries—the *glomerulus*—comes to lie within the expanded end of the tubule, which thus forms a two-layered capsule for the glomerulus. One layer of the capsule closely invests the tuft of capillaries, dipping down into it and separating the

groups of capillaries (see p. 294). This layer by modification of the original epithelium of the tubule is finally composed of a single layer of flat epithelial cells with projecting nuclei. The outer layer of the capsule lies against the delicate connective tissue which surrounds the Malpighian body. This layer consists of a similar though slightly higher epithelium and is known as *Bowman's capsule*. Between the glomerular layer of the capsule and Bowman's capsule proper is a space which represents the beginning of the lumen of the uriniferous tubule (Fig. 198), the epithelium of Bowman's capsule being directly continuous with that of the neck of the tubule.

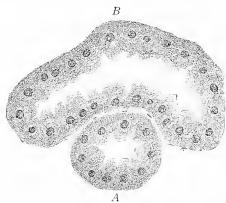


Fig. 199.—Proximal Convoluted Tubules of Human Kidney. × 350. (Technic 2, p, 302.) A, Cross-section; B, oblique section.

- 2. The Neck.—This is short and narrow, and is lined by a few cuboidal epithelial cells. Toward its glomerular end the epithelium is transitional between the flat epithelium of Bowman's capsule and the cuboidal epithelium of the neck proper. At its other end the epithelium of the neck becomes larger and more irregular as it passes over into that lining the next division of the tubule (Fig. 198).
- 3. The first convoluted tubule (Fig. 199) measures from 40 to  $70\mu$  in diameter. It is lined by irregularly cuboidal or pyramidal epithelium, with very indistinct demarcation between the cells. The cytoplasm is granular, and the granules are arranged in rows, giving the cell a striated appearance. This is especially marked at the basal end of the cell where the nucleus is situated. A zone of fine striations along the free surface frequently presents somewhat the appearance of cilia.
- 4. The descending arm of Henle's loop is narrow (Fig. 200, 1), 10 to  $15\mu$  in diameter. It is lined by a simple flat epithelium. The part of the cell which contains the nucleus bulges into the lumen, and as the

nuclei of opposite sides of the tubule usually alternate, the lumen is apt to present a wavy appearance in longitudinal sections.

5. Henle's Loop.—The epithelium here changes from the flat of the descending arm to the cuboidal of the ascending arm. The exact point where the transition occurs varies. It may take place during the turn of the loop, or in either the ascending or descending arm.

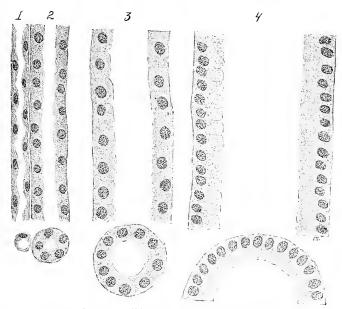


Fig. 200.—Tubules of Human Kidney.  $\times$  560. From longitudinal section. (Technic 2, p. 302.) I, Descending arm of Henle's loop; 2, ascending arm of Henle's loop; 3, collecting tubule; 4, duct of Bellini. Beneath the longitudinal sections are seen cross sections of the same tubules.

- 6. The ascending arm of Henle's loop (Fig. 200, 2) is broader than the descending, measuring from 20 to 30µ in diameter. Its epithelium is cuboidal with granular striated protoplasm. The cells thus resemble those of the convoluted tubule, but are smaller, more regular, and less granular.
- 7. The second convoluted tubule has a diameter of 40 to 50 $\mu$ . It is much less tortuous than the first convoluted tubule. Its epithelium is similar to that lining the first convoluted tubule except that it is slightly lower and less distinctly striated.
- 8. The *arched tubule* has a somewhat narrower lumen (about  $25\mu$ ) than the second convoluted. It is lined with a low cuboidal epithelium with only slightly granular cytoplasm.
  - 9. The straight or collecting tubule (Fig. 200, 3) has at its commence-

ment at the apex of a medullary ray a diameter of from 40 to  $50\mu$  As it descends it receives other arched tubules, and increases in diameter until in the *ducts of Bellini* (Fig. 200, 4) of the papilla it has a diameter of from 200 to  $300\mu$  and a widely open lumen. The epithelium is at first low and gradually increases in height. In the ducts of Bellini it is

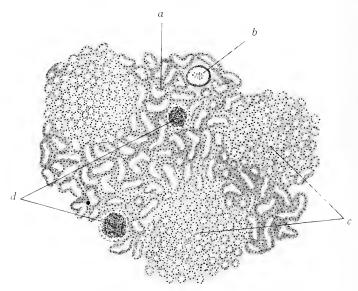


Fig. 201.—Cross Section Through Cortex of Human Kidney.  $\times$  60. (Technic 2, p. 302.) a, Convoluted tubules of cortical pyramid; b, interlobular artery; c, medullary rays; d, Malpighian bodies.

of the high columnar type. The cytoplasm of these cells contains comparatively few granules, thus appearing transparent in contrast with the granular cytoplasm of the ascending arms of Henle's loops and of the convoluted tubules.

Location in kidney	Portion of tubule	<i>Epithelium</i>
Cortical labyrinth	Bowman's capsule Neck First convoluted	Flat with bulging nuclei. Cuboidal granular. Pyramidal, granular; large cells with granules in rows, giving striated appearance;
	Second convoluted	striated free border; indistinct cell outline. Similar to preceding, but cells not so distinctly striated and more regular in shape.

Location in kidney	Portion of tubule	Epithelium
Medullary ray in cortex.	Arched (passing from labyrinth to ray)	Rather clear cuboidal cells.
	Part of ascending arm Henle's loop	Cuboidal, granular, regular.
	Collecting tubule	Cuboidal or columnar, clear; varying in height with diameter of tubule.
Medulla	Decending arm, Hen- le's loop	Clear flat cells with bulging nuclei.
	Henle's loop	Usually like descending, rarely like ascending arm.
	Part of ascending arm Henle's loop	Cuboidal, granular.
Papilla	Collecting tubule	Cuboidal or columnar, clear; varying in height with diameter of tubule.
	Ducts of Bellini	Clear, cuboidal or columnar cells according to diameter of tubule.

The epithelium of the uriniferous tubule rests upon an apparently structureless basement membrane. Rühle describes the basement membrane as consisting of delicate longitudinal and circular connective-tissue fibrils. He regards the fibrils as merely a more regular arrangement of the interstitial connective tissue. According to Rühle the epithelium simply rests upon the basement membrane, being in no way connected with it. In the cortex the tubules are closely packed and the amount of interstitial connective tissue is extremely small. In the medulla the connective tissue is more abundant.

Of the function of the different parts of the uriniferous tubule our knowledge is extremely limited. The water of the urine is secreted in the Malpighian body, some specific action of the cells covering the glomerulus, allowing the water, normally free from albumen, to pass from the capillaries into the lumen of the tubule. The urinary solids are secreted mainly or wholly by the cells of the convoluted tubule and of the ascending arm of Henle's loop.

**Blood-vessels** (diagram, Fig. 203).—The blood supply to the kidney is rich and the blood-vessels come into intimate relations with the tubules. The *renal artery* enters the kidney at the hilum, and immediately splits up into a number of branches—the *interlobar arteries* (Fig 203, g). These give off twigs to the calyces and to the capsule, then

without further branching pass between the papillæ through the medulla to the junction of medulla and cortex. Here they bend sharply at right angles and following the boundary line between cortex and medulla, form a series of arches, the *arteriæ arciformes* or *arcuate arteries* (Fig. 203, d). From the arcuate arteries two sets of vessels arise, one supplying the cortex, the other the medulla (Figs. 196 and 203).

The arteries to the cortex spring from the outer (Fig. 203, b) sides of the arterial arches, and as interlobular arteries pursue a quite straight

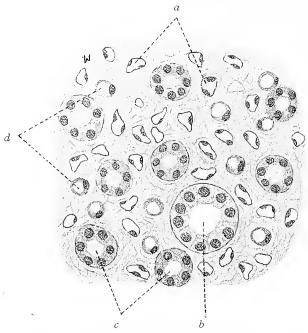


Fig. 202.—Cross Section through Medulla of Human Kidney.  $\times$  465. (Technic 2, p. 302.) a, Capillaries; b, collecting tubule; c, ascending arms of Henle's loops; d, descending arms of Henle's loops.

course through the cortical pyramids toward the surface, about midway between adjacent medullary rays. From each interlobular artery are given off numerous short lateral branches, each one of which passes to a Malpighian body. Entering a Malpighian body as its afferent vessel, the artery breaks up into a number of small arterioles, which in turn give rise to the groups of capillaries which form the glomerulus. Each group of glomerular capillaries arising from a single arteriole is separated from its neighbors by a rather larger amount of connective tissue than that which separates the individual capillaries. This gives to the glomerulus its lobular appearance. From the smaller glomerular capillaries the blood passes into somewhat larger capillaries, which unite to form the efferent vessel of the glomerulus. As afferent

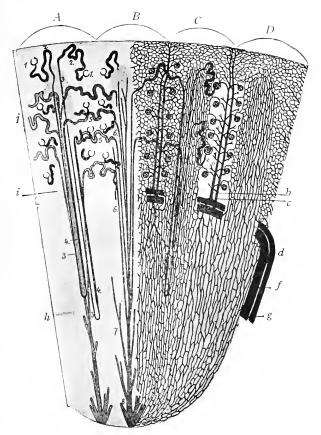


Fig. 203.—Diagram to Illustrate (left) the Course of the Uriniferous Tubule; (right) the Course of the Renal Vessels. (Szymonowicz.) A, B, C, D, form the kidney *lobules*; a, afferent vessel; e, efferent vessel of glomerulus; e, Bowman's capsule; e, first convoluted tubule; e, descending arm of Henle's loop; e, ascending arm of Henle's loop; e, second convoluted tubule; e and e, collecting tubules; e, duct of Bellini; e, interlobular artery; e, interlobular vein; e, renal arch (arcuate artery above and arcuate vein below); e, interlobar vein; e, interlobar artery; e, medulla; e, medullary ray; e, cortex.

and efferent vessels lie side by side, the glomerulus has the appearance of being suspended from this point (Figs. 196, 198). The entire vascular system of the glomerulus is arterial.

After leaving the glomerulus, the efferent vessel breaks up into a second system of capillaries, which form a dense network among the

tubules of the cortical pyramids and of the medullary rays. The mesh corresponds to the shape of the tubules, being irregular in the pyramids, long and narrow in the rays. In these capillaries the blood gradually becomes venous and passes into the interlobular veins (Fig. 203.c). These accompany the interlobular arteries to the boundary between cortex and medulla, where they enter the arcuate veins, which accompany the arcuate arteries (Fig. 203.d).

The main arteries to the medulla arise from the inner concave sides of the arterial arches. They pass straight down among the tubules of the medulla and are known as arteriæ rectæ. Branching, they give rise to a long-meshed capillary network which surrounds the tubules. This capillary network is also supplied by  $(\mathfrak{1})$  efferent vessels from the more deeply situated glomeruli (false arteriæ rectæ) and  $(\mathfrak{2})$  by medullary branches from the interlobular arteries. The veins of the medulla arise from the capillary network and follow the arteries back to the junction of medulla and cortex, where they empty into the arcuate veins (Fig. 203, d).

In addition to the distribution just described, some of the interlobular arteries extend to the surface of the kidney, where they enter the capsule and form a network of capillaries which anastomose with capillaries of the suprarenal, recurrent, and phrenic arteries. A further collateral circulation is established by branches of the abovenamed arteries penetrating the kidney and forming capillary networks within the cortex, even supplying some of the more superficial glomeruli. The most superficial of the small veins which enter the interlobular are arranged in radial groups, having the interlobular veins as their centres. These lie just beneath the capsule, and are known as the stellate veins of Verheyn. In addition to capillary anastomoses, direct communication between arteries and veins of both cortex and medulla, by means of trunks of considerable size, has been described.

The lymph vessels of the kidney are arranged in two systems, a superficial system which ramifies in the capsule, and a deep system which accompanies the arteries to the parenchyma of the organ. Little is known of the relation of the lymphatics to the kidney tubules.

Nerves.—These are derived from both cerebro-spinal and sympathetic systems. The medullated fibres appear to pass mainly to the walls of the blood-vessels which supply the kidney capsule. Plexuses of fine non-medullated fibres (sympathetic) accompany the arteries to the glomeruli. Delicate terminals have been described as

passing from these plexuses, piercing the basement membrane and ending freely between the epithelial cells of the tubules.

### The Kidney-Pelvis and Ureter.

The kidney-pelvis, with its subdivisions the calyces, and the ureter constitute the *main excretory duct* of the kidney. Their walls consist of three coats: an inner mucous, a middle muscular, and an outer fibrous.

The mucosa is lined by epithelium of the transitional type. There are from four to eight layers of cells, the cell outlines are usually well defined, and the surface cells instead of being distinctly squamous are only slightly flattened. Less commonly large flat plate-like cells, each containing several nuclei, are present. The cells rest upon a basement membrane, beneath which is a stroma of delicate fibro-elastic tissue rich in cells. Diffuse lymphatic tissue frequently occurs in the stroma, especially of the pelvis. Occasionally the lymphatic tissue takes the form of small nodules. Mucous glands in small numbers are found in the stroma of the pelvis and upper part of the ureter. There is no distinct submucosa, although the outer part of the stroma is sometimes referred to as such.

The muscularis consists of an inner longitudinal and an outer circular layer. In the lower part of the ureter a discontinuous outer longitudinal layer is added.

The fibrosa consists of loosely arranged connective tissue and contains many large blood-vessels. It is not sharply limited externally, but blends with the connective tissue of surrounding structures, and serves to attach the ureter to the latter.

The larger **blood-vessels** run in the fibrous coat. From these, branches pierce the muscular layer, give rise to a capillary network among the muscle cells, and then pass to the mucosa, in the stroma of which they break up into a rich network of capillaries. The veins follow the arteries.

The **lymphatics** follow the blood-vessels, being especially numerous in the stroma of the mucosa.

Nerves.—Plexuses of both medullated and non-medullated fibres occur in the walls of the ureter and pelvis. The non-medullated fibres pass mainly to the cells of the muscularis. Medullated fibres enter the mucosa where they lose their medullary sheaths. Terminals of these fibres have been traced to the lining epithelium.

### The Urinary Bladder.

The walls of the bladder are similar in structure to those of the ureter.

The mucous membrane is thrown up into folds or is comparatively smooth, according to the degree of distention of the organ. The epithelium is of the same general type—transitional epithelium (see page 67)—as that of the ureter. The number of layers of cells and the shapes of the cells depend largely upon whether the bladder is

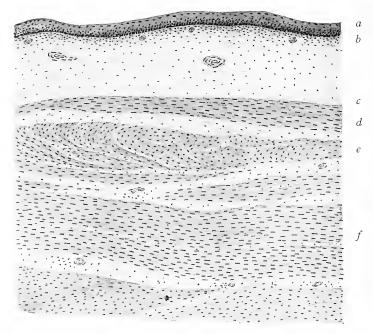


Fig. 204.—Vertical Section through Wall of moderately distended Human Bladder.  $\times$  60. (Technic 5, p. 302.) a, Epithelium, b, stroma, of mucous membrane; c, submucosa; d, inner muscle layer; e, middle muscle layer; f, outer muscle layer.

full or empty. In the collapsed organ the superficial cells are cuboidal or even columnar, their under surfaces being marked by pit-like depressions caused by pressure of underlying cells. Beneath the superficial cells are several layers of polygonal cells, while upon the basement membrane is the usual single layer of small cuboidal cells. In the moderately distended bladder the superficial cells become flatter and the entire epithelium thinner (Fig. 204). In the distended organ there is still further flattening of the superficial cells and thinning of the entire epithelium. The stroma consists of fine loosely arranged

connective tissue containing many lymphoid cells and sometimes small lymph nodules. It merges without distinct demarcation into the less cellular *submucosa* (Fig. 204,  $\epsilon$ ).

The three **muscular layers** of the lower part of the ureter are continued on to the bladder, where the muscle bundles of the different layers interlace and anastomose, but can be still indistinctly differentiated into an inner longitudinal, a middle circular, and an outer longitudinal layer (Fig. 204, d, e, f).

The **fibrous layer** is similar to that of the ureter, and attaches the organ to the surrounding structures.

The blood- and lymph-vessels have a distribution similar to those of the ureter.

Nerves.—Sensory medullated fibres pierce the muscularis, branch repeatedly in the stroma, lose their medullary sheaths, and terminate among the cells of the lining epithelium. Sympathetic fibres form plexuses in the fibrous coat, where they are interspersed with numerous small groups of ganglion cells. Axones of these sympathetic neurones penetrate the muscularis. Here they form plexuses, from which are given off terminals to the individual muscle cells.

For development of urinary system see page 346.

# The Suprarenal Gland.

The suprarenal is a ductless gland situated on the upper and anterior surface of the kidney. It is surrounded by a *capsule* and consists of an outer zone or *cortex* and a central porton or *medulla*. The cortex and medulla are sharply differentiated both in general appearance, and in histological structure. The former is of rather firm consistency, its cells are arranged in rows with the blood-vessels between them, giving the zone a striated appearance. Its cells contain fat droplets and peculiar granules known as *lipoid granules* which give the cortex a yellowish tint. In contrast the medulla is soft, vascular, has a dark reddish appearance, and its cells contain granules known as *chromaffin* or *phæochrome granules*.

The Capsule (Fig. 205, A) is composed of fibrous connective tissue and smooth muscle. In the outer part of the capsule the connective tissue is loosely arranged and merges with the surrounding fatty areolar tissue. The inner layer of the capsule is more dense and forms a firm investment for the underlying glandular tissue. From the capsule trabeculæ extend into the organ forming its framework and outlining

compartments, which contain the glandular epithelium. This connective tissue is reticular in character.

The CORTEX (Fig. 205, B) is subdivided into three layers or zones:

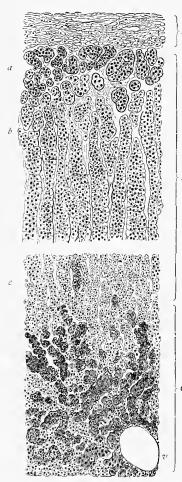


Fig. 205.—Vertical Section of Suprarenal. (Merkel-Henle.) Λ, Capsule; Β, cortex; C, medulla; a, glomerular zone; b, fascicular zone; ε, reticular zone; v, vein in medulla.

(a) A narrow, superficial layer, the glomerular zone; (b) a broad middle layer, the fascicular zone; and (c) a narrow deep layer, the reticular zone. The names of the layers are indicative of the shape of the connective-tissueenclosed compartments and of the contained groups of gland cells. In the glomerular zone (Fig. 205, a) the high, irregularly columnar epithelium is arranged in spherical or oval groups. The protoplasm of the cells is granular, and their nuclei are rich in chromatin. In the fascicular zone (Fig. 205, b) polyhedral cells are arranged in long columns or fascicles. The cytoplasm is granular and usually contains some or many fat droplets. The nuclei contain less chromatin than those in the glomerular zone. In the reticular zone (Fig. 205, c) similar though somewhat more darkly staining cells form a coarse reticulum of irregular anastomosing cords.

The MEDULLA (Fig. 205, C) consists of spherical and oval groups and cords of polygonal cells. After alcohol or formalin fixation these cells take a paler stain than those of the cortex. After fixation in solutions containing chromic acid or chrome salts the cells of the medulla assume a peculiar

characteristic deep brown color, which cannot be removed by washing in water and which is due to chromaffin granules which they contain. Scattered in irregular groups among these cells are many sympathetic ganglion cells.

Blood-vessels.—The arteries supplying the suprarenal first form a

poorly defined plexus in the capsule. From this are given off three sets of vessels—one to the capsule, one to the cortex, and one to the medulla. The first set breaks up into a network of capillaries, which supply the capsule. The vessels to the cortex break up into capillary networks, the shape of the mesh corresponding to the arrangement of the connective tissue in the different zones. The vessels to the medulla pass directly through the cortex without branching and form dense capillary networks among the groups of medullary cells. The relations of the capillaries to these gland cells are extremely intimate, especially in the reticular zone and medulla, where the cells in many cases immediately surround the capillaries in much the same manner as the glandular cells of a tubular gland surround their lumina. From the capillaries of both cortex and medulla small veins arise. These unite to form larger veins which empty into one or two main veins situated in the centre of the medulla.

**Lymphatics.**—These follow in general the course of the blood-vessels. The exact distribution of the suprarenal lymph system has not been as yet satisfactorily determined.

Nerves.—The nerve supply of the suprarenal is so rich and the nerve elements of the gland are so abundant as to have led to its classification by some among the organs of the nervous system. Both medullated and non-medullated fibres—but chiefly the latter—form plexuses in the capsule, where they are associated with groups of sympathetic ganglion cells. From the capsular plexuses fine fibres pass into the cortex, where they form networks around the groups of cortical cells. The nerve terminals of the cortex apparently do not penetrate the groups of cells. Bundles of nerve fibres, larger and more numerous than those to the cortex, pass through the cortex to the medulla. Here they form unusually dense plexuses of fibres, which not only surround the groups of cells, but penetrate the groups and surround the individual cells. Associated with the plexuses of the medulla, less commonly of the cortex, are numerous conspicuous groups of sympathetic ganglion cells.

Development.—The cortex and medulla have entirely different developmental histories. In the lower vertebrates (fishes) the two parts of the gland continue separate throughout life. In the ascending mammalian scale, the two parts become more and more closely united until in mammals they form a single organ. The cortex develops from mesoderm, first appearing in embryos of about five to six mm. At about the level of the cephalic third of the mesonephros the mesothelium

sends outgrowths into the mesenchyme. These outgrowths soon lose their connection with the main mass of mesothelium and constitute the anlage of the suprarenal cortex. The medulla has an entirely independent origin, being derived from ectoderm, as part of the peripheral sympathetic nervous system. The cells of some of the sympathetic ganglia differentiate into sympathoblasts and phaochromoblasts, which give rise to the sympathetic cells and chromaffin cells respectively. These cells soon separate from their ganglia of origin and come to lie first near, then within, the developing cortex, thus forming the medulla.

### TECHNIC.

(1) Fix the simple kidney of a rabbit or guinea-pig in formalin-Müller's fluid (technic 5, p. 7). Make sections through the entire organ including the papilla and pelvis, stain with hæmatoxylin-eosin (technic 1, p. 18), and mount in balsam. This section is for the study of the general topography of the kidney.

(2) Fix small pieces from the different parts of a human kidney in formalin-Müller's fluid or in Zenker's fluid. Thin sections should be made, some cutting the tubules longitudinally, others transversely, stained with hæmatoxylin-eosin and

mounted in balsam.

- (3) Blood-vessels.—For the purpose of demonstrating blood vessels of the kidney the method of double injection is useful (page 24).
- (4) Ureter.—Cut transversely into short segments, fix in formalin-Müller's fluid (technic 5, p. 7), and stain transverse sections with hæmatoxylin-eosin (technic 1, p. 18), or with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19). Mount in balsam.
- (5) Bladder (technic 1, p. 223, or technic 2, p. 223). By the latter method any desired degree of distention may be obtained.
- (6) Suprarenal. Technic same as (2) above. Thin vertical sections should include both cortex and medulla.

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## CHAPTER IX.

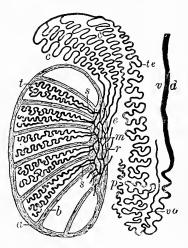
#### THE REPRODUCTIVE SYSTEM.

#### I. MALE ORGANS.

### The Testis.

THE testes are compound tubular glands. Each testis is enclosed in a dense connective-tissue capsule, the *tunica albuginea* (Fig. 206, a). Outside the latter is a closed serous sac, the *tunica vaginalis*, the

visceral layer of which is attached to the tunica albuginea, while the parietal layer lines the inner surface of the scrotum. Posteriorly the serous sac is wanting, the testis lying behind and outside of the tunica vaginalis. As the latter is derived from the peritoneum, being brought down with and invaginated by the testes in their descent to the scrotum, it is lined by mesothelial cells. To the inner side of the tunica albuginea is a layer of loose connective tissue rich in blood-vessels, the tunica vasculosa. Posteriorly the tunica albuginea is greatly thickened to form the corpus Highmori, or mediastinum testis, from which strong connective-tissue septa radiate (Figs. 206, m and 207, b). These septa pass completely through the organ and blend with the tunica albuginea at various points. In this way the interior of the testis is subdivided into a number of pyramidal



F16. 206.—Diagram illustrating the Course and Relations of the Seminiferous Tubules and their Excretory Ducts. (Piersol.) a, Tunica albuginea; b, connective-tissue septum between lobules; m, mediastinum; t, convoluted portion of seminiferous tubule; s, straight tubule; r, rete testis; e, vasa efferentia; c, tubules of head of epididymis; te, vas epididymis; vd, vas deferens; va, vas aberrans; p, paradidymis.

chambers or *lobules*, with bases directed toward the periphery and apices at the mediastinum (Figs. 206 and 207).

Behind the testis and outside of its tunica albuginea is an elongated body—the *epididymis* (Figs. 206, c and 207, c), consisting of convoluted

tubules continuous with those of the mediastinum. The epididymis is divided into three parts: an expanded upper extremity, the *head* or *globus major* (Figs. 206 and 207, c); a *middle piece*, the *body* (Fig. 207, d); and a slightly expanded *lower extremity*, the *tail* or *globus minor*. From the last named passes off the main excretory duct of the testis, the *vas deferens* (Fig. 206, vd). All of the tubules of the epididymis

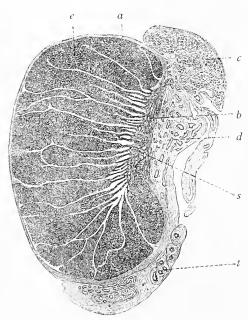


FIG. 207.—Longitudinal Section through Human Testis and Epididymis.  $\times$  2. (Böhm and von Davidoff.) The light strands are connective-tissue septa. a, Tunica albuginea; b, mediastinum and rete testis; c, head of epididymis; d, body of epididymis; e, lobule; s, straight tubules; t, vas epididymis.

are continuous on the one hand with the tubules of the testicle, and on the other with the vas deferens. They thus constitute a portion of the complex system of excretory ducts of the testicle.

The seminiferous tubule may be divided with reference to structure and location into three parts. (1) A much convoluted part, the convoluted tubule, which begins at the base and occupies the greater portion of a lobule of the testis (Fig. 210, a). As they approach the apex of a lobule several of these convoluted tubules unite to form (2) the straight tubule (Fig. 206, s, 210). This passes through the apex of

the lobule to the mediastinum, where it unites with other straight tubules to form (3) the irregular network of tubules of the mediastinum, the *rete testis* (Fig. 210, c).

1. The Convoluted Tubule.—This, which may be considered the most important secreting portion of the lobule, since it is here that the spermatozoa are formed, has a diameter of from 150 to 250 $\mu$ . The tubules begin, some blindly, others by anastomoses with neighboring tubules, near the periphery of the lobule, and pursue a tortuous course toward its apex (Fig. 210, a).

The wall of the convoluted tubule (Fig. 208) consists of three

layers: (a) An outer layer composed of several rows of flattened connective-tissue cells which closely invest the tubule; (b) a thin basement membrane; and (c) a lining epithelium. The epithelium consists of two kinds of cells, the so-called *supporting* or *sustentacular cells* and the *glandular cells proper*, the *spermatogenic cells*.

The sustentacular cells, or columns of Sertoli, are irregular, high, epithelial structures, whose bases rest upon the basement membrane,

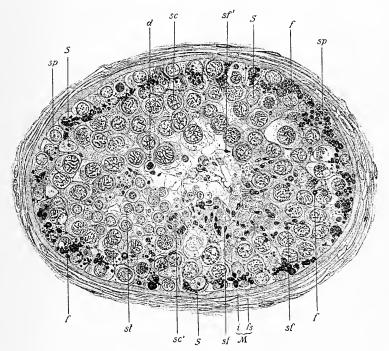


Fig. 208.—Cross Section of Convoluted Portion of Human Seminiferous Tubule.  $\times$  480. (Kölliker.) M, Basement membrane; i, its inner homogeneous layer, fs, its outer fibrous layer; s, nucleus of Sertoli cell; sp, spermatogone; sc, spermatozoër, sf, spermatozoër mitosis; sf, nearly mature spermatozoër; sf, spermatozoër free in lumen of tubule; d, degenerating nucleus in lumen; f, fat droplets stained by osmic acid.

and which extend through or nearly through the entire epithelium (Fig. 209, s). Their sides show marked irregularities and depressions, due to the pressure of surrounding spermatogenic cells. Their nuclei are clear, being poor in chromatin and their protoplasm contains brownish fat droplets. The cells of Sertoli have long been considered as sustentacular in character. It has recently been suggested that these cells are derived from the spermatogenic cells, but that, instead of developing into spermatozoa, they undergo retrograde changes, their

protoplasm mingling with the intercellular substance, their nuclei becoming lost and the cells finally disappearing. According to this theory the tuft-like arrangement of the spermatozoa about the ends of the Sertoli cells is due to pressure by surrounding spermatogenic cells (Figs. 200, h and 211, l).

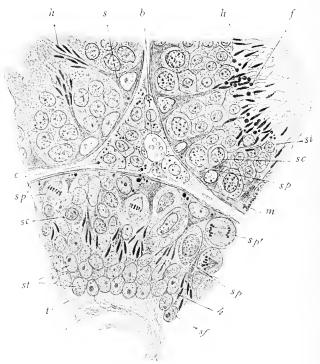


Fig. 209.—Parts of Transverse Section of three Seminiferous Tubules from Testis of White Mouse.  $\times$  600. (Szymonowicz.) s, Sertoli cell with nucleus; sp, spermatogone, resting state; sp', spermatogone in mitosis; sc, spermatocyte; st, spermatid; sf, spermatid developing into spermatozoön; h, head of spermatozoön; t, tails of developing spermatozoa; t, blood-vessel; t, interstitial cell; t, basal membrane; t, fat droplets.

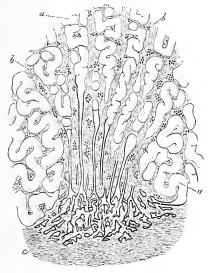
The appearance which the spermatogenic cells present depends upon the functional condition of the tubule. In the resting state the epithelium consists of several layers of spherical cells containing nuclei which stain with varying degrees of intensity. In the active state several distinct layers of spermatogenic cells can be differentiated. These from without inward are as follows:

(1) Spermatogones (Figs. 208 and 209, sp).—These are small cuboidal cells which lie against the basement membrane. Their nuclei are spherical and rich in chromatin. By mitotic division of the spermatogones are formed the cells of the second layer, the spermatocytes.

(2) Spermatocytes (Figs. 208 and 209. sc).—These are larger spherical cells with abundant cytoplasm and large vesicular nuclei showing various stages of mitosis. They form from two to four layers

to the inner side of the spermatogones, and are sometimes differentiated into spermatocytes of the first order and spermatocytes of the second order. By mitotic division of the innermost spermatocytes are formed the spermatids.

(3) The *spermatids* (Figs. 208 and 209. *st*) are small round cells which line the lumen



F1G. 210.

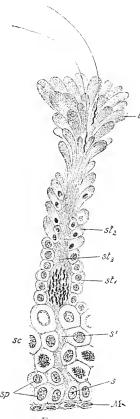


FIG. 211.

FIG. 210.—Passage of Convoluted Part of Seminiferous Tt bules into Straight Tubules and of these into the Rete Testis (Milhalkowicz.) a, Convoluted part of tubule; b, fibrous stroma continued from the mediastinum testis; c, rete testis.

Fig. 211.—Spermatoblast with some Adjacent Sperm Cells, from Testis of Sparrow. (From Kölliker, after Etzold.) M, Basement membrane; s, nucleus of Sertoli cell; sp, spermatogones; sc, spermatocyte;  $st_1$  and  $st_2$ , spermatids lying along the surface of the Sertoli cell, s' and  $st_3$ ; at  $st_3$  are seen the nearly mature spermatozoa; l, tuft-like arrangement of bodies of spermatids around free end of Sertoli cell, with two mature spermatozoa.

of the seminiferous tubule. They are the direct progenitors of the spermatozoa. (For details of spermatogenesis see page 314.)

In the actively secreting testicle *spermatozoa* are frequently found either free in the lumen of the tubule or with their heads among the superficial cells and their tails extending out into the lumen (Figs. 208,  $sf^1$  and 211). There are also found in the lumen many small

cells with dark nuclei. These are spermatids which have become free and which degenerate without forming spermatozoa.

Separating and supporting the convoluted tubules is a small amount of interstitial connective tissue in which are the blood-vessels and nerves. Among the usual connective-tissue elements are found



F16. 212.—From Section through Human Mediastinum and Rete Testis.  $\times$  96. (Kölliker.) A, Artery; V, vein; L, lymph space; C, canals of rete testis; s, cords of tissue projecting into the lumina of the tubules and so cut transversely or obliquely; Sk, section of convoluted portion of seminiferous tubule.

groups of rather large spherical cells with large nuclei—interstitial cells. They are believed to represent remains of the Wolffian body (Fig. 209, c).

2. The Straight Tubule.—With the termination of the convoluted portion, the spermatogenic tissue of the gland ends, the remainder of the tubule constituting a complex system of excretory ducts. The straight tubule is much narrower than the convoluted,

having a diameter of from 20 to 40 µ. It is lined by a single layer of cuboidal cells resting upon a thin basement membrane. At the apex

of the lobule the straight tubules become continuous with the tubules of the rete testis.

3. THE TUBULES OF THE RETE TESTIS.—These are irregular canals which vary greatly in shape and size. They are lined with a single layer of low cuboidal or flat epithelial cells (Fig. 212, C).

The Seminal Ducts.— While the already described

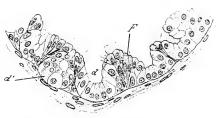


FIG. 213.—Part of a Cross Section through a Vas Efferens of the Human Epididymis. X 140. (Kölliker.) F, High columnar ciliated epithelium; d, lower non-ciliated epithelium, presenting appearance of a gland; d', the same cut obliquely.

straight tubules and the tubules of the rete testis must be regarded as part of the complex excretory duct system of the testis, there are certain structures which are wholly outside the testis proper, which serve to transmit the secretion of the testis, and are known as the seminal

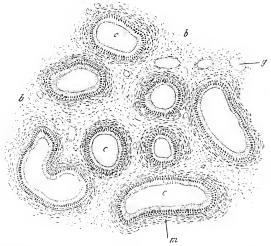


Fig. 214.—From Cross Section through Head of Epididymis.  $\times$  35. (Kölliker.) b, Interstitial connective tissue;  $\epsilon$ , sections through tubules of epididymis, showing two-layered columnar epithelium; g, blood-vessel.

ducts. On leaving the testis these ducts form the epididymis, after which they converge to form the main excretory duct of the testis, the vas deferens.

THE EPIDIDYMIS.—From the tubules of the rete testis arise from eight to fifteen tubules, the vasa efferentia, or efferent ducts of the

testis (Fig. 206, e). Each vas efferens pursues a tortuous course, is separated from its fellows by connective tissue, and forms one of the lobules of the head of the epididymis. The epithelium of the vasa efferentia consists of two kinds of cells, high columnar ciliated cells (Fig. 213, F), and, interspersed among these, low cuboidal non-ciliated cells (Fig. 213, d). Occasionally some of the high cells are free from cilia and some of the cuboidal cells may bear cilia. The cuboidal cells

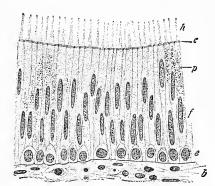


Fig. 215.—Vertical Section through Wall of Tubule of Epididymis. X 700. (Kölliform the vas epididymis (Fig. 214). Connective-tissue and smooth muscle cells; e, basal layer of epithelial cells; f, high columnar epithelial cells; p, pigment granules in columnar cells; c, cuticula; h, cilia.

lie in groups between groups of the higher cells, often giving the appearance of crypt-like depressions. These have been referred to as intraepithelial glands. They do not, however, invaginate the underlying tissues. The epithelium rests upon a basement membrane, beneath which are several layers of circularly disposed smooth muscle cells.

The vasa efferentia converge to Here the epithelium is of the stratified variety, there being two or three rows of cells. The surface cells are narrow, high, and ciliated,

and their nuclei are placed at different levels (Fig. 215). The cilia are long and each cell has only a few cilia. The deeper cells are irregular in shape. The basement membrane and muscular layers are the same as in the vasa efferentia. As the vas deferens is approached the muscular coat becomes thickened, and is sometimes strengthened by the addition of scattered bundles of longitudinally disposed cells.

THE VAS DEFERENS.—The walls of the vas deferens consist of four coats—mucosa, submucosa, muscularis, and fibrosa (Fig. 216).

The mucosa is folded longitudinally, and is composed of a stroma and a lining epithelium. The epithelium is of the stratified columnar type with two or three rows of cells, being similar to that lining the vas epididymis. The extent to which the epithelium is ciliated varies greatly. In some cases the entire vas is ciliated, in others only the upper portion, in still others no cilia are present beyond the epididymis. The epithelium rests upon a basement membrane beneath which is a

fibro-elastic cellular stroma. The stroma merges without distinct demarcation into the more vascular *submucosa*.

The muscularis consists of two strongly developed layers of smooth muscle, an inner circular and an outer longitudinal (Fig. 216), which together constitute about seven-eighths of the wall of the vas. At the beginning of the vas deferens a third layer of muscle is added

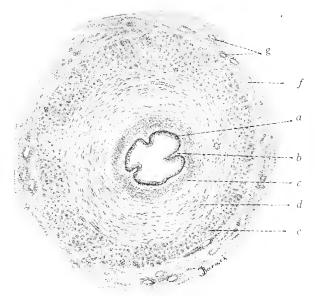


Fig. 216.—Cross Section of Human Vas Deferens.  $\times$  37. (Szymonowicz.) a, Epithelium; b, stroma; c, submucosa; d, inner circular muscle layer; e, outer longitudinal muscle layer; f, fibrous layer; g, blood-vessels.

composed of longitudinal bundles, and situated between the inner circular layer and the submucosa.

The *fibrosa* consists of fibrous tissue containing many elastic fibres. Near its termination the vas dilates to form the *ampulla*, the walls of which present essentially the same structure as those of the vas. The lining epithelium is, however, frequently markedly pigmented and the mucosa contains branched tubular glands.

The Seminal Vesicles and Ejaculatory Ducts.—The seminal vesicles. The walls of the seminal vesicles are similar in structure to those of the ampulla. The epithelium is pseudo-stratified with two or three rows of nuclei and contains a yellow pigment. When the vesicles are distended the epithelium flattens out and the nuclei lie more in one plane, thus giving the appearance of an ordinary simple columnar epithelium. Beneath the epithelium is a thin stroma, out-

side of which is an inner circular and an outer longitudinal layer of smooth muscle, both layers being much less developed than in the vas. The seminal vesicles are to be regarded as accessory genital glands.

The *ejaculatory ducts* are lined with a single layer of columnar cells. The muscularis is the same as in the ampulla except that the inner circular layer is thinner. In the prostatic portion of the duct the muscularis is indistinct, merging with the muscle tissue of the gland. The ducts empty either directly into the urethra or into the urethra through the vesicula prostatica.

Rudimentary Structures Connected with the Development of the Genital System.—Connected with the testicle and its ducts are remains of certain feetal structures. These are:

- (1) The paradidymis, or organ of Giraldes, situated between the vessels of the spermatic cord near the testis. It consists of several blind tubules lined with simple columnar ciliated epithelium.
- (2) The ductus aberrans Halleri, found in the epididymis. It is lined with simple columnar ciliated epithelium and opens into the vas epididymis. Instead of a single ductus aberrans, several ducts may be present.
- (3) The appendix testis (stalked hydatid or hydatid of Morgagni), in the upper part of the globus major. It consists of a vascular connective tissue surrounding a cavity lined with simple columnar ciliated epithelium:
- (4) The appendix epididymidis, a vascular structure, not always present, lying near the appendix testis. It resembles the latter in structure.

The paradidymis and ductus aberrans Halleri probably represent remains of the embryonal mesonephros. The appendix testis and the appendix epididymidis are believed by some to be derived from the primitive kidney, by others from the embryonal duct of Müller.

Blood-vessels.—Branches of the spermatic artery ramify in the mediastinum and in the tunica vasculosa. These send branches into the septa of the testicle, which give rise to a capillary network among the convoluted tubules. From the capillaries arise veins which accompany the arteries.

Lymph capillaries begin as clefts in the tunica albuginea and in the connective tissue surrounding the seminiferous tubules. These connect with the more definite lymph vessels of the mediastinum and of the spermatic cord. Nerves.—Non-medullated nerve fibres form plexuses around the blood-vessels. From these, fibres pass to plexuses among the semi-

niferous tubules. Their exact method of termination in connection with the epithelium has not been determined. In the epididymis are found small sympathetic ganglia. The walls of the vasa efferentia, vas epididymis, and vas deferens contain plexuses of non-medullated nerve fibres, which give off terminals to the smooth muscle cells and to the mucosa.

The Spermatozoa.—The spermatozoa are the specific secretion of the testicle. Human spermatozoa are long, slender flagellate bodies, from 50 to 70 m in length, and are suspended in the semen, which is a secretion of the accessory sexual glands. The general shape is that of a tadpole; and by means of an undulatory motion of the tail, the spermatozoön is capable of swimming about freely in a suitable medium. It has been estimated that the human spermatozoa average about sixty thousand per cubic millimetre of semen.

The human spermatozoön consists of (1) a head, (2) a middle piece or body, and (3) a tail or flagellum (Fig. 217).

The *head*, from 3 to 5µ long and about half that in breadth, is oval in shape when seen on flat, pear-shaped when seen on edge. It con-

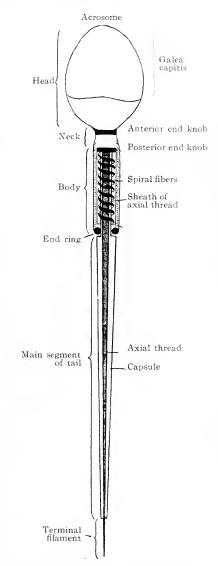


Fig. 217.—Diagram of a Human Spermatozoön. (Meves, Bonnet.)

sists mainly of chromatin derived from the nucleus of the parent cell. Enveloping the nuclear material of the head is a thin layer or delicate membrane of cytoplasm, the galea capitis. The front of the head

ends in a sharp edge, the *apical body* or *acrosome*. In some lower forms the acrosome is much more highly developed than in man and extends forward as a pointed or barbed spear, the *perforatorium*. The acrosome is differentiated from the nuclear portion of the head by taking an acid dye, the chromatin, of course, taking a basic stain.

The body is cylindrical, about the same length as the head, and consists of a fibrillated central core, the axial thread, surrounded by a protoplasmic capsule. A short clear portion, the neck, unites the head and body. Just behind the head the axial thread presents a bulbous thickening, the anterior end knob, which fits into a depression in the head. At the junction of neck and body are one or several posterior end knobs to which the axial thread is attached. The latter leaves the body through a perforated ring, the end ring or end disk. Delicate fibrils—spiral fibres—run spirally around the body portion of the axial thread.

The tail consists of a main segment, from 40 to 60µ in length, and a terminal segment having a length of from 5 to 10µ. The main segment has a central fibrillated axial thread which is continuous with the axial thread of the body. This is enclosed in a thin cytoplasmic membrane or capsule continuous with the capsule of the body. This membrane, inconspicuous and apparently structureless in man, is remarkably developed in some lower forms, e.g., the membrana undulata of birds. The terminal segment consists of the axial thread alone. The motility of the spermatozoön depends entirely upon the flagellate movements of the tail. In many of the lower animals the spermatozoön has a much more complicated structure.

Of the above-described parts of the spermatozoön only the head and tail can usually be differentiated, except by the use of special methods and very high-power objectives.

Development of the Spermatozoa.—As already noted in describing the testicle, the spermatozoa are developed from the epithelial cells of the seminiferous tubules. The most peripheral of the tubule cells, the *spermatogones* (Fig. 208, *sp* and Fig. 209, *sp*) are small round cells with nuclei rich in chromatin. By mitosis the spermatogone gives rise to two daughter cells, one of which remains at the periphery as a spermatogone, while the other takes up a more central position as a *spermatocyte* (Fig. 209, *sc* and Fig. 211, *sc*). The latter are rather large spherical cells, whose nuclei show very distinct chromatin networks. By mitotic division of the spermatocytes of the innermost row are formed the *spermatids* (Fig. 209, *st* and Fig. 211, *st*).

These are small spherical cells, which line the lumen of the tubule and are the *direct progenitors of the spermatozoa*. In the transformation of spermatocyte into spermatid an extremely important change takes place in the nucleus. This consists in a *reduction of its chromosomes to one-half the number specific for the species* (page 52). The transformation of the spermatid into the spermatozoön differs somewhat in different animals and the details of the process must be regarded as not

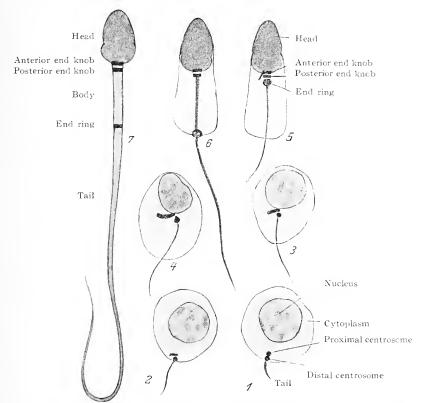


Fig. 218.—Transformation of a Spermatid into a Spermatozoön (human). Schematic. (Meyes, Bonnet.)

yet definitely determined. The nucleus of the spermatid first becomes oval in shape, and its chromosomes become condensed into a small homogeneous mass, which forms the head of the spermatozoön. During their transformation into the heads of the spermatozoa, the nuclei of the spermatids arrange themselves in tufts against the inner ends of the cells of Sertoli. This compound structure, consisting of a Sertoli cell and of a group of developing spermatozoa attached to its

central end, is known as a spermatoblast (Fig. 211). The body or middle piece of the spermatozoön is described by most investigators as derived from the centrosome, while the tail is a derivative of the cytoplasm.

The details of the transformation of the spermatid into the spermatozoon are illustrated in Fig. 218. The centrosome either divides completely, forming two centrosomes, or incompletely, forming a dumb-bell-shaped body. The nuclear material becomes very compact and passes to one end of the cell, forming the bulk of the head. Both centrosomes help to form the body. They first become diskshaped. The one lying nearer the center of the cell becomes attached to the posterior end of the head as the anterior end-knob, the other takes a position a little more posteriorly as the posterior end-knob and from it grows out the axial filament. Some of this centrosome passes to the posterior limits of the body and then becomes As the two parts of this centrosome separate the delicate cytoplasm between them forms the spiral fibres. During these changes the axial filament has been growing and projects beyond the limits of the cell. Most of the cytoplasm of the spermatid is not used in the formation of the spermatozoön, but is cast off and degenerates. A small amount is used for the sheath of the body, and for the galea capitis. The sheath of the main part of the filament appears to develop from the filament itself.

The significance of the different parts of the spermatozoön has been brought out in describing its development. From this it is seen that the spermatozoön, like the mature ovum, is a true sexual element with one-half the somatic number of chromosomes. The head and body, containing the chromatin and the centrosomes, are the parts of the spermatozoön essential to fertilization. The acrosome is an accessory which in some forms at least aids the spermatozoön in attaching itself to and in entering the ovum. The tail is an accessory structure which provides motion, enabling the spermatozoön to move about freely in the semen and in the fluids of the female generative tract. Considering ther minuteness, their speed is considerable, having been estimated at from 1.5 to 3.5 mm. per minute; enough to allow them to ascend through uterus and oviduct against the adverse action of the cilia. When in a favorable environment, such as the fluids of the female generative tract, the spermatozoon is capable of living for some time after leaving the testicle. Living spermatozoa have been found in the uterus or tubes one to three and a half weeks after coitus.

#### TECHNIC.

- (1) For the study of the general topography of the testis, remove the testis of a new-born child, make a deep incision through the tunica albuginea in order to allow the fixative to penetrate quickly, and fix in formalin-Müller's fluid (technic 5, p. 7). Antero-posterior longitudinal sections through the entire organ and including the epididymis should be stained with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) or with hæmatoxylin-eosin (technic 1, p. 18) and mounted in balsam.
  - (2) The testis of a young adult is removed as soon after death as possible, is

cut into thin transverse slices, which include the epididymis, and is fixed in formalin-Müller's or in Zenker's fluid (technic 9, p. 8). Select a slice which includes the head of the epididymis, cut away the anterior half or two-thirds of the testis proper in order to reduce the size of the block, and, after the usual hardening and embedding, cut thin sections through the remaining posterior portion of the testis, the mediastinum, and epididymis. Stain with hæmatoxylin-eosin (technic 1, p. 18) and mount in balsam.

- (3) For the study of spermatogenesis fix a mouse's testis in chrome-acetic-osmic mixture (technic 7, p. 7). Harden in alcohol and mount thin unstained sections in balsam or in glycerin.
- (4) Spermatozoa.—Human spermatozoa may be examined fresh in warm normal saline solution or fixed in saturated aqueous solution of picric acid and mounted in glycerin. Mammalian spermatozoa may be obtained from the vagina after intercourse, or by incision into the head of the epididymis. Technic same as for human.
- (5) A portion of the vas deferens is usually removed with the testis and may be subjected to technic (2) above. Transverse sections are stained with hæmatoxylineosin and mounted in balsam.

### The Prostate Gland.

The prostate is described by some as a compound tubular, by others as a compound alveolar gland. It is perhaps best regarded as a collection of simple branched tubular glands with dilated terminal tubules. These number from forty to fifty, and their ducts converge to form about twenty main ducts, which open into the urethra. The gland is surrounded by a capsule of fibro-elastic tissue and smooth muscle cells, the muscle cells predominating. From the capsule broad trabeculæ of the same structure as the capsule pass into the gland. The amount of connective tissue is large. It is less in the prostate of the young than of the old. The hypertrophied prestate of age is due mainly to an increase in the connective-tissue elements. The tubules have wide lumina and are lined with simple cuboidal epithelium of the serous type, resting upon a delicate basement membrane (Fig. 210). Less commonly the epithelium is pseudo-stratified. The ducts are lined with simple columnar epithelium until near their terminations, where they are lined with transitional epithelium similar to that lining the urethra. Peculiar concentrically laminated bodies. crescentic corpuscles, or corpora amylacea, are frequently present in the terminal tubules (Fig. 219, c). They are more numerous after middle Through the prostate runs the prostatic portion of the urethra. Within the prostate is found the vesicula prostatica (utriculus prostaticus—uterus masculinus). It represents the remains of a fœtal structure, the  $M\ddot{u}llerian\ duct$  and consists of a blind sac with folded mucous membrane lined with a two-rowed ciliated epithelium which dips down to form short tubular glands. The prostatic secretion is serous.

The **blood-vessels** of the prostate ramify in the capsule and trabeculæ. The small arteries give rise to a capillary network which surrounds the gland tubules. From these arise small veins, which accompany the arteries in the septa and unite to form venous plexuses in the capsule.

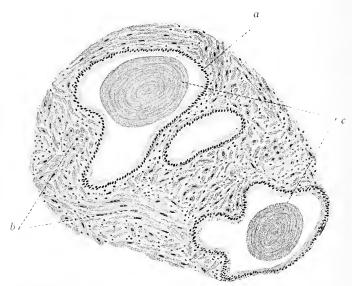


Fig. 219.—Section of Human Prostate.  $\times$  150. (Technic 1, p. 319.) a, Epithelium of tubule; b, interstitial connective tissue; c, corpora amylacea.

The **lymphatics** begin as blind clefts in the trabeculæ and follow the general course of the blood-vessels.

Nerves.—Small groups of sympathetic ganglion cells are found in the larger trabeculæ and beneath the capsule. Axones of these cells pass to the smooth muscle of the trabeculæ and of the walls of the blood-vessels. Their mode of termination is not known. Timofeew describes afferent medullated fibres ending within capsular structures of flat nucleated cells. Two kinds of fibres pass to each capsule: one a large medullated fibre which loses its sheath and gives rise within the capsule to several flat fibres with serrated edges, the other small medullated fibres which lose their sheaths and split up into

small varicose fibrils which form a network around the terminals of the large fibre.

## Cowper's Glands.

The bulbo-urethral glands, or glands of Cowper, are small, compound tubular glands. Both tubules and ducts are irregular in diameter so that some of them have more the character of alveoli than of tubules. They are lined with mucous cells. The smaller ducts are lined with simple cuboidal epithelium. They unite to form two main excretory ducts which open into the urethra and are lined with stratified columnar epithelium consisting of two or three layers of cells. In the main duct, as well as in its branches, smooth muscle occurs.

### TECHNIC.

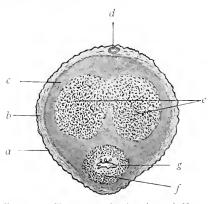
- (1) Fix small pieces of the prostate of a young man in formalin-Müller's fluid (technic 5, p. 7). Stain sections with hæmatoxylin-eosin (technic 1, p. 18) and mount in balsam.
- (2) The prostate of an old man should be treated with the same technic and compared with the above.
  - (3) Cowper's glands. Same technic as prostate (1).

### The Penis.

The penis consists largely of three long cylindrical bodies, the corpus spongiosum and the two corpora cavernosa. The latter lie side

by side, dorsally, while the corpus spongiosum occupies a medial ventral position (Fig. 220). All three are enclosed in a common connective-tissue capsule which is loosely attached to the overlying skin. In addition each corpus has its own special capsule or tunica albuginea, about a millimetre in thickness, and composed of dense connective tissue containing many elastic fibres.

The *corpus spongiosum* and *corpora cavernosa* have essentially



F16. 220.—Transverse Section through Human Penis. a, Skin; b, subcutaneous tissue; c, fibrous tunic; d, dorsal vein; c, corpora cavernosa; f, corpus spongiosum; g, urethra.

the same structure, being composed of so-called *erectile tissue* (Fig. 221). This consists of thick trabeculæ of intermingled fibro-elastic tissue and bundles of smooth muscle cells, which anastomose to form a coarse

meshed network, the spaces of which are lined with endothelium. The spaces are known as *cavernous sinuses*, and communicate with one another, and with the blood-vessels of the penis. In the flaccid condition of the organ these sinuses are empty and their sides are in apposition. In erection these sinuses become filled with venous blood.

The arteries have thick muscular walls and run in the septa. A few of them open directly into the venous sinuses. Most of them give rise to a superficial capillary network beneath the tunica albuginea. From this capillary plexus the blood passes into a plexus of

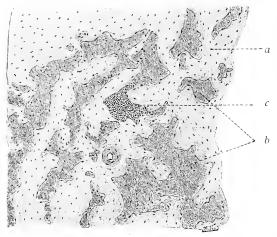


Fig. 221.—Erectile Tissue of Corpus Spongiosum of Human Penis.  $\times$  60. a, Trabeculæ of connective tissue and smooth muscle; b, cavernous sinuses; c, groups of leucocytes in sinus.

broader venous channels in the periphery of the erectile tissue, and these in turn communicate with the cavernous sinuses. The usual direct anastomoses between arterial and venous capillaries also occur. The blood may therefore pass either through the usual course—arteries, capillaries, veins—or, under certain conditions, may pass through the cavernous sinuses. This determines the flaccid or the erect condition of the organ. The veins arise partly from the capillaries and partly from the cavernous sinuses. They pass through the tunica albuginea and empty into the dorsal vein of the penis (Fig. 220). In the corpus spongiosum there is probably no direct opening of arteries into sinuses. Both trabeculæ and sinuses are also smaller.

Of the lymphatics of the penis little definite is known.

The nerve endings, according to Dogiel, consist of: (a) free sensory endings, (b) deeply situated genital corpuscles, (c) Pacinian corpus-

cles and Krause's end-bulbs in the more superficial connective tissue, and (d) Meissner's corpuscles in the papillæ. (For details see pages 387 and 388.)

The *glans penis* consists of erectile tissue similar in structure to that of the corpus cavernosum, except that the venous spaces are smaller and more regular. The mucous membrane is very closely at-

tached to the fibrous sheath of the underlying erectile tissue. A few small sebaceous glands, unconnected with hairs—the glands of Tyson—are found in the mucous membrane of the base of the glans penis.

The *prepuce* is a fold of skin which overlies the glans penis. Its inner surface is lined with mucous membrane.



FIG. 222.

FIG. 223.

Fig. 222.—From Transverse Section of Urethra and Corpus Spongiosum, including Mucous Membrane and part of Submucosa.  $\times$  15. The dark spots represent the cavernous veins.

F16. 223.—Vertical Section through Portion of Wall of Human Male Urethra.  $\times$  350. A, Mucous membrane; B, submucosa; a, epithelium; b, stroma; c, cavernous veins; d, connective tissue of submucosa.

## The Urethra.1

The MALE URETHRA is divided into three parts—prostatic, membranous, and penile. The wall of the urethra consists of three coats

¹ The female urethra, while not so distinctly divisible into sections, presents essentially the same structure as the male urethra. The epithelium begins at the bladder as stratified squamous of the transitional type, changes to a two-layered stratified or pseudostratified, and finally passes over into stratified squamous near the urethral opening. Glands of Littré are present, but are fewer than in the male.

—mucous, submucous, and muscular. The structure of the wall differs in the different parts of the urethra.

The mucous membrane (Fig. 223) consists of epithelium and stroma. The epithelium of the prostatic part is stratified squamous (transitional), resembling that of the bladder. In the membranous part it is stratified columnar or pseudostratified. In the penile portion it is pseudostratified up to the fossa navicularis, where it changes to stratified squamous. The epithelium rests upon a basement membrane, beneath which is a thin stroma rich in elastic fibres and having papillæ which are especially prominent in the terminal dilated portion of the urethra, the fossa navicularis. The stroma merges without distinct demarcation into the submucosa.

The *submucosa* consists of connective tissue and, in the penile portion, of more or less longitudinally disposed smooth muscle. It contains a dense network of veins—cavernous veins—which give it the character of erectile tissue (Fig. 223).

The *muscular coat* is thickest in the prostatic and membranous portions. Here it consists of a thin inner longitudinal and a thicker outer circular layer. A definite muscular wall ceases at the beginning of the penile portion, although circularly disposed smooth muscle cells are found in the outer part of the submucosa of the penile urethra.

Throughout the mucosa of the entire urethra, but most numerous in the penile portion, are simple branched tubular mucous glands, the glands of Littré. They are lined with columnar epithelium and the longer extend into the submucosa.

#### TECHNIC.

- (1) For the study of the general topography of the penis, remove the skin from the organ and cut into transverse slices about 0.5 cm. in thickness. Fix in formalin-Müller's fluid (technic 5, p. 7), cut rather thick sections across the entire penis, stain with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) or with hæmatoxylin-cosin (technic 1, p. 18) and mount in balsam.
- (2) For the study of the structure of the penile portion of the urethra and of the erectile tissue of the corpus spongiosum, cut away the corpora cavernosa, leaving only the corpus spongiosum and contained urethra, and treat as above. Sections should be thin and stained with hæmatoxylin-cosin.
- (3) The same technic is to be used for the membranous and prostatic portions of the urethra.

### II. FEMALE ORGANS.

## The Ovary.

The ovary is classed as one of the ductless glands. Its specific secretion is the ovum. The ovary has no duct system which is directly continuous with its structure. In place of this it is provided with what may be considered to be a highly specialized disconnected excretory duct—the *oviduct* or *Fallopian tube*—which serves for the transmission of its secretion to the uterus.

On one side the ovary is attached by a broad base, the *hilum*, to the broad ligament. Elsewhere the surface of the ovary is covered

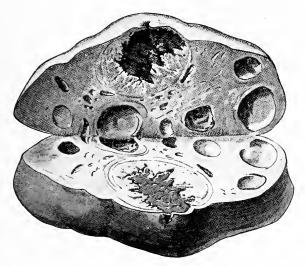


Fig. 224.—Ovary opened by Longitudinal Incision. Ovum has Escaped through Tear in Surface. Cavity of follicle filled with blood clot (corpus hæmorrhagicum) and irregular projections composed of lutein cells. (Kollmann's Atlas.)

by a modified peritoneum. At the hilum the tissues of the broad ligament pass into the ovary and spread out there to form the *ovarian stroma*. This consists of fibrous connective tissue rich in elastic fibres and containing many smooth muscle cells. In the deeper central portion of the organ, stroma alone is found. Here it contains many large blood-vessels, and constitutes the *medulla* or *zona vasculosa* of the ovary (Fig. 225, 2). From the medulla the stroma radiates toward the surface of the ovary and becomes interspersed with glandular elements forming the *ovarian cortex* (Fig. 225, 3, 3'). At the surface of the ovary, just beneath the peritoneum, the stroma forms a rather

dense layer of fibrous tissue, the *tunica albuginea*. At the margin of the peritoneal surface of the ovary the connective tissue of the peritoneum becomes continuous with the stroma of the ovary, while the flat mesothelium of the general peritoneum is replaced by a single layer of cuboidal cells, which covers the surface of the ovary and is known from its function as the *germinal epithelium* (Fig. 226, *he*). The parenchyma or secreting portion of the ovary consists of peculiar glandular elements, the *Graafian follicles*.

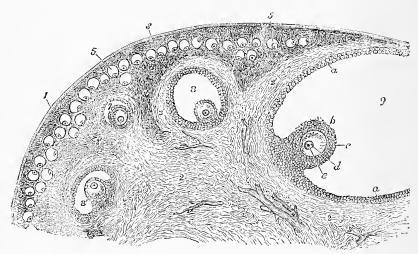
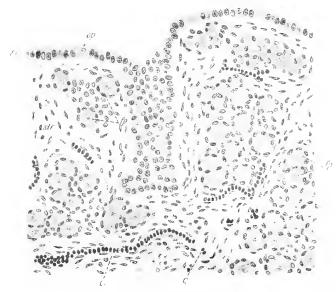


FIG. 225.—Semidiagrammatic Drawing of Part of Cortex and Medulla of Cat's Ovary. (From Schrön, in Quain's "Anatomy.") I, Germinal epithelium, beneath which is 3, the tunica albuginea; 2, medulla, containing large blood-vessels, 4; 2,2', fibrous stroma, arranged around mature Graafian follicle as its theca folliculi; 3', stroma of cortex; 5, small (primitive) Graafian follicles near surface; 6, same deeper in cortex; 7, later stage of Graafian follicle, beginning of cavity; 8 and 8', still later stages in development of follicle; 0, mature follicle; a, stratum granulosum; b, germ hill; c, ovum; d, nucleus (germinal vesicle); e, nucleolus (germinal spot).

The structure of the Graasian follicle can be best appreciated by studying its development. The follicles originate from the germinal epithelium during fœtal life. At this time the germinal epithelium is proliferating, and certain of its cells differentiate into larger spherical cells—primitive ova (Fig. 226, op). The primitive ova pass down into the stroma accompanied by a considerable number of the undifferentiated cells of the germinal epithelium. A cord-like mass of cells is thus formed, extending from the surface into the stroma. This is known as  $Pfl\ddot{u}ger$ 's egg cord (Fig. 226). Each cord usually contains several ova. In some cases the differentiation of the ova cells does not occur upon the surface but in the cords after they have extended

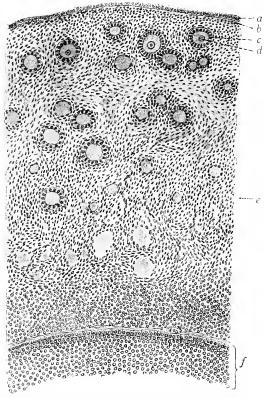
down from the surface. The connection of the cord with the surface epithelium is next broken so that each cord becomes completely surrounded by stroma. It is now known as an egg nest (Fig. 226). During this process proliferation of the epithelial cells of the cords and nests has been going on, and each ovum surrounded by a layer of epithelial cells becomes separated from its neighbors (Fig. 226, fp). This central ovum surrounded by a single layer of epithelial cells (follicular cells) is the primitive Graafian follicle (Fig. 226, fp, Fig. 227, and Fig. 228, a). Rarely a follicle may contain more than one ovum, of which, however,



F16. 226.—From Transverse Section of Ovary of New-born Child.  $\times$  280 (Sobotta). Shows primitive ova in germinal epithelium; Pflüger's egg cords and nests of cells;  $\epsilon$ , capillaries;  $h\epsilon$ , germinal epithelium; str, stroma; fp, primitive follicles; op, primitive ova.

only one goes on to maturity, the others degenerating. The follicle increases in size, mainly on account of proliferation of the follicular cells, which soon form several layers instead of a single layer, but also partly on account of growth of the ovum itself (Fig. 228). The latter now leaves the centre of the follicle and takes up an eccentric position. At the same time a cavity (or several small cavities which later unite) appears near the centre of the follicle (Fig. 228, c and Fig. 225, 7). This is filled with fluid which seems to be in part a secretion of the follicular cells, in part a result of their disintegration. The cavity is known as the *follicular cavity* or *antrum*, the fluid as the *liquor folliculi*.

Lining the follicular cavity are several rows of follicular cells with granular protoplasm—the *stratum granulosum*. With increase in the liquor folliculi the ovum becomes still further pressed to one side of the follicle, where, surrounded by an accumulation of follicular cells, it forms a distinct projection into the cavity (Fig. 230, and Fig. 225,

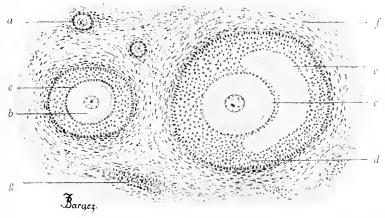


F16. 227.—Vertical Section through Cortex of Ovary of Young Girl.  $\times$  190. (Böhm and von Davidoff.) a, Germinal epithelium; b, tunica albuginea; c, follicular epithelium; d, ovum; e, primitive Graafian follicles in ovarian cortex; f, granular layer of large Graafian follicle.

8 and 9). This is known as the germ hill (discus proligerus—cumulus ovigerus). The cells of the germ hill nearest the ovum become columnar and arranged in a regular single layer around the ovum—the corona radiata (Fig. 231). The ovarian stroma immediately surrounding the Graasian follicle becomes somewhat modified to form a sheath for the follicle—the theca folliculi (Fig. 229). This consists of two layers, an outer more dense fibrous layer, the tunica fibrosa,

and an inner more cellular and vascular, the *tunica vasculosa*. Between the theca folliculi and the stratum granulosum is an apparently structureless basement membrane.

While these changes are taking place in the follicle, the ovum is also undergoing development. The ovum of the primitive follicle is a spherical cell, having a diameter of from 40 to 70  $\mu$  and the structure of a typical cell. The nucleus or germinal vesicle (so called on account of the part it takes in reproduction) is about half the diameter of the cell, and is spherical and centrally placed (Fig. 228). It is surrounded



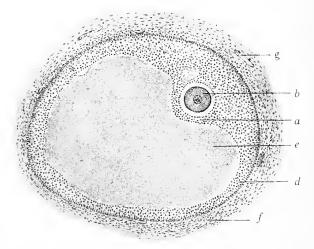
F16. 228.—From Section through Cortex of Ape's Ovary.  $\times$  150. (Szymonowicz.) a, Primitive follicle; b, ovum, with nucleus and nucleolus; c, zona pellucida; d, follicular epithelium; e, follicular cavity; f, ovarian stroma; g, blood-vessel in stroma.

by a double-contoured nuclear membrane, and contains a distinct chromatic network and nucleolus or *germinal spot*. The cytoplasm is quite easily differentiated into a spongioplasm network and a homogeneous hyaloplasm. Such ova are present in all active ovaries, *i.e.*, during the childbearing period, but are especially numerous in the ovary of the infant and child (Fig. 227.)

With the development of the follicle the ovum increases in size and becomes surrounded by a clear membrane, the zona pellucida, believed by some to be a cuticular formation deposited by the egg cell, by others to be a product of the surrounding follicular cells. Minute canals extend into the zona pellucida from its outer surface. These contain processes of the cells of the corona radiata. A narrow cleft, the perivitelline space, has been described as separating the ovum from the zona pellucida. During the growth of the ovum its cytoplasm

becomes coarsely granular from the development of yolk or deutoplasm granules (Fig. 231). Immediately surrounding the nucleus, and just beneath the zona pellucida, the egg protoplasm is fairly free from yolk granules.

The further maturation of the ovum, which is necessary before the egg cell is in condition to be fertilized, consists in changes in the chromatic elements of the nucleus, which result in the extrusion of the polar bodies, and apparently have as their main object the reduction in number of chromosomes to one-half the number characteristic of the species. This process has been described (page 53). In many



F16. 229.—Section through Graafian Follicle of Ape's Ovary.  $\times$  90. (Szymonowicz.) Later stage of development than Fig. 228. a, Germ hill; b, ovum with clear zona pellucida, germinal vesicle, and germinal spot; d, follicular epithelium (membrana granulosa); e, follicular cavity; f, theca folliculi; g, blood-vessel.

of the lower animals maturation of the ovum is completed outside the ovary. In man and the higher animals the entire process takes place within the ovary, the second polar body being extruded just before the escape of the ovum from its follicle.

The youngest of the Graasian follicles are found just under the tunica albuginea near the germinal epithelium, from which they originate (Fig. 225, 5). As the follicle matures it passes deeper into the cortex. With complete maturity the follicle usually assumes macroscopic proportions—8 to 12 mm.—and often occupies the entire thickness of the cortex, its theca at one point touching the tunica albuginea. Thinning of the follicular wall nearest the surface of the ovary next takes place (Fig. 232), while at the same time an increase in

the liquor folliculi determines increased intrafollicular pressure. This results in rupture of the Graafian follicle and the discharge of its ovum, together with the liquor folliculi and some of the follicular cells.

An escape of blood into the follicle from the torn vessels of the theca always accompanies the discharge of the ovum. The follicle again becomes a closed cavity, while the contained blood clot becomes

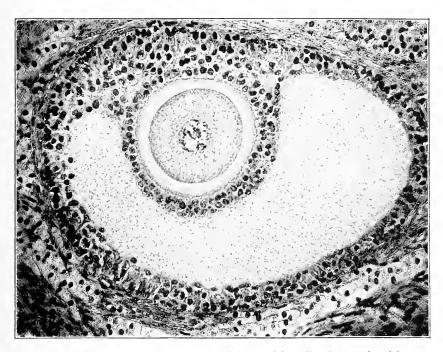


Fig. 230—Graafian Follicle and Contained Ovum of Cat; directly reproduced from a photograph of a preparation by Dahlgren. × 235. (From "The Cell in Development and Inheritance," Prof. E. B. Wilson; The Macmillan Company, publishers.) The ovum is seen lying in the Graafian follicle within the germ hill, the cells of the latter immediately surrounding the ovum forming the corona radiata. The clear zone within the corona is the zona pellucida, within which are the egg protoplasm, nucleus, and nucleolus. Encircling the follicle is the connective tissue of the theca folliculi.

organized by the ingrowth of vessels from the theca, to form the corpus hæmorrhagicum (Fig. 233), which represents the earliest stage in the development of the corpus luteum.

The *corpus luteum* (Fig. 234), which replaces the corpus hæmorrhagicum, consists of large yellow cells—*lutein cells*—and of connective tissue. The latter with its blood-vessels is derived from the inner layer of the theca. The origin of the lutein cells is not clear. They are described by some as derived from the connective-tissue cells of

the theca; by others as the result of proliferation of the cells of the stratum granulosum. The cells have a yellow color from the presence of fatty (lutein) granules in their protoplasm, and it is to these granules that the characteristic yellow color of the corpus luteum is due. A definite cellular structure with a supporting connective-tissue framework thus replaces the corpus hæmorrhagicum, remains of which are usually

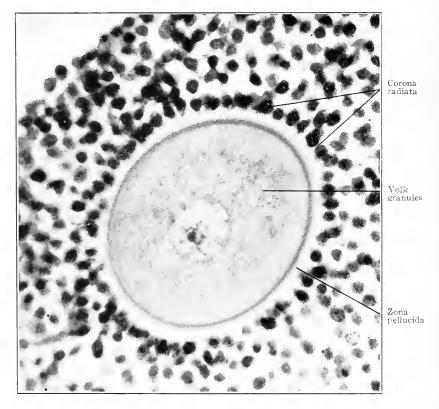


Fig. 231.—From a Section of a Human Ovum. Section taken from the ovary of a 12 year old girl. The ovum lies in a large mature Graafian follicle and is surrounded by the cells of the "germ hill" (the inner edge of which is shown in the upper left-hand corner of the figure). Photograph. (Bailey and Miller).

present in the shape of orange-colored crystals of hæmatoidin. By degeneration and subsequent absorption of its tissues the corpus luteum becomes gradually reduced in size, loses its yellow color, and is then known as the *corpus albicans*. This also is mostly absorbed, being finally represented merely by a small area of fibrous tissue.

Corpora lutea are divided into true corpora lutea (corpora lutea vera or corpora lutea of pregnancy) and false corpora lutea (corpora

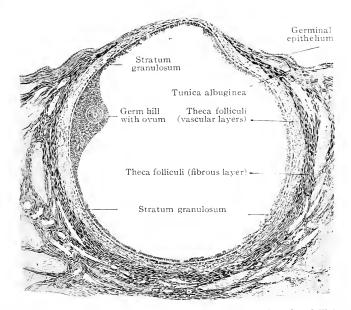


Fig. 232.—From Section of Human Ovary, showing mature Graafian follicle ready to rupture. (Kollmann's Atlas.)

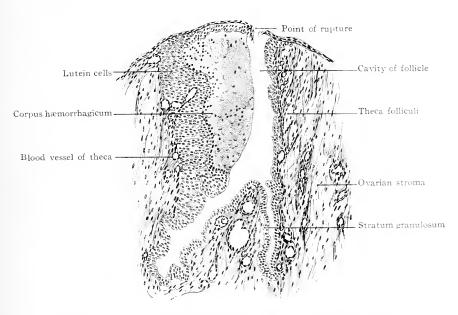


Fig. 233.—From Section of Human Ovary, showing early stage in formation of Corpus Luteum. (Kollmann's Atlas.)

lutea spuria). The former replace follicles whose ova have undergone fertilization, the latter, follicles whose ova have not been fertilized. The structure of both is similar, but the true corpus luteum is larger, and both it and its corpus albicans are slower in passing through their retrogressive changes, thus remaining much longer in the ovary.

While the function of the curpus luteum is not known, the recent experiments of Fraenkel seem to be confirmatory of the theory ad-

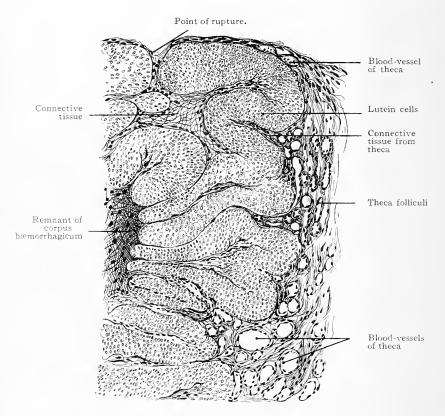


Fig. 234.—From Section of Human Ovary, showing later stage of Corpus Luteum than Fig. 233. (Kollmann's Atlas.)

vanced by Born, that the corpus luteum is a gland having an internal secretion, which appears to have some influence upon the attachment of the fecundated ovum to the uterus and upon its nutrition during the first few weeks of its development. According to Fraenkel the corpus luteum is a periodically rejuvenated ovarian gland, which gives to the uterus a cyclic nutritional impulse, which prepares it for

the implantation of the ovum or favors menstruation whenever the ovum is not fertilized.

Of the large number of ova—estimated at seventy-two thousand in the human ovaries—only comparatively few, according to Henle about four hundred, reach maturity. The majority undergo, together with their follicles, retrogressive changes known as atresia of the follicle. The nucleus of the ovum, as well as the nuclei of the follicular cells, passes through a series of chromatolytic changes, or in some cases apparently simply atrophies. The cell bodies undergo fatty or albuminous degeneration and the cell becomes reduced to a homogeneous mass, which is finally absorbed, leaving in its place a connective-tissue scar, probably the remains of the theca folliculi.

Blood-vessels.—The arteries, branches of the ovarian and uterine, enter the ovary at the hilum and ramify in the medulla. From these are given off branches which pass to the cortex and end in a capillary network in the tunica albuginea. In the outer layer of the theca folliculi the capillaries form a wide-meshed network, which gives rise to a fine-meshed network of capillaries in the inner layer of the theca. From the capillaries veins arise which form a plexus in the medulla and leave the ovary at the hilum.

**Lymphatics.**—These begin as small lymph spaces in the cortex, which communicate with more definite lymph vessels in the medulla, the latter leaving the organ at the hilum.

Nerves.—Medullated and non-medullated fibres enter the ovary at the hilum and follow the course taken by the blood-vessels. Many of the fibres end in the vessel walls; others form plexuses around the follicle and end in the theca folliculi. Some describe fibres as passing through the theca and ending in the follicular epithelium. Others claim that nerve fibres do not enter the follicle proper. Groups of sympathetic ganglion cells occur in the medulla near the hilum.

As is the case with the testicle, certain rudimentary organs, the remains of fœtal structures, are found connected with the ovary.

The *poroöphoron* consists of a number of cords or tubules of epithelial cells, sometimes ciliated, sometimes non-ciliated. It is found in the medulla, or, more commonly, in the connective tissue of the hilum.

The *cpoöphoron* is a similar structure found in the folds of the broad ligament. Its tubules open into a duct known as Gärtner's duct. In man this duct ends blindly. In some of the lower animals it opens into the vagina. Both paroöphoron and epoöphoron are

remains of the embryonal mesonephros, the former of its posterior segment, the latter of its middle segment.

## The Oviduct.

The oviduct or Fallopian tube is the excretory duct of the ovary, serving for the transmission of the discharged ovum from ovary to uterus. Although there is no sharp demarcation between them, it is convenient to divide the tube into three segments: (1) The isthmus, beginning at the uterus and extending about one-third the length of

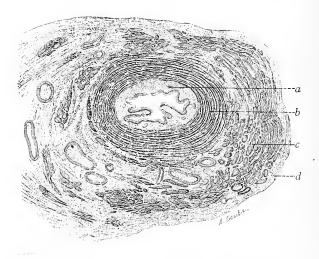


Fig. 235—Cross Section of Oviduct near Uterine End. a, Mucous membrane; b, circular muscle coat; c, longitudinal muscle coat; d, connective tissue of serous coat, (Orthmann.)

the tube; (2) the ampulla, about twice the diameter of the isthmus, and occupying somewhat more than the middle third; and (3) the fimbriated or ovarian extremity.

The walls of the oviduct consist of three coats: (1) Mucous, (2) muscular, and (3) serous (Figs. 235 and 236).

The mucous membrane presents numerous longitudinal foldings. In the embryo four of these folds can usually be distinguished, and these are known as primary folds. In the adult many secondary folds have developed upon the primary, especially in the ampulla and fimbriated extremity where the folds are high and complicated (Fig. 236). The epithelium lining the tube is of the simple columnar ciliated type, and completely covers the foldings of the mucous mem-

brane. The ciliary motion is toward the uterus. The stroma consists of a cellular connective tissue, quite compact in structure in the isthmus, where the folds are low, more loosely arranged in the high folds of the ampulla and fimbriated extremity.

The *muscular coat* consists of an inner circular and an outer longitudinal layer. The latter is a comparatively thin layer in the isthmus, consists of discontinuous groups of muscle cells in the ampulla, and in the fimbriated extremity is frequently absent.

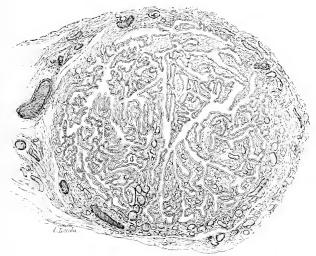


Fig. 236.—Cross Section of Oviduct near Fimbriated Extremity, showing complicated foldings of mucous membrane. (Orthmann.)

The serous coat has the usual structure of peritoneum.

The larger **blood-vessels** run in the stroma along the bases of the folds. They send off branches which give rise to a dense capillary network in the stroma.

Of the **lymphatics** of the tube little is known.

The **nerves** form a rich plexus in the stroma, from which branches pass to the blood-vessels and muscular tissue of the walls of the tube and internally as far as the epithelial lining.

#### TECHNIC.

- (1) Child's Ovary.—Remove the ovary of a new-born child, being careful not to touch the surface epithelium, fix in Zenker's fluid (technic 9, p. 8), and harden in alcohol. Cut sections of the entire organ through the hilum. Stain with hæmatoxylin-eosin (technic 1, p. 18) and mount in balsam.
  - (2) For the purpose of studying the Graafian follicle in the different stages of

its development remove an ovary from an adult cat or dog and treat as above. Technic (1). These sections also, as a rule, are satisfactory for the study of the corpus luteum.

(3) The adult human ovary is little used for histological purposes on account of the few follicles it usually contains and its proneness to pathological changes.

Its study is, however, so extremely important, especially with reference to the pathology of the ovary, that if possible a normal human ovary should be obtained from a young subject for purposes of comparison with the above. Technic (1).

- (4) For studying the egg cords of Pflüger and their relation to the germ epithelium, ovaries of the human fœtus, and of very young cats, dogs, and rabbits are satisfactory. Technic (1).
- (5) Sections of the fimbriated end of the oviduct are usually found in the sections of ovary. For the study of other parts of the tube, cut out thin pieces from different regions, fix in formalin-Müller's fluid, stain transverse sections with hæmatoxylin-eosin, and mount in balsam.

## The Uterus.

The wall of the uterus consists of three coats which from without inward are serous, muscular, and mucous.

The *serous coat* is a reflection of the peritoneum, and has the usual structure of a serous membrane.

The *muscularis* consists of bundles of smooth muscle cells separated by connective tissue. The muscle has a general arrangement into three layers, an inner, a middle, and an outer, which are distinct in the cervix, but not well defined in the body and fundus.

The inner layer—stratum submucosum—is mainly longitudinal, although some obliquely running bundles are usually present.

The middle layer—called from the large venous channels which it contains, the *stratum vasculare*—is the thickest of the three layers, forming the main

bulk of the muscular wall. It consists mainly of circularly disposed muscle bundles.

The outer layer—stratum supravasculare—is thin and consists partly of circular bundles, partly of longitudinal. The latter predominate and form a fairly distinct layer just beneath the serosa.

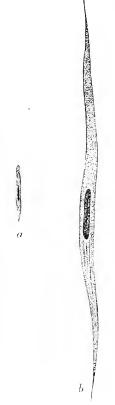


Fig. 237.— Muscle cells from (a) non-pregnant uterus; b, pregnant uterus; drawn to same scale. (Sellheim.)

The muscle cells of the uterus are long spindle-shaped elements, some having pointed, others blunt, branched, or frayed ends. In the virgin uterus they have a length of from 40 to 60  $\mu$ . During pregnancy the muscular tissue of the uterus is greatly increased. This is due partly to increase in the number, partly to increase in the size of the muscle cells. At term the muscle cells frequently have a length of from 250 to 600  $\mu$ . (Fig. 237.)

The *mucous membrane*. As the mucosa presents marked variation in structure, dependent upon the functional condition of the organ, it is necessary to describe:

- 1. The mucosa of the resting uterus.
- 2. The mucosa of the menstruating uterus.
- 3. The mucosa of the pregnant uterus.

## I. THE MUCOSA OF THE REST-ING UTERUS.

This is from 1 to 2 mm. thick, and consists of a stroma, glands, and a lining epithelium (Fig. 238). The stroma resembles embryonal connective tissue, consisting of fine fibrils and long, irregular branching cells which form a sort of network, the meshes of which are filled in with lymphoid cells and leucocytes. The epithelium is of the simple high columnar ciliated

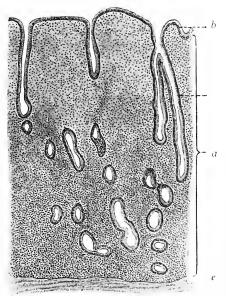


Fig. 238.—From Uterus of Young Woman. (Böhm and von Davidoff; preparation by Dr. J. Amann.)  $\times$  34. a, Mucous membrane: b, surface epithelium;  $\epsilon$ , gland;  $\epsilon$ , muscle.

variety, the ciliary motion being toward the cervix. A basement membrane separates the epithelium from the underlying stroma. The glands are simple forked tubules lined by a single layer of columnar ciliated cells resting upon a basement membrane and continuous with the surface cells. The glands extend completely through the stroma. Near the surface they run a comparatively straight course. Deeper in the stroma their course is more tortuous, while the fundus is frequently turned at right angles to the rest of the tubule.

In the cervix the stroma is firmer and less cellular, and the mu-

cous membrane is thicker and presents numerous folds—the *plicæ* palmatæ. The epithelium is higher than in the body of the organ. In addition to glands like those found in the body of the uterus, the cervical mucosa contains peculiar short, sac-like invaginations, lined with a continuation of the surface epithelium, which secrete a glairy

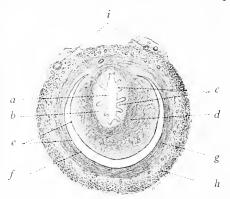


Fig. 230.—From Section of Dog's Cervix. × 4. (Technic 2, p. 340.) a, Cervical canal; b, mucosa; c, folds of mucosa (plicæ palmatæ); d, muscle layers of cervix; e, epithelium of vagina and vaginal surface of cervix; f, vaginal epithelium; g, vaginal mucosa; h, submucosa and muscularis of vagina; i, blood-vessels.

mucus. Closure of the mouths of some of these sacs frequently occurs, leading to the formation of retention cysts, the so-called ovula Nabothi. At about the junction of middle and lower thirds of the cervical canal a change takes place in the epithelium. Here the simple columnar ciliated epithelium of the upper part of the cervix gradually passes over into a stratified squamous epithelium. Near the external os papillæ appear, the vaginal surface of the cervix being covered with a stratified

squamous epithelium with underlying papillæ similar to and continuous with that of the vagina.

Near the external os the epithelium changes over into the stratified squamous epithelium with underlying papillæ, similar to that of the external surface of the cervix.

## 2. The Mucosa of the Menstruating Uterus.

This consists of the same structural elements as the mucosa of the resting uterus: stroma, glands, and lining epithelium. These, however, undergo certain changes which may be conveniently divided into three stages:

- (a) The stage of preparation.
- (b) The stage of menstruation proper.
- (c) The stage of reparation.
- (a) THE STAGE OF PREPARATION.—This begins several days before the actual flow of blood, and is marked by an intense hyperæmia determining a swelling and growth of the entire mucosa. The

blood-vessels, especially the capillaries and veins, become greatly distended, thus contributing largely to the increase in thickness of the mucosa. There are also proliferation of the connective-tissue cells, an increase in the number of leucocytes, and a growth of the uterine glands. The surface at the same time becomes irregular, the

glands opening into deep pits or depressions, and the glands themselves become more tortuous and their lumina more widely open. The mucous membrane has now reached a thickness of about 6 mm., and is known as the *decidua menstrualis* (Fig. 240).

(b) THE STAGE OF MEN-STRUATION PROPER.—This is marked by the escape of blood from the engorged vessels and the appearance of the external phenomena of menstruation. The blood escapes partly by rupture of the vessel walls, partly by diapedesis. The hemorrhage is at first subepithelial, but the epithelium soon gives way and the blood escapes into the cavity of the uterus. Much difference of opinion exists as to the amount of epithelial destruction during menstruation, some claiming that the entire epithelium is de-

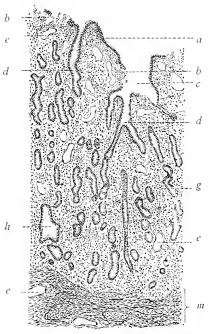


Fig. 240.—Section through Mucous Membrane of Virgin Uterus during First Day of Menstruation. × 30. (Schaper.) a, Surface epithelium; b, disintegrating surface: c, pit-like depression in mucous membrane; d, excretory duct; e, blood-vessels; g, gland tubule; h, dilated gland tubule: m, muscularis.

stroyed with each menstrual period, others that the epithelium remains almost intact. Complete destruction of the epithelium is hardly compatible with the restoration of the epithelium which always follows menstruation. While there is undoubtedly destruction of most or all of the surface epithelium and of the glands to some considerable depth, the deeper portions of the glands always remain to take part in the succeeding regenerative phenomena.

(c) THE STAGE OF REPARATION.—After from three to five days the bleeding from the uterine mucosa ceases and the return to the resting condition begins. This is marked by disappearance of the

congestion, by decrease in thickness of the mucosa and in the size of the glands, and by restoration of the surface epithelium.

# 3. The Mucosa of the Pregnant Uterus.

This is known as the *decidua graviditatis*, and presents changes in structure somewhat similar to those which occur during menstruation, but more extensive. It is divided into three parts:

- (a) The decidua serotina or decidua basalis-- that part of the mucosa to which the ovum is attached.
- (b) The decidua reflexa or decidua capsularis—that part of the mucosa which surrounds the ovum.
  - (c) The decidua vera—which consist of all the remaining mucosa.

The development of the decidua vera resembles the changes which take place in the mucosa during menstruation. There is the same thickening of the mucosa, and this thickening is due to the same factor, i.e., distention of the blood-vessels and proliferation of the tissue elements. These changes are, however, much more extensive than during menstruation. The superficial part of the stroma between the mouths of the glands becomes quite dense and firm, forming the compact layer. The deeper part of the stroma contains numerous cavities, which are the lumina of the now widely distended and tortuous glands. This is known as the spongy layer.

Within the stroma, especially of the compact layer, develop the so-called *decidual cells*. These are peculiar typical cells derived from connective tissue. They are of large size (30 to  $100\mu$ ), vary greatly in shape, and in the later months of pregnancy have a rather characteristic brown color, which they impart to the superficial layers of the decidua vera. They are mostly mononuclear, although polynuclear forms occur.

During the latter half of pregnancy there is a gradual thinning of the decidua vera, due apparently to pressure. The necks of the glands in the compact layer disappear, and the gland lumina in the spongy layer are changed into elongated spaces, which lie parallel to the muscular layer.

The decidua reflexa and decidua serotina have at first the same structure as the decidua vera. The decidua reflexa undergoes hyaline degeneration during the early part of pregnancy, and by the end of gestation has either completely disappeared (Minot) or has fused with the decidua vera (Leopold).

The decidua serotina undergoes changes connected with the development of the placenta.

### The Placenta.1

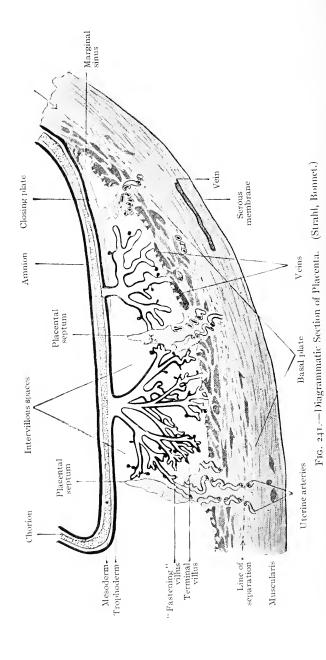
The placenta consists of two parts, one of which is of maternal origin—placenta uterina—the other of fœtal origin—the placenta fætalis. As it is in the placenta that the interchange takes place between the maternal and the fœtal blood, the relations between the maternal and fœtal parts of the placenta are extremely intimate. This relation consists essentially in the growing out from the fœtal placenta of finger-like projections—villi—which penetrate the maternal placenta, the latter being especially modified for their reception.

The Placenta Fœtalis.—This is a differentiated portion of the chorion. On the surface directed toward the fœtus the chorion after the third month is covered by a delicate fœtal membrane, the placental portion of the amnion. This consists of a surface epithelium, resting upon a layer of embryonal connective tissue which attaches it to the chorion. The chorion consists of (a) a compact layer—the membrana chorii—composed at first of embryonal, later of fibrous, connective tissue, and containing the main branches of the umbilical vessels and (b) an inner villous layer, which gives rise to finger-like projections which extend down from the the fœtal into the maternal placenta and serve to connect the two.

The chorionic villi first appear as short projections composed entirely of epithelium. Each of these primary villi branches dichotomously, giving rise to a number of secondary villi. As they develop, the central portion of the original solid epithelial structure is replaced by connective tissue. Septa of connective tissue from the maternal placenta pass down among the villi and separate them into groups or cotyledons. The main or primary villi run a quite straight course from the chorion into the maternal placental tissue, apparently serving to secure firm union between the two. They are thus known as roots of attachment or fastening villi (Fig. 241). The secondary villi are given off laterally from the primary villi, end freely in the spaces between the latter—intervillous spaces (Fig. 241)—and are known as free, terminal or floating villi (Fig. 241).

The chorionic villus thus consists of a central core of connective tissue covered by a layer of epithelium. The connective tissue is of the mucous type and serves for the transmission of numerous bloodvessels. In the villi of early pregnancy the epithelium consists of an

<sup>&</sup>lt;sup>1</sup> For many facts as to the structure of the placenta, the writer is indebted to the excellent chapter on the subject added by Prof. Alfred Schaper to the fifth edition of Stöhr's "Textbook of Histology."



inner layer of distinctly outlined cells and an outer layer of fused cell bodies—a syncytium (Fig. 243, A, a)—containing small scattered nuclei. The villi of the later months of pregnancy have no definite epithelial covering, but are surrounded by a delicate homogeneous membrane, probably the remains of the syncytium. At various points on the surface of the villus are groups of nuclei. These stain intensely, are surrounded by a homogeneous protoplasm, and form knob-like projections above the general surface of the villus. They are known as

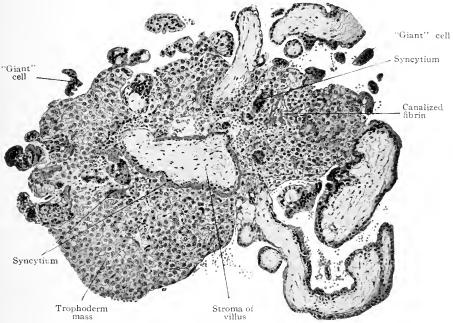


Fig. 242.—Section of Chorion of Human Embryo of one month (9 mm.). (Grosser.)

cell patches, or more properly as nuclear groups (Fig. 243, c), and represent remains of the nuclei of the epithelium of the younger villus. Between the nuclear groups the villus is covered only by a thin homogeneous membrane. Small villi usually resemble more closely in structure the younger villus, being frequently covered by a nucleated syncytium. Portions of the syncytium, especially of older villi, sometimes become changed into a peculiar hyaline substance containing numerous channels. This is known as canalized fibrin, and may form dense layers upon the surface of the chorion. (Fig. 242.)

THE PLACENTA UTERINA.—This develops from the decidua serotina. The latter becomes much thinner than the rest of the decidua

(decidua vera), but still shows a division into a deeper spongy portion containing gland tubules, and a superficial compact portion in which are large numbers of decidual cells. From the superficial portion connective-tissue septa—placental septa—grow into the fœtal placenta, as described above, separating its villi into cotyledons. Near the margins of the placenta these septa pass to the chorionic membrane

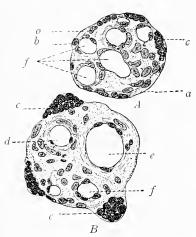


FIG. 243.—Cross Sections of Human Chorionic Villi at End of Pregnancy. × 250. (Schaper.) A, Small villus; B, larger villus. a, Protoplasmic coat (syncytium); b, epithelial nucleus; ε, nuclear groups; d, small artery; ε, small vein; f, capillaries.

and form beneath it a thin membrane, the *subchorionic placental decidua*. At the edge of the placenta, where decidua serotina passes over into the thicker decidua vera, there is a close attachment of the chorion to the former.

As the placenta serves as the place of interchange of materials between the maternal and the fœtal circulations, the arrangement of the placental blood-vessels is of especial importance. Arterial branches from vessels of the uterine muscularis enter the serotina. In the very tortuous course which these vessels take through the serotina (Fig. 241) their walls lose their muscular and connective-tissue elements and be-

come reduced to epithelial tubes. These branch in the placental septa and finally open into the intervillous spaces along the edges of the cotyledons. The veins take origin from these spaces near the centres of the cotyledons. The maternal blood thus passes through the intervillous spaces from periphery to centre, and in its course comes into direct contact with the freely terminating chorionic villi. It is to be noted that the blood-vessel systems of the mother and of the fœtus are both closed systems, and that consequently there is no direct admixture of maternal and fœtal blood. Interchange of materials must therefore always take place through the capillary walls and through the walls of the chorionic villi. (Fig. 241.)

Blood-vessels.—The arteries enter the uterus from the broad ligament and pass to the stratum vasculare of the muscularis, where they undergo extensive ramification. From the arteries of the stratum vasculare branches pass to the mucosa and give rise to capillary net-

works, which surround the glands and are especially dense just beneath the surface epithelium. From these capillaries the blood passes into a plexus of veins in the deeper portion of the mucosa, and these in turn empty into the venous plexuses of the stratum vasculare. Thence the veins accompany the arteries, leaving the uterus through the broad ligament.

Lymphatics.—These begin as minute spaces in the stroma and empty into the more definite lymph channels of the muscularis, which are especially well developed in the stratum vasculare. These in turn communicate with the larger lymph vessels in the subserous connective tissue.

Nerves.—Both medullated and non-medullated nerve fibres occur in the uterus. The latter are associated with minute sympathetic ganglia and supply the muscular tissue. The medullated fibres form plexuses in the mucosa, from which are given off fine fibres which terminate freely between the cells of the surface epithelium and of the uterine glands.

## The Vagina.

The wall of the vagina consists of four coats, which from without inward are fibrous, muscular, submucous, and mucous.

The *fibrous coat* consists of dense connective tissue with many coarse elastic fibres. It serves to connect the vagina with the surrounding structures.

The *muscular coat* is indistinctly divided into an outer longitudinal and an inner circular layer. The latter is usually not well developed and may be absent.

The *submucosa* is a layer of loose connective tissue, especially rich in elastic fibres and blood-vessels. Numerous large venous channels give to the submucosa the character of erectile tissue.

The *mucous membrane* consists of a papillated connective-tissue stroma of mixed fibrous and elastic tissue. The stroma usually contains diffuse lymphoid tissue and more rarely solitary nodules. Covering the stroma is a stratified squamous epithelium, the surface cells of which are extremely thin. The surface of the mucosa is not smooth. but is folded transversely, forming the so-called *ruga*. Most authorities agree that glands are wanting in the vagina, the mucus found there being derived from the glands of the cervix.

**Blood-vessels.**—The larger blood-vessels run in the submucosa, giving off branches which break up into capillary networks in the sub-

mucosa, muscularis, and stroma. The vascular networks have a general direction parallel to the surface. The capillaries empty into veins which form a plexus of broad venous channels in the muscularis.

The Lymphatics.—These follow in general the distribution of the blood-vessels.

Nerves.—Nerve fibres from both cerebro-spinal and sympathetic systems are found in the vagina. Medullated (sensory) fibres, the dendrites of spinal ganglion cells, form plexuses in the mucosa, from which are given off delicate non-medullated terminals to the epithelial cells. Non-medullated sympathetic fibres supply the muscularis and the muscle of the vessel walls. Along these nerves are small sympathetic ganglia.

In the vestibule the epithelium gradually takes on the structure of epidermis. Here are located small mucous glands—glandulæ vestibulares minores—especially numerous around the clitoris and opening of the urethra. Larger mucous glands—glandulæ vestibulares majores, or glands of Bartholin—analogous to Cowper's glands in the male, are also found in the walls of the vestibule.

The *clitoris* consists mainly of erectile tissue similar to that of the corpora cavernosa of the penis. It is covered with a thin epithelium with underlying papillæ, and is richly supplied with nerves having highly specialized terminations.

## DEVELOPMENT OF THE URINARY AND REPRODUCTIVE SYSTEMS.

The development of the genito-urinary system is complicated by the appearance, and disappearance for the most part, of two sets of urinary organs, and the final formation of the permanent set. The three sets, in the order of their appearance, are the pronephroi, mesonephroi, and metanephroi. The first two sets, which are present only in the embryo in the higher animals, are the representatives of organs that function in the adult in the lower vertebrates. They are also intimately concerned in the development of the efferent duct system of the male reproductive organs in higher animals. The metanephroi, generally known as the kidneys, are the functional urinary organs in the majority of reptiles and in all birds and mammals.

The **pronephroi** are represented in the human embryo of 3 to 5 mm. by one or two small, condensed masses of mesoderm just lateral to the primitive segments on each side in the cervical region. These masses, which are probably derived from the mesothelial lining of the

body cavity, may or may not become hollow, but do not connect with the pronephric duct, and soon disappear. The *pronephric duct* appears about the same time as a derivative of the mesoderm just lateral to the primitive segments. It extends from the cervical region to the caudal region of the embryo where it bends mesially and opens into the gut. These ducts persist and become the ducts of the mesonephroi.

The mesonephroi begin to develop almost as soon as the pronephroi and just caudal to them. Condensations appear in the mesodermal tissue lateral to the primitive segments and become more or less tortuous. Lamina appear in these condensations, thus forming tubules which then connect at one end with the pronephric duct (now the mesonephric or Wolffian duct). The tubules develop progressively from before backward and finally form a series extending from the cervical region to the pelvic region of the embryo. At the distal end of each tubule a glomerulus, containing branches from the aorta. develops. The tubules increase in length and number and come to form a pair of large structures which project into the dorsal part of the body cavity. These are often spoken of as the Wolffian bodies. They reach the height of their development during the fifth or sixth week.

During the period of their existence in the embryo in higher animals, the mesonephroi functionate as urinary organs, not only through the agency of the glomeruli but also by means of the epithelium of the tubules themselves, among which numerous branches of the posterior cardinal veins ramify.

From the sixth week on, and coincident with the development of the metanephroi or kidneys, the mesonephroi atrophy, leaving finally only certain parts which differ in the two sexes. In the male some of the tubules in the cephalic portion persist as the vasa efferentia, while a few in the caudal portion remain as the paradidymis and vasa aberrantia; the duct persists as the vas epididymidis, vas deferens, and ejaculatory duct. In the female the mesonephric tubules disappear for the most part, only a few remaining to form the epophoron and paroöphoron, while the duct persists in part as Gärtner's canal.

Each **kidney** begins in embryos of 5 to 6 mm. as a hollow bud on the dorsal side of each mesonephric duct near its opening into the gut. This bud grows dorsally, and then turns cranially in the mesoderm between the vertebral column and the mesonephros. The proximal portion remains more slender as the ureter, while the distal end be-

comes dilated to form the primitive renal pelvis. From this dilated end a number of secondary evaginations grow out to form the papillary ducts and straight collecting tubules.

The mesodermal tissue surrounding the outgrowths from the primitive renal pelvis becomes condensed in places and gives rise to the convoluted portions of the uriniferous tubules and to Henle's loops. A glomerulus develops in connection with the distal end of each convoluted tubule. The portion of each tubule derived from the mesodermal tissue unites secondarily at the arched (junctional) tubule with the portion derived from the renal pelvis. Thus the kidney tubules are derived in part directly from undifferentiated mesoderm (convoluted tubules and Henle's loops) and in part from an outgrowth from the mesonephric duct (straight collecting tubules and papillary ducts).

During feetal life the kidneys are distinctly lobulated, but after birth the surface becomes quite smooth.

The genital gland on each side appears on the mesial surface of the mesonephros as a thickening of a narrow band of the mesothelial lining of the body cavity. The cells in the band become differentiated into two kinds—small cuboidal cells which stain rather intensely, and larger spherical cells with clearer cytoplasm and vesicular nuclei. The latter are the sex cells which are destined to give rise to the ova in the female or the spermatozoa in the male. The whole thickened band is known as the germinal epithelium.

The cells of the germinal epithelium increase in number by mitosis and soon become differentiated into two layers—a superficial layer which retains its epithelial character and contains the sex cells, and a deeper layer which is destined to give rise in part to the stroma of the genital gland. The elevation caused by the increased number of cells projects into the body cavity as the *genital ridge*. From the superficial layer containing the sex cells a number of plugs or columns of cells grow down into the deeper layer carrying some of the sex cells with them. Thus far (up to about the fifth week) the changes are common to both sexes, and only later does the sex differentiation occur.

After about the fifth week certain changes occur in the genital ridge which differ accordingly as the ridge is to become an ovary or a testicle. In the case of the ovary a layer of loose connective tissue grows in between the surface epithelium and the cell columns or plugs mentioned above. The cell columns are thus pushed farther from the surface and constitute the medullary cords. These ultimately disap-

pear. The surface epithelium again sends plugs of cells (Pflüger's egg cords) down into the underlying tissue. These cords are made up for the most part of epithelial cells which give rise to the follicular cells. but contain also a considerable number of sex cells (primitive ova). The egg cords then become broken up into smaller masses each of which contains a single primitive ovum (rarely more) and constitutes a primitive Graafian follicle. The sex cell grows in size and becomes the primary occyte (and finally the mature ovum), while the epithelial cells around it give rise to the stratum granulosum and germ hill of the mature Graafian follicle. During these processes the stroma also increases in amount, while the original germinal epithelium becomes reduced to a single layer of cuboidal cells. The formation of egg cords is usually completed before birth. (See also p. 324.)

In the case of the testicle a layer of dense connective tissue, the tunica albuginea, develops between the germinal epithelium and the sex cords. The epithelium becomes reduced to a single layer of flat cells. The sex cords which first grew into the underlying tissue and which contain the sex cells, are destined to give rise to the convoluted seminiferous tubules. This phase of development differs from that in the ovary inasmuch as in the latter case the first formed sex cords (medullary cords) disappear, Pflüger's egg cords being formed later and having no homologue in the testicle. The sex cords of the testicle become more and more convoluted and the sex cells (spermatogonia) proliferate rapidly. Beginning after birth and continuing up to the time of puberty, lumina appear in the sex cords and they thus give rise to the convoluted seminiferous tubules. The supporting cells (of Sertoli) are probably derived from the undifferentiated epithelial cells of the sex cords. (See also p. 305.)

#### TECHNIC.

- (1) A human uterus—if possible from a young adult—or, if this cannot be obtained, the uterus of a cat or dog, is cut transversely into slices about 1 cm. thick and fixed in Zenker's fluid (technic 9, p. 8) or in formalin-Müller's fluid (technic 5, p. 7). For topography these slices are cut in half through the middle of the uterine cavity and sections made through the entire half organ. These are stained with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) and mounted in balsam. For details of the mucous membrane, cut away most of the muscle from around the half slice, being careful not to touch the mucous surface; make thin sections, stain with hæmatoxylin-eosin (technic 1, p. 18), and mount in balsam.
  - (2) Sections of the cervix may be prepared in the same manner as the preceding.
- (3) Placental tissue may be cut into small cubes and treated with the same technic (1).

- (4) If a human or animal uterus with the placenta *in situ* is obtainable it should be cut into thin slices and fixed in formalin-Müller's fluid. The blocks of tissue should be so arranged that sections include the utero-placental junction. They may be stained with hæmatoxylin-eosin or with hæmatoxylin-picro-acid-fuch-sin (see above).
  - (5) Treat pieces of the human vagina according to technic 1, p. 223.

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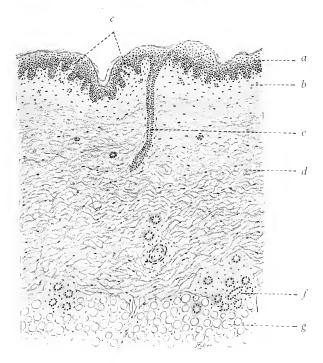
### CHAPTER X.

## THE SKIN AND ITS APPENDAGES.

### The Skin.

THE skin or cutis consists of two parts: (1) The derma, corium, or true skin, and covering this, (2) the epidermis or cuticle. The derma is a connective-tissue derivative of the mesoderm, the epidermis an epithelial derivative of the ectoderm.

THE DERMA.—This is divided into two layers which blend with-



F16. 244.—Vertical Section of Thin Skin, Human.  $\times$  60. (Technic 2, p. 356.) a. Epidermis; b, pars papillaris of derma; c, papillæ; d, pars reticularis of derma; c, duct of sweat gland; f, sweat gland; g, subcutaneous fat.

out distinct demarcation. The deeper is known as the pars reticularis, the more superficial as the pars papillaris (Fig. 244).

The pars reticularis is made up of rather coarse, loosely arranged

white and elastic fibres with connective-tissue cells in varying numbers. The fibres run for the most part parallel to the surface of the skin.

The pars papillaris is similar in structure to the preceding, but both white and elastic fibres are finer and more closely arranged. Externally this layer is marked by minute folds which are visible to the naked eye, and can be seen intersecting one another and enclosing small irregular areas of skin. In the thick skin of the palms and soles these furrows are close together and parallel, while between them are long corresponding ridges. In addition to the furrows and

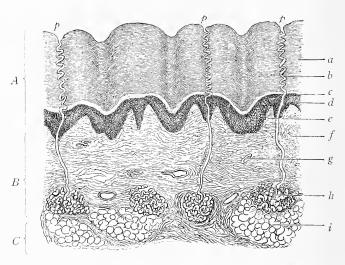


Fig. 245.—Thick Vertical Section through Skin of Finger Tip. (Merkel-Henle.) A, Epidermis; B, derma; C, subcutis. a, Stratum corneum; b, duct of sweat gland; c, stratum lucidum; d, stratum germinativum; e, papilla of derma; f, derma; g, blood-vessel; h, sweat gland; f, fat lobule; g, sweat pore.

ridges the entire surface of the corium is beset with minute papillæ. These vary in structure, some ending in a single point—simple papillæ—others in several points—compound papillæ; some containing blood-vessels—vascular papillæ; others containing special nerve terminations—nerve papillæ (Fig. 246).

Smooth muscle cells occur in the corium in connection with the sweat glands. In the skin of the scrotum—tunica dartos—and of the nipple, the smooth muscle cells are arranged in a network parallel to the surface. In the face and neck striated muscle fibres penetrate the corium.

Beneath the corium is the subcutaneous tissue. This consists of

vertically disposed bands of connective tissue—the *retinaculæ cutis*—which serve to unite the corium to the underlying structures and enclose fat lobules. In some parts of the body this subcutaneous fat forms a thick layer—the *panniculus adiposus*.

THE EPIDERMIS.—This is composed of stratified squamous epithelium. In the comparatively thin skin of the general body surface the epidermis is divided into two sub-layers: (1) One lying just above the papillary layer of the derma, and known as the stratum germina-

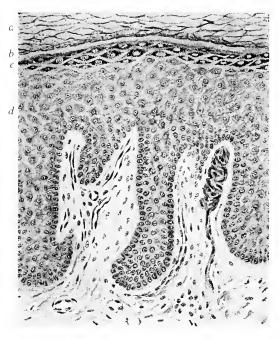


Fig. 246.—From Vertical Section through Skin of Human Finger Tip.  $\times$  200. (Schäfer.) a, Stratum corneum; b, stratum lucidum; c, stratum granulosum; d, stratum germinativum. To the left a vascular papilla; to the right a nerve papilla containing tactile corpuscle.

tivum (stratum mucosum—stratum Malpighii); (2) the other constituting the superficial layer of the skin—the horny layer or stratum corneum. In the thick skin of the palms and soles two additional layers are developed; (3) the stratum granulosum; and (4) the stratum lucidum (Fig. 245).

(1) The *stratum germinativum* consists of several layers of cells. The deepest cells are columnar and form a single layer (stratum cylindricum), which rests upon a basement membrane separating it

from the derma. The membrane and cells follow the elevations and depressions caused by the papillæ. The rest of the stratum germinativum consists of large polygonal cells. These cells have well-

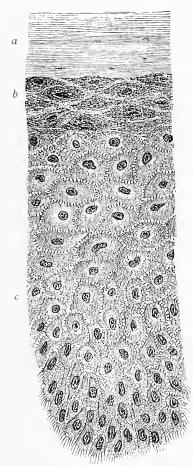


Fig. 247.—From Vertical Section through Thick Skin. (Merkel-Henle.) a, Stratum lucidum; b, stratum granulosum; c, stratum germinativum, showing intercellular bridges.

developed intercellular bridges, which appear as spines projecting from the surfaces of the cells. For this reason the cells are sometimes called "prickle" cells, and the layer, the "stratum spinosum." The spines cross minute spaces between the cells, which are believed to communicate with the lymph spaces of the derma (Fig. 247, c). The cells of the stratum germinativum are usually in a state of active mitosis.

- (2) The stratum granulosum is well developed only where the skin is thick. It consists of from one to three layers of flattened polygonal cells. protoplasm of these cells contains deeply staining granules—keratohyaline granules—which probably represent a stage in the formation of the substance—keratin—of corneum cells. The nuclei of these show degenerative always changes, and there is reason for believing that this karyolysis is closely associated with the formation of the keratohvaline granules (Fig. 247, b).
- (3) The *stratum lucidum* is also best developed where the skin is thickest. It consists of two or three layers of flat clear cells, the outlines of which are frequently so indistinct that

the layer appears homogeneous. The transparency of the cells is due to the presence of a substance known as *eleidin*, and derived from the keratohyaline granules of the stratum granulosum (Fig. 247, a).

(4) The *stratum corneum* varies greatly in thickness, reaching its greatest development in the skin of the palms and soles. The cells

are flattened and horny, especially near the surface. Some appear homogeneous, others have a lamellated appearance. They contain pareleidin, a derivative of the eleidin of the stratum lucidum. Nuclei are lost, but in many of the cells can be seen the spaces which the nuclei once occupied. Constant desquamation of these cells goes on, cells from the deeper layers taking their place.

The color of the skin in the white races is due to pigmentation of the deeper layers of the epidermis. In certain parts of the body pigmentation of the connective-tissue cells of the derma also occurs. In the dark races all cells of the epidermis are pigmented, although there is less pigment in the surface cells than in the cells more deeply situated.

Two kinds of glands occur in the skin—sebaceous glands and sweat glands.

Sebaceous Glands.—These are usually associated with the hair follicles, and will be described in that connection. Sebaceous glands unconnected with hair occur along the margin of the lips, in the glans and prepuce of the penis, and in the labia minora.

SWEAT GLANDS (glandulæ sudoriparæ).—These are found throughout the entire skin with the exception of the margin of the lips, the inner surface of the prepuce, and the glans penis. They are simple coiled tubular glands. The coiled portion of the gland usually lies in the subcutis, although it may lie wholly or partly in the deeper portion of the pars reticularis. The excretory duct runs a quite straight course through the derma, and enters the epidermis in one of the depressions between the papillæ. In the epidermis the duct takes a spiral course to the surface, where it opens into a minute pit just visible to the naked eye—the sweat pore (Fig. 245, p). The coiled portion of the gland is lined with a simple cuboidal epithelium, having a granular protoplasm. In the smaller glands the epithelium rests directly upon the basement membrane. In the larger glands a longitudinal layer of smooth muscle cells separates the glandular epithelium from the basement membrane. The walls of the ducts consist of two or three layers of cuboidal epithelial cells, resting upon a delicate basement membrane, outside of which are longitudinally disposed connective-tissue fibres. On reaching the horny layer the epithelial wall of the duct ceases, the duct consisting of a mere channel through the epithelium. (Fig. 245.)

#### TECHNIC.

(1) Fix the volar half of a finger-tip in formalin-Müller's fluid (technic 5, p. 7) or in absolute alcohol. Curling may be prevented by pinning to a piece of

cork. Sections are cut transversely to the ridges, stained with hæmatoxylin-picroacid-fuchsin (technic 3, p. 19), and mounted in balsam. Thick sections should be cut for the study of the coil glands with their ducts; thin sections for cellular details of the layers.

- (2) Prepare in the same manner and for contrast with the preceding, sections of thin skin from almost any part of the body.
- (3) Prepare a piece of negro skin in the same manner and note the position of the pigment.

#### The Nails.

The nails are modified epidermis. Each nail consists of: (a) a body, the attached uncovered portion of the nail; (b) a free edge, the anterior unattached extension of the body; (c) the nail root, the posterior part of the nail which lies under the skin (Fig. 248).

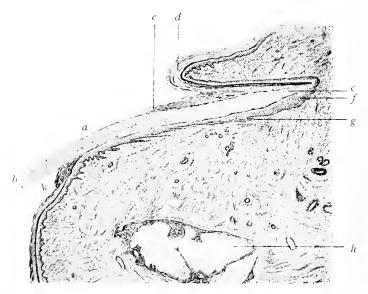


Fig. 248.—Longitudinal Section through Root of Human Nail and Nail Bed.  $\times$  10. (Schaper.) a, Body of nail; b, free edge; c, root of nail; d, epidermis; e, eponychium; f, stratum germinativum of nail; g, folds in derma of nail bed; h, bone of finger; k, hyponychium.

The nail lies upon a specially modified portion of the corium, the *nail bed*, which beneath the nail root and somewhat forward of the root is known as the *matrix*. The nail bed is bounded on either side by folds of skin, the *nail wall*, while between the nail wall and the nail bed is a furrow, the *nail groove* (Fig. 249).

The nail bed consists of corium. Its connective-tissue fibres are

arranged partly horizontal to the long axis of the nail, partly in a vertical plane extending from the periosteum to the nail. Papillæ are not present, but in their place are minute longitudinal ridges,

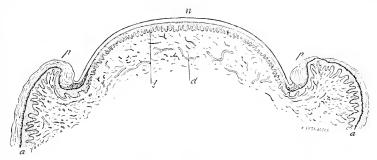


Fig. 249.—Transverse Section of Nail and Nail Bed. (Rannie.) n, Nail; a, epidermis: p, nail wall, to inner side of which is the nail groove; l, folds of derma; d, nail bed.

which begin at the matrix and, increasing in height as they pass forward, terminate abruptly at the end of the nail bed, beyond which are the usual papillæ of the derma.

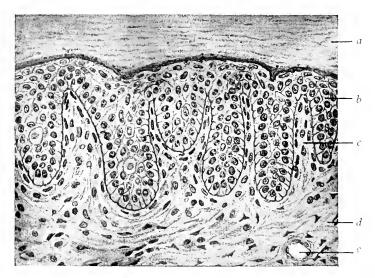


Fig. 250.—Vertical Transverse Section through Nail Body.  $\times$  280. (Szymonowicz.) a, Nail; b, stratum germinativum; c, ridge of nail bed; d, derma; e, blood-vessel.

The nail itself consists of two parts<sup>1</sup>—an outer harder part or true nail, and an under softer part. The outer portion is hard and horny, is developed from the stratum lucidum, and consists of several layers

<sup>1</sup> Another division of nail and nail bed considers the nail as composed of the hard part only, the soft stratum germinativum being considered a part of the nail bed.

of clear, flat, nucleated cells. These layers overlap in such a manner that each layer extends a little farther forward than the layer above. The under softer portion of the nail corresponds to the stratum germinativum of the skin and, like the latter, consists of polygonal "prickle" cells and a stratum cylindricum resting upon a basement membrane. In the matrix where the process of nail formation is going on, this layer is thicker than elsewhere and is white and opaque from the presence of keratohyalin. The convex anterior margin of this area can be seen with the naked eye and is known as the *lunula*.

At the junction of nail and skin, in the nail groove, the stratum corneum extends somewhat over the nail as its *eponychium*. A similar extension of the stratum corneum occurs on the under surface of the nail where the nail becomes free from the nail bed. This is known as the *hyponychium* (Fig. 248).

Growth of nail takes place by a transformation of the cells of the matrix into true nail cells. In this process the outer hard layer is pushed forward over the stratum germinativum, the latter remaining always in the same position.

#### TECHNIC.

- (1) Remove two or more distal phalanges from the fingers of a new-born child and fix in absolute alcohol or in formalin-Müller's fluid (technic 5, p. 7). After fixing, the bone should be carefully removed. Both longitudinal and transverse sections are made, stained with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19), and mounted in balsam. In cutting the sections it is usually best so to place the block that the knife passes through volar surface first, through nail last.
- (2) The cellular elements of nail do not show well in sections. For demonstrating the nail cells, boil a piece of nail in concentrated potash lye or warm it in strong sulphuric acid, scrape off cells from the softened surface, and mount in glycerin.

#### The Hair.

The hair, like the nail, is a development of the epidermis. The hair itself consists of a *shaft*, that portion of the hair which projects above the skin, and a *root*, that portion embedded within the skin. At its lower end the root presents a knob-like expansion, the *hair bulb*, in the under surface of which is a cup-like depression, which receives an extension of corium. This is known as the *papilla*. Enclosing the hair root is the *hair follicle*.

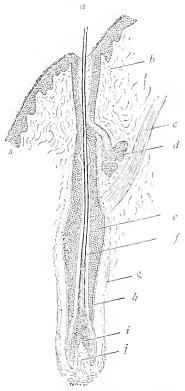
THE HAIR.—This is composed of epithelial cells arranged in three layers, which from within outward are medulla, cortex, and cuticle (Fig. 252).

(1) The medulla occupies the central axis of the hair. It is absent

in small hairs, and in the large hairs does not extend throughout their entire length. It is from 16 to 20 $\mu$  in diameter, and consists of from two to four layers of polygonal or cuboidal cells with finely granular, usually pigmented protoplasm and rudimentary nuclei.

- (2) The cortex makes up the main bulk of the hair and consists of several layers of long spindle-shaped cells, the protoplasm of which shows distinct longitudinal striations, while the nuclei appear atrophied. As these striations give the hair the appearance of being composed of fibrille, the term "cortical fibres" has been applied to them. In colored hair, pigment granules and pigment in solution are found in and between the cells of this layer. This pigment determines the color of the hair. In the root the cortical cells are less flattened than in the shaft.
- (3) The *cuticle* has a thickness of about  $1\mu$ , and consists of clear scale-like, non-nucleated epithelial cells. These overlap one another like shingles on a roof, giving to the surface of the hair a serrated appearance (Fig. 252.)

THE HAIR FOLLICLE.—This is also a modification of the skin. In the formation of the follicles of the finer (lanugo) hairs the epidermis alone is concerned. The follicles of the larger hairs contain both epidermal and dermal elements. The latter form the connective tissue follicle, while the epi



F16. 251.—Longitudinal Section of Hair and its Follicle from Vertical Section of Scalp. (Ranvier.) a, Shaft of hair; b, derma; c, arrector pili muscle; d, sebaceous gland; e, outer root sheath; f, inner root sheath; g, connective-tissue follicle; h, vitreous membrane; i, hair bulb; j, papilla; s, epidermis.

- connective-tissue follicle, while the epidermis forms the root sheaths.
- (1) The *root sheath* consists of two sub-layers—the *inner root sheath* and the *outer root sheath* (Figs, 253, 254, and 255).
- (a) The inner root sheath consists of three layers, which from within outward are the cuticle of the root sheath, Huxley's layer, and Henle's layer.

The cuticle of the root sheath lies against the cuticle of the hair and

is similar to the latter in structure. It consists of thin scale-like over-lapping cells, nucleated in the deeper parts of the sheath, non-nucleated nearer the surface (Figs. 253, 254 and 255,  $\epsilon$ ).

Huxley's layer lies immediately outside the cuticle of the root sheath, constituting the middle layer of the inner root sheath. It consists of about two rows of elongated cells with slightly granular protoplasm containing eleidin. In the deeper portion of the root these

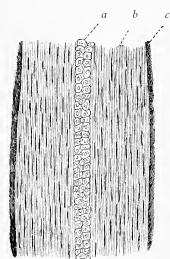


Fig. 252.—Longitudinal Section of Hair.  $\times$  350. (Kölliker.) a, Medulla; b, cortex; c, cuticle.

cells contain nuclei. Nearer the surface the nuclei are rudimentary or absent (Figs. 253, 254 and 255, d).

Henle's layer is a single row of clear flat cells. In the bulb these cells may contain nuclei; elsewhere they are non-nucleated (Fig. 255, e).

- (b) The outer root sheath is derived from the stratum germinativum to which it corresponds in structure. Next to the vitreous membrane is a single layer of columnar cells (stratum cylindricum). Inside of this are several layers of "prickle" cells (Figs. 253, 254 and 255, f).
- (2) The connective-tissue follicle consists of three layers—an inner vitreous membrane, a middle vascular layer, and an outer fibrous layer.
- (a) The vitreous or hyaline membrane is a thin homogeneous structure of the nature of an elastic membrane. It lies next to the outer root sheath and corresponds to the basement membrane of the derma (Figs. 253, 254 and 255, g).
- (b) The middle or vascular layer is composed of fine connective-tissue fibres, the general arrangement of which is circular. Cellular elements are quite abundant, while elastic fibres are, as a rule, absent. As its name would indicate, this layer is especially rich in blood-vessels (Figs. 253, 254 and 255, i).
- (c) The outer or fibrous layer consists of rather coarse, loosely woven bundles of white fibres, which run mainly in a longitudinal direction. Among these are elastic fibres and a few connective-tissue cells.

In the deeper portion of the root, some little distance above the

bulb, all the layers of the hair and its follicle can be distinctly seen. The differentiation of the layers becomes less marked as one passes in either direction. At about the level of the entrance of the ducts of the sebaceous glands (see p. 362) the inner root sheath disappears, and the outer root sheath passes over into the stratum germinativum of the skin, while between the outer root sheath (now stratum germi-

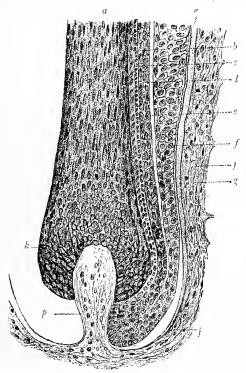


Fig. 253.—Longitudinal Section of Lower End of Root of Hair, including Papilla. (Kölliker.) a, Root of hair; b, cuticle of hair; c, cuticle of root sheath; d, Huxley's layer of inner root sheath; e, Henle's layer of inner root sheath; f, outer root sheath; g, vitreous membrane: g, connective-tissue follicle; g, bulb of hair; g, papilla.

nativum) and the hair are interposed the outer layers of the skin, stratum granulosum and stratum lucidum, when present, and stratum corneum. All of these are continuous with the same layers of the skin. In the region of the bulb the outer root sheath first becomes thinner, then disappears, while the layers of the inner root sheath retain their identity until the neck of the papilla is reached, at which point the different layers coalesce.

The arrector pili muscle (Fig. 251, c) is a narrow band, or bands, of smooth muscle connected with the hair follicle. It arises from the

outer layer of the derma on the side toward which the hair slants, and is inserted into the wall of the follicle at the junction of its middle and lower thirds, the sebaceous gland being usually included between the muscle and the hair (see below). The contraction of the muscle thus tends to straighten the hair and to compress the gland.

The sebaceous glands are with few exceptions connected with the hair follicles. They are simple or branched alveolar glands. The

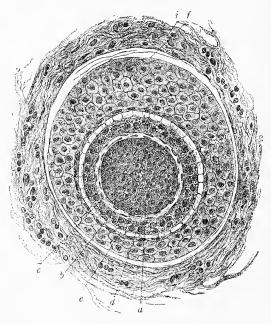


FIG. 254.—Transverse Section through Root of Hair and Hair Follicle. (Kölliker.) a, Hair; b, hair cuticle; c, cuticle of root sheath; d, Huxley's layer; e, Henle's layer; f, outer root sheath; i, connective-tissue follicle.

size of the gland bears no relation to the size of the hair, the largest glands being frequently connected with the smallest hairs. The glands are spherical or oval in shape and each gland is enclosed by a connective-tissue capsule derived from the follicle or from the derma. Beneath the capsule is a basement membrane continuous with the vitreous membrane of the follicle. The wide excretory duct empties into the upper third of the follicle and is lined with stratified squamous epithelium continuous with the outer root sheath and stratum germinativum. The lower end of the duct opens into several simple or branched alveoli, at the mouths of which the epithelium becomes reduced to a single layer of cuboidal cells. In the alveoli themselves

the cells are spheroidal or polyhedral, and usually fill the entire alveolus. These cells, like those lining the duct, are derivatives of the outer root sheath. The secretion of the gland—an oily substance called *sebum*—appears to be the direct product of disintegration of the alveolar cells,

which can usually be seen in all stages of the process of transformation of the cell into the secretion of the gland. The most peripheral cells show the least secretory changes, containing a few small fat droplets. The central cells and those in the lumen of the duct show the most marked changes, their protoplasm being almost wholly converted into fat, their nuclei shrunken or disintegrated or lost. In the middle zone are cells showing intermediary stages in the process.

Shedding of hair occurs in most mammalia at regularly recurring periods. In man there is a constant death and replacement of hair. In a hair about to be shed, the bulb becomes cornified and splits up into a number of fibres. The hair next becomes detached from the papilla and from the root sheath and is cast off, the empty root sheaths collapsing and forming a cord of cells between the papilla and lower end of the shedding hair. If the dead hair is to be replaced by a new one, there sooner or later occurs a proliferation of the cells of the outer root sheath in the region of the old papilla. From this "hair germ" the new hair is formed in a manner similar to embryonal hair formation,

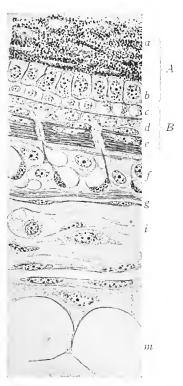


Fig. 255.—From Longitudinal Section through Hair and Hair Follicle. Enlarged to 800 diameters. (Schäfer.) A, Hair. a, Cortex of hair; b, cuticle of hair. B, Inner sheath. c, Cuticle of root sheath; d, Huxley's layer; c. Henle's layer; f, outer root sheath; g, vitreous membrane; i. connective-tissue follicle; m, fat cells.

the new hair growing upward under or to one side of the dead hair, which it finally replaces.

As to the manner in which growth of hair takes place, two views are held. According to one of these, the hair, cuticle, and inner root sheath are replenished by proliferation of the epithelial cells surrounding the papilla. These parts thus grow from below toward

the surface. The oldest cells of the outer root-sheath, on the other hand, lie against the vitreous membrane, so that growth of this sheath takes place from without inward. According to the second view, the various parts of the hair and its follicle are direct derivatives of the different layers of the skin, and their growth takes place by a continuous process of invagination. Thus the most peripheral cells of the outer root-sheath—stratum cylindricum—pass over the papilla and turn upward to form the medulla of the hair; the deeper cells—stratum spinosum—of the outer root-sheath become continuous with the cortex of the hair; the stratum lucidum, with the sheath of Henle, which turns up on the hair as its cuticle; Huxley's layer, with the cuticle of the inner root-sheath. According to this view growth of hair is accomplished by continuous growth downward from the surface, and turning up into the hair, of these layers.

#### TECHNIC.

Pin out small pieces of human scalp on cork and fix in absolute alcohol or in formalin-Müller's fluid (technic 5, p. 7). From one block cut sections perpendicular to the surface of the scalp and in the long axes of the hair and follicles. From a second block cut sections at right angles to the hair follicles, *i.e.*, not quite parallel to the surface of the scalp but a little obliquely. By this means not only are transverse sections secured, but if the block be sufficiently long the follicles are cut through at all levels. Sections are stained with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19) and mounted in balsam.

Blood-vessels of the skin. From the larger arteries in the subcutaneous tissue branches penetrate the pars reticularis of the derma, where they anastomose to form cutaneous networks. The latter give off branches, which pass to the papillary layer of the derma and there form a second series of networks, the subpapillary, just beneath the papillæ. From the cutaneous networks arise two sets of capillaries, one supplying the fat lobules, the other supplying the region of the sweat glands. From the subpapillary networks are given off small arteries which break up into capillary networks for the supply of the papilke, sebaceous glands, and hair follicles. The return blood from these capillaries first enters a horizontal plexus of veins just under the papille. This communicates with a second plexus just beneath the first. Small veins from this second plexus pass alongside the arteries to the deeper part of the corium, where they form a third plexus with larger, more irregular meshes. Into this plexus pass most of the veins from the fat lobules and sweat glands, although one or two small veins from the sweat glands usually follow the duct and

empty into the subpapillary plexus. The blood next passes into a fourth plexus in the subcutaneous tissue, from which arise veins of considerable size. These accompany the arteries.

Small arteries from the plexuses of the skin and subcutis pass to the hair follicle. The larger arterioles run longitudinally in the outer layer of the follicle. From these are given off branches which form a rich plexus of small arterioles and capillaries in the vascular layer of the follicle. Capillaries from this plexus also pass to the sebaceous glands, the arrectores pilorum muscles, and the papillæ.

The lymphatics of the skin. These begin as clefts in the papillæ, which open into a horizontal network of lymph capillaries in the pars papillaris. This communicates with a network of larger lymph capillaries with wider meshes in the subcutaneous tissue. The latter also receives lymph capillaries from plexuses which surround the sebaceous glands, the sweat glands, and the hair follicles.

The nerves of the skin. These are mainly sensory. Efferent sympathetic axones supply the smooth muscle of the walls of the bloodvessels, the arrectores pilorum, and secretory fibres to the sweat glands. The medullated sensory nerves are peripheral processes of spinal ganglion cells. The larger trunks lie in the subcutis, giving off branches which pass to the corium, where they form a rich subpapillary plexus of both medullated and non-medullated fibres. From the subcutaneous nerve-trunks and from the subpapillary plexus are given off fibres which terminate in more or less elaborate special nerve endings (see page 386). Their location is as follows: (1) In the subcutis: Vater-Pacinian corpuscles, the corpuscles of Ruffini, and the Golgi-Mazzoni corpuscles of the finger-tip. The first two forms are most numerous in the palms and soles. (2) In the derma: Tactile corpuscles of Meissner and Wagner. These are found in the papille, especially of the finger-tip, palm, and sole. Krause's end bulbs—usually in the derma just beneath the papillæ, more rarely in the papillæ themselves. (3) In the epithelium: Free nerve endings among the epithelial cells.

Branches of the cutaneous nerves supply the hair follicles. As a rule but one nerve passes to each follicle, entering it just below the entrance of the duct of the sebaceous gland. As it enters the follicle the nerve fibre loses its medullary sheath and divides into two branches, which further subdivide to form a ring-like plexus of fine fibres encircling the follicle. From this ring, small varicose fibrils run for a short distance up the follicle, terminating mainly in slight expansions on the vitreous membrane.

#### TECHNIC.

For the study of the blood-vessels of the skin inject (technic p. 22) the entire hand or foot of a new-born child. Examine rather thick sections either mounted unstained or stained only with eosin.

## DEVELOPMENT OF THE SKIN, NAILS, AND HAIR.

The epidermis is, as already noted, of ectodermic origin. It consists at first of a single layer of cuboidal cells. This soon differentiates into two layers—an outer, the future stratum corneum, and an inner, the future stratum germinativum. The stratum granulosum and stratum lucidum are special developments of the stratum germinativum. The corium is of mesoblastic origin. It is at first smooth, the papillæ being a secondary development.

The nail first appears as a thickening of the stratum lucidum. This spreads until the future nail bed is completely covered. During development the stratum corneum extends completely over the nail as its eponychium. During the ninth month (intra-uterine) the nail begins to grow forward free from its bed and the eponychium disappears, except as already noted.

The hair also develops from ectoderm. It first appears about the end of the third fœtal month as a small local thickening of the epidermis. This thickening is due mainly to proliferation of the cells of the stratum mucosum, and soon pushes its way down into the underlying corium, forming a long slender cord of cells—the hair germ. Differentiation of the surrounding connective tissue of the corium forms the follicle wall, while an invagination of this connective tissue into the lower end of the hair germ forms the papilla. The cells of the hair germ now differentiate into two layers: a central core the middle portion of which forms the hair, while the peripheral portion forms the inner root sheath; and an outer layer which becomes the outer root sheath. The sublayers are formed from these by subsequent differentiation. The hair when first formed lies wholly beneath the surface of the skin. As the hair reaches the surface its pointed extremity pierces the surface epithelium to become the hair shaft (Fig. 256).

The sebaceous gland develops as an outgrowth from the outer root sheath. This is a flask-shaped and at first solid mass of cells, which later differentiate to form the ducts and alveoli of the gland.

The sweat glands first appear as solid ingrowths of the stratum germinativum into the underlying corium. The lower end of the ingrowth becomes thickened and convoluted to form the coiled por-

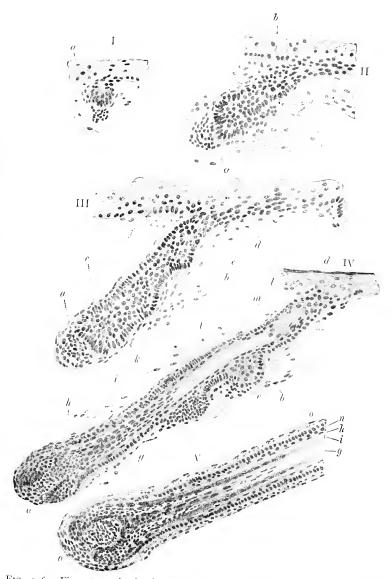


Fig. 256.—Five stages in the development of a human hair. (Stōhr.) a, Papilla: b, arrector pili muscle; c, beginning of hair shaft; d, point where hair shaft grows through epidermis; e, anlage of sebaceous gland; f, hair germ; g, hair shaft: h, Henle's layer; i, Huxley's layer; k, cuticle of root sheath; i, inner root sheat ; i, outer root sheath in tangential section; i, outer root sheath; i, connective-tissue follicle.

tion of the gland, and somewhat later the central portion becomes channelled out to form the lumen. The muscle tissue of the sweat glands, which lies between the epithelium and the basement membrane, is the only muscle of the body derived from the ectoderm.

## The Mammary Gland.

The mammary gland is a compound alveolar gland. It consists of from fifteen to twenty lobes, each of which is subdivided into lobules. The gland is surrounded by a layer of connective tissue containing more or less fat. From this periglandular connective tissue broad septa extend into the gland, separating the lobes (interlobar septa). From the latter finer connective-tissue bands pass in between the lobules (interlobular septa). From the interlobular septa strands of connective tissue extend into the lobule where they act as support for the glandular structures proper. An excretory duct passes to each lobe where it divides into a number of smaller ducts (lobular ducts), one of which runs to each lobule. Within the latter the lobular duct breaks up into a number of terminal ducts, which in turn open into groups of alveoli. The fifteen to twenty main excretory ducts pass through the nipple and open on its surface. At the base of the nipple each main duct presents a sac-like dilatation, the ampulla, which appears to act as a reservoir for the storage of the milk.

Until puberty the gland continues to develop alike in both sexes, but after about the twelfth year the male gland undergoes retrogressive changes, while the female gland continues its development.

The inactive mammary gland, by which is meant the female gland up to the advent of the first pregnancy and between periods of lactation, consists mainly of connective tissue and a few scattered groups of excretory ducts (Fig. 257). Around the ends of some of the ducts are small groups of collapsed alveoli. Both ducts and alveoli are lined with a low columnar, often rather flat epithelium. In some cases the flat cells are two or three layers thick, forming a thin stratified squamous epithelium. The relative amount of fat and connective tissue varies greatly, some inactive mammæ consisting almost wholly of fat tissue.

THE ACTIVE MAMMARY GLAND.—Throughout pregnancy the gland undergoes extensive developmental changes and becomes functional at about the time of birth of the child. The microscopic appearance of the active gland differs greatly from that of the inactive

(Fig. 258). There is a marked reduction in the connective tissue of the gland, its place being taken by newly developed ducts and alveoli. The alveoli are spheroidal, oval, or irregular in shape, and vary considerably in size. The alveoli are lined by a single layer of low columnar or cuboidal epithelial cells which rest upon a homogeneous basement membrane. The appearance of the cells differs according to their secretory conditions. The resting cell is cuboidal and its protoplasm granular. With the onset of secretion the cell elongates,

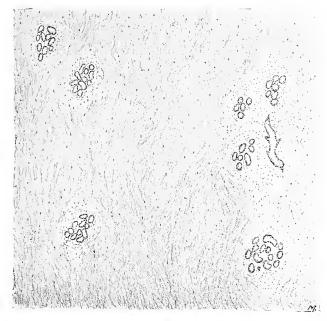


Fig. 257.—From Section of Human Inactive Mammary Gland. × 25. (Technic 1, p. 371.) Gland composed almost wholly of connective tissue; few scattered groups of tubules.

and a number of minute fat droplets appear. These unite to form one or two large globules of fat in the free end of the cell. The fat is next discharged into the lumen of the alveolus, and regeneration of the cell takes place from the unchanged basal portion. As to the number of times a cell is able to go through this process of secretion and repair before it must be replaced by a new cell, nothing definite is known. Active secretion does not as a rule take place in all the aiveoli of a lobule at the same time. Each lobule thus contains both active and inactive alveoli. The smallest ducts are lined with a low columnar or cuboidal epithelium. This increases in height with

increase in the diameter of the duct until in the largest ducts the epithelium is of the high columnar type.

The secretion of the gland is milk. This consists microscopically of a clear fluid or plasma in which are suspended the milk globules. The latter are droplets of fat from 3 to  $5\mu$  in diameter, each enclosed in a thin albuminous membrane which prevents the droplets from coalescing. Cells, probably leucocytes, containing fat droplets may also be present. In the secretion of the gland during the later months of pregnancy, and also for a few days following the birth of the child,

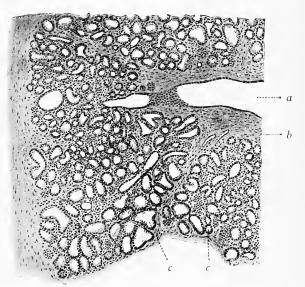


Fig. 258.—From Section of Human Mammary Gland during Lactation.  $\times$  50. (Stöhr.) a, Branch of excretory duct; b, interlobular connective tissue; c, alveoli.

a relatively large number of large fat-containing leucocytes—colostrum corpuscles—are found.

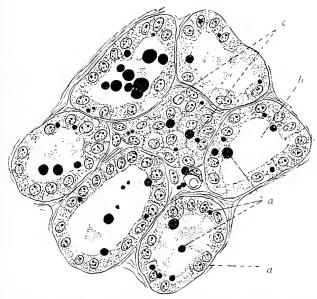
**Blood-vessels.**—These enter the gland, branch and ramify in the interlobar and interlobular connective tissue, and finally terminate in capillary networks among the alveoli and ducts. From the capillaries arise veins which accompany the arteries.

Lymphatics.—Lymph capillaries form networks among the alveoli and terminal ducts. The lymph capillaries empty into larger lymphatics in the connective tissue. These in turn communicate with several lymph vessels which convey the lymph to the axillary glands.

Nerves.—Both cerebro-spinal and sympathetic nerves supply the gland, the larger trunks following the interlobar and interlobular

connective-tissue septa. The nerve terminals break up into plexuses which surround the alveoli just outside their basement membranes. From these plexuses, delicate fibrils have been described passing through the basement membrane and ending between the secreting cells.

Development.—The development of the mammary gland is quite similar to the development of the sebaceous glands. The gland first appears as a dipping down of solid cord-like masses of cells from the stratum mucosum. The alveoli remain rudimentary until the advent



F16. 259.—From Section of Mammary Gland of Guinea-pig during Lactation.  $\times$  500. (Osmic acid.) (Szymonowicz.) a, Basement membrane; b, lumen of alveolus; c, tangential section of alveolus; d, fat globules.

of pregnancy. After lactation the alveoli atrophy, being replaced by connective tissue, and the gland returns to the resting state. After the menopause a permanent atrophy of the gland begins, fat and connective tissue ultimately almost wholly replacing the glandular elements.

#### TECHNIC.

- (1) Fix thin slices of an inactive mammary gland in formalin-Müller's fluid (technic 5, p. 7). Stain sections with hæmatoxylin-eosin (technic 1, p. 18), and mount in balsam.
  - (2) Prepare sections of an active mammary gland, as in preceding technic (1).

(3) Fix very thin small pieces of an active gland in one-per-cent. aqueous solution of osmic acid. After twenty-four hours wash in water and harden in graded alcohols. Thin sections may be mounted unstained, or after slight eosin stain, in glycerin.

### General References for Further Study.

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### CHAPTER XI.

### THE NERVOUS SYSTEM.

The nervous mechanism in man consists of two distinct though associated systems, the *cerebro-spinal nervous system* and the *sympathetic nervous system*. Each of these systems is composed of a central portion which is its centre of nervous activity, and of a peripheral portion which serves to place the centre in connection with the organs which it controls. In the cerebro-spinal system the central portion is known as the central nervous system and consists of the cerebro-spinal axis, or brain and spinal cord. The peripheral portion is formed by the cranial and spinal nerves. The central portion of the sympathetic system consists of a series of ganglia from which the sympathetic nerves take origin. These latter constitute its peripheral portion.

# HISTOLOGICAL DEVELOPMENT AND GENERAL STRUCTURE.

The beginning differentiation of the nervous system appears very early in embryonic life. It is first indicated by a longitudinal median thickening of the outer embryonic layer or ectoderm, to form the neural plate. The sides of the plate become elevated to form the neural folds, leaving between them the neural groove. By the dorsal union of these folds the neural groove is converted into the neural tube. The lumen of the neural tube corresponds to the central canal of the cord and the ventricles of the brain in the adult, and it is from the ectodermic cells which form the walls of this tube that the entire nervous system is developed. The caudal portion of the tube is of nearly uniform diameter—the spinal cord. At the cephalic end, the neural plate, even before its closure, is wider and forms, when closed, an expanded portion of the tube, the brain. In their further development, the walls of the brain form three expansions—the three brain "vesicles" known as the forebrain (prosence phalon), midbrain (mesence phalon), and hindbrain (rhombencephalon). In the forebrain two main divisions are usually distinguished, the endbrain (telencephalon) and the interbrain (dience phalon). The basal part of the endbrain forms the corpora striata and rhinencephalon, while the dorsal part expands into the pallium (cerebral hemispheres). In the interbrain may be distinguished a dorsal part, the *epithalamus*; a middle (largest) part, the *thalamus*; and a ventral expansion, the hypothalamus. In the midbrain the basal part becomes the tegmentum, and the dorsal part expands into the corpora quadrigemina or inferior and superior colliculi. The narrower part, connecting midbrain and hindbrain, is the isthmus. The basal part of the hindbrain forms the medulla oblongata and part of the dorsal wall expands into the cerebellum. In the later development of the brain, the pallium, and with it parts of the cerebellum, becomes enormously enlarged and structures are formed constituting connections between the pallium and the rest of the brain. The most massive of these are the pes pedunculi, added ventrally to the thalamus and midbrain; the pons Varolii, added ventrally to part of the midbrain, isthmus and part of the hindbrain; and the pyramids, added ventrally to the medulla. The basal part of the mid- and hindbrain, thus covered ventrally by the pes and pons, is the tegmentum. Other portions of the dorsal walls of the forebrain and hindbrain form thin-walled expansions which, together with vascular mesodermic coverings, are the chorioid plexuses of the lateral, third, and fourth ventricles. ties of the cerebral hemispheres are the lateral ventricles; the cavity of the interbrain is the third ventricle; that of the midbrain is the iter or aquæductus Sylvii; that of the hindbrain is the fourth ventricle.

The wall of the neural tube is at first composed of a single layer of epithelial cells. By proliferation of these cells the epithelium soon becomes many-layered, and forms a syncytium—the *myelospongium* of His—although some of the original epithelial cells appear to extend through the entire thickness of the wall.

Some of the syncytial cells which extend through the entire thickness of the wall of the neural tube (*spongioblasts* of His) increase in length as the wall increases in thickness. The inner ends of these cells form the lining of the tube, while other parts of the cells between the lumen and the surface tend to collapse, forming cord-like structures. The outer ends of the cells, on the other hand, become perforated and unite to form a thick network—the *marginal veil* of His. Of these cells, some retain this position, with nuclei near the lumen, in the adult and are known as *ependymal cells*; others move away from the central canal and become *neuroglia cells*.

Still other of the cells of the neural tube are destined to become neurones, and as such are known as neuroblasts. From the neuro-

blast a neurofibrillated process grows out—the future axone. Dendrites which at this stage are absent develop later in a similar manner, i.e., by extensions of the cell protoplasm. The neuroblasts soon leave their original position near the lumen and pass outward along the spaces between the elongated ependymal cells, but their bodies do not usually penetrate the marginal veil. Some may, however, pass through and even leave the neural tube along with the efferent roots. The axones of many neuroblasts located in the ventral part of the neural tube pierce the marginal veil and leave the neural tube as the efferent root fibres. These pass to sympathetic ganglia or to various structures (muscles, glandular epithelia) the activities of which they affect. Such structures may be collectively termed effectors. These nerve cells together with many of the sympathetic neurones (see below) are the efferent peripheral neurones. The axones of other neuroblasts do not completely pierce the marginal veil, but are directed upward and downward within it, thus forming fibres connecting various parts of the central nervous system. Axones of still other neuroblasts, especially in suprasegmental structures (see p. 377), are directed toward the lumen. All such neurones whose axones do not leave the neural tube may be termed intermediate or central neurones, as distinguished from the peripheral neurones: intermediate, because they serve as intermediate links connecting, within the central nervous system, the terminations of the afferent peripheral neurones (see below) with the bodies of the efferent peripheral neurones; central, because they are confined to the central nervous system. Later becoming medullated, their axones constitute the great majority of the fibres of the white matter of the central nervous system.

During the closure of the neural groove, groups of cells from the crest of each neural fold become separated from the rest of the developing nervous system. Some of these cells form the *cerebro-spinal ganglia*, while, according to most authorities, others migrate still further from the neural tube and form the various *sympathetic ganglia*. Some cells (neuroblasts) develop into the *nerve cells* of the cerebro-spinal and sympathetic ganglia. Others form, according to some authorities, enveloping cells, such as the *capsule cells* around the ganglion cell bodies and the *neurilemma cells* around the peripheral nerve fibres. These latter would thus correspond to the neuroglia cells of the central nervous system. The majority of the neuroblasts of the cerebro-

<sup>&</sup>lt;sup>1</sup>According to other views, other cells may participate in the formation of the axone, and the dendrites may anastomose with other neuroblasts (see Chap. VI).

spinal ganglia develop two processes: peripheral processes (afferent nerve fibres) to various structures (receptors) which receive stimuli; and central processes, forming the afferent roots and passing into the central nervous system where they usually bifurcate and form longitudinal ascending and descending arms. These cells are at first bipolar, later the cell body withdraws from the two processes and thus assumes the adult unipolar condition (see page 383). Other processes may also appear. Many of the neuroblasts of the sympathetic ganglia develop dendrites and axones while others form branching cells in which the two kinds of processes cannot be easily distinguished. Sympathetic cells are also derived from cells which migrate from the neural tube along the efferent root (p. 375).

The cerebro-spinal ganglionic neurones, together with some sympathetic neurones, certain neurones in the olfactory mucous membrane, retina, and possibly midbrain roof, constitute the afferent peripheral neurones of the entire nervous system. Most of the sympathetic neurones are efferent. The peripheral processes of the afferent peripheral neurones, the axones of the efferent peripheral neurones after they have emerged from the central nervous system, and the axones of the sympathetic ganglion cells, together with all their sheaths and connective-tissue investments, form the peripheral nerves. The bodies of the afferent peripheral neurones and sympathetic neurones form groups known as ganglia. The peripheral neurones are arranged segmentally, as shown by the series of ganglia and nerves.

The sympathetic neurones and those cerebro-spinal neurones which innervate sympathetic ganglia, viscera, glands, blood-vessels, and smooth and heart muscle are peripheral *visceral* or *splanchnic* neurones. Those cranial nerve neurones which innervate the striated voluntary muscles of jaw, face, pharynx, and larynx are usually also classed as splanchnic. The remainder of the cerebro-spinal peripheral neurones are peripheral *somatic* neurones.

From the foregoing it will be seen that all the neurones of the nervous system fall into two categories: I, *Peripheral* neurones, a part of whose processes, at least, lie outside the central nervous system, forming the peripheral nerves. II, *Central* or *intermediate* neurones. These lie entirely within the central nervous system. The peripheral neurones may be classified as follows: A. *Afferent* (all the neurone bodies outside the central nervous system, except possibly some in midbrain roof). The afferent neurones are (1) the cerebrospinal ganglion cells, (a) somatic, (b) splanchnic; (2) cells in olfactory

membrane, retina, and possibly midbrain; (3) some sympathetic neurones (splanchnic). B. Efferent neurones. These are (1) cerebrospinal (neurone bodies in ventral part of central nervous system), (a) somatic (to voluntary striated muscles), (b) splanchnic (to sympathetic ganglia, smooth and heart muscle, glands); (2) sympathetic (splanchnic, bodies in sympathetic ganglia, to smooth and heart muscle, glands).

In the central nervous system the bodies and dendrites are usually aggregated in certain localities which, on account of their appearance when examined in fresh condition, are collectively termed the *gray matter (substantia grisea)*. The gray matter also contains the beginnings and endings of the nerve fibres. The parts of the nervous system where the bodies and dendrites are absent and which are composed (exclusive of the neuroglia, blood-vessels, etc.) of the medullated nerve fibres are collectively termed the *white matter (substantia alba)*.

The central nervous system may be divided into a *segmental* part and a *suprasegmental* part. The former is in more immediate relation with the peripheral (segmental) nerves. It comprises the spinal cord and basal part of the brain (*segmental* brain). It contains all the bodies of the efferent cerebro-spinal neurones and practically all the terminations of the central processes (afferent root fibres) of the afferent peripheral neurones. In it the gray matter is internal, as a rule, and the white matter external. The suprasegmental part comprises the expanded portions of the dorsal wall of the neural tube already mentioned, namely the pallium, corpora quadrigemina, and cerebellum. These constitute the highest coördinating centers of the nervous system. Here the gray matter is external, constituting a *cortex*, and the white matter is internal.

The grouping of peripheral neurones into ganglia and nerves has already been mentioned. In the central nervous system more or less definite groups or *systems* of neurones having certain definite connections may also be distinguished. The axones of such a system constitute a *tract* or, when aggregated into a definite bundle, a *fasciculus*. The groups of neurone bodies are termed *nuclei*. The group or collection of bodies whose axones form a certain tract is the *nucleus of origin* of that tract. The same nucleus may receive the terminations of some other tract and is then the *terminal nucleus* of that tract. A given neurone system serves as a path for the conduction of some particular kind of nerve impulse. A *conduction path*, however, is

often composed of several neurone systems linked together, thus forming a series of relays.

All reactions performed by the nervous system must ultimately take effect upon some part of the body or effector and are usually initiated by changes in some receptor. Such a circuit from receptor to effector may be termed a neural arc (Fig. 260), and will involve afferent peripheral neurones, efferent peripheral neurones and usually intermediate neurones. The complexity of such arcs depends largely

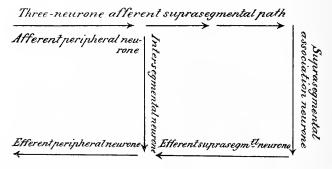


Fig. 260.—Diagram illustrating an arc transversing only the segmental, and an arc transversing the suprasegmental part of the nervous system.

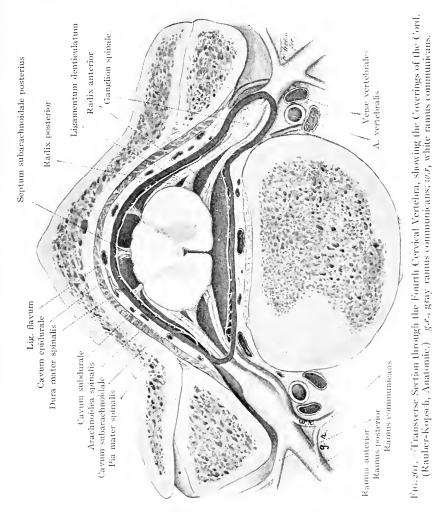
upon the number and character of intermediate neurones intercalated in the arc between the afferent and efferent peripheral neurones. Such arcs may obviously traverse centrally only the cord or segmental brain or may also traverse one or more of the suprasegmental parts of the nervous system. Intermediate neurones which link together different segments of the cord and segmental brain may be termed intersegmental neurones. Other intermediate neurones form paths to and from suprasegmental parts (afferent and efferent suprasegmental neurones) and still others are suprasegmental associative neurones confined to suprasegmental structures (Fig. 260).

### MEMBRANES OF THE BRAIN AND CORD.

The brain and cord are enclosed by two connective-tissue membranes, the dura mater and the pia mater (Fig. 261).

The *dura mater* is the outer of the two membranes and consists of dense fibrous tissue. The *cerebral dura* serves both as an investing membrane for the brain and as periosteum for the inner surfaces of the cranial bones. It consists of two layers: (a) An inner layer of closely packed fibro-elastic tissue containing many connective

tissue cells, and lined on its brain surface with a single layer of flat cells; and (b) an outer layer, which forms the periosteum and is similar in structure to the inner layer, but much richer in blood-vessels and nerves. Between the two layers are large venous sinuses. The *spinal dura* corresponds to the inner layer of the cerebral dura, which



it resembles in structure, the vertebre having their own separate periosteum. The outer surface of the spinal dura is covered with a single layer of flat cells, and is separated from the periosteum by the epidural space, which contains anastomosing venous channels lying in an areolar tissue rich in fat.

The pia mater closely invests the brain and cord, extending into the sulci and sending prolongations into the ventricles. It consists of fibro-elastic tissue arranged in irregular lamellæ, forming a spongy tissue, the cavities of which contain more or less fluid. The outer lamellæ are the most compact, and are covered on the dural surface by a single layer of flat cells. It is this external layer of the pia which is frequently described as a separate membrane, the arachnoid. The inner lamellæ of the pia are more loosely arranged, are more cellular and more vascular. Especially conspicuous are large, irregular cells with delicate bodies and large distinct nuclei. They lie upon the connective-tissue bundles partially lining the spaces.

The *Pacchionian bodies* are peculiar outgrowths from the outer layer of the pia mater cerebralis, which are most numerous along the longitudinal fissure. They are composed of fibrous tissue, and frequently contain fat cells and calcareous deposits.

Blood-vessels.—The spinal dura and the inner layer of the cerebral dura are poor in blood-vessels. The outer layer of the cerebral dura, forming as it does the periosteum of the cranial bones, is rich in blood-vessels which pass into and supply the bones. The pia is very vascular, especially its inner layers, from which vessels pass into the brain and cord.

#### TECHNIC.

For the study of the structure of the membranes of the brain and spinal cord, fix pieces of the cord with its membranes, and of the surface of the brain with membranes attached, in formalin-Müller's fluid (technic 5, p. 7) and stain sections with hæmatoxylin-eosin (technic 1, p. 18).

### THE PERIPHERAL NERVES.

The peripheral nerves are divided into spinal nerves and cranial nerves, the former being connected with the cord, the latter with the brain. Each spinal nerve consists of two parts—a motor or efferent part and a sensory or afferent part. Of the cranial nerves some are purely efferent, others purely afferent, while still others consist like the spinal nerves of both efferent and afferent fibres. The efferent fibres of the spinal nerves are axones of cell bodies situated in the anterior horns of the cord (see p. 404, and Figs. 279 and 289) and axones of sympathetic ganglion cells. The former leave the cord as separate bundles, which join to form the motor or efferent root. The

afferent fibres are peripheral processes of cell bodies situated in the spinal ganglia (p. 385 and Figs. 279, 264). These leave the ganglion and join with the fibres of the motor root to form the mixed spinal nerve (Fig. 279, f). The connection of the ganglion with the cord is by means of the central processes of the spinal ganglion cells. which enter the cord as the posterior root. Among the afferent fibres of the posterior root are also found, in some animals, a few efferent

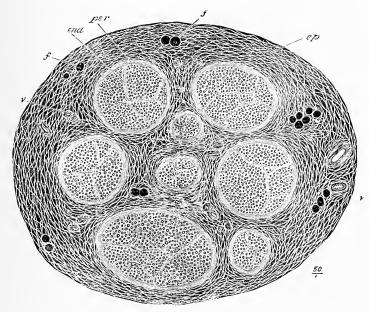


Fig. 262.—From Transverse Section of Human Nerve Trunk. (Osmic acid fixation.) (Quain.) *ep*, Nerve sheath or epineurium surrounding the entire nerve and containing blood-vessels (*v*) and small groups of fat cells (*f*); *per*, perifascicular sheath or perineurium surrounding each bundle or fascicle of nerve fibres; *end*, interior of fascicle showing supporting connective tissue, the endoneurium.

fibres (Fig. 279, c), processes of cells in the cord. Some fibres from the spinal ganglion and from the efferent roots form the white ramus communicans to the sympathetic ganglia. Fibres from the sympathetic ganglia form the gray ramus communicans to the mixed spinal nerve (Figs. 261 and 273). For further details regarding cranial nerves see pp. 425, 426.

The peripheral nerve consists of nerve fibres supported by connective tissue (Fig. 262). Enclosing the entire nerve is a sheath of dense connective tissue, the *epineurium*. This sends septa into the nerve which divide the fibres into a number of bundles or *fascicles*.

Surrounding each fascicle the connective tissue forms a fairly distinct sheath, the *perifascicular sheath* or *perineurium*. From the latter, delicate strands of connective tissue pass into the fascicle, separating the individual nerve fibres. This constitutes the *intrafascicular connective tissue* or *endoneurium*. In the connective-tissue layers of the perineurium are blood-vessels, and lymph spaces lined with endothelium, which communicate with lymph channels within the fascicle. When nerves branch, the connective-tissue sheaths follow the branchings. When the nerve becomes reduced to a single fibre, the connective tissue still remaining constitutes the sheath of Henle. On emerging from the central nervous system, the root fibres receive an investment of connective tissue as they pass through the pia mater. This is reinforced by additional connective tissue, as the nerve passes through the dura mater. For description of medullated and non-medullated nerve fibres see Chap. VI.

#### TECHNIC.

Fix a medium-sized nerve, such as the human radial or ulnar, by suspending it, with a weight attached to the lower end, in formalin-Müller's fluid (technic 5, p. 7). Stain transverse sections in hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19), or hæmatoxylin-eosin (technic 1, p. 18), and mount in balsam. Pieces of nerve should also be fixed in osmic acid imbedded, cut, and mounted without further staining. Pieces of fresh nerve may be teased and examined without staining.

### THE AFFERENT PERIPHERAL NEURONES.

These consist, as already stated, of the bodies and processes of the cerebro-spinal ganglion cells, probably some of the sympathetic ganglion cells, certain cells of the retina and certain cells of the olfactory mucous membrane. The two last named are described in connection with the organs of special sense.

# The Cerebro-spinal Ganglia.

The cerebro-spinal ganglia are groups of nerve cells connected with the afferent roots of the cerebro-spinal nerves. Each ganglion is surrounded by a connective-tissue capsule which is continuous with the perineurium and epineurium of the peripheral nerves. (Fig. 261.) From this capsule connective-tissue trabeculæ extend into the ganglion, forming a connective-tissue framework. Within the ganglion the nerve cells are separated into irregular groups by strands of connective tissue

and by bundles of nerve fibres. Each ganglion cell contains a centrally located nucleus and a distinct nucleolus, and is surrounded by a capsule of flat, concentrically arranged cells which are probably derived from the neural plate (p. 375) and are often called *amphicytes* or *satellite* cells (Fig. 265). Stained by Nissl's method the cytoplasm is seen to contain rather small, finely granular chromophilic bodies, which show a tendency to concentric arrangement around the nucleus. Pigmentation is common, the granules usually forming a group in the

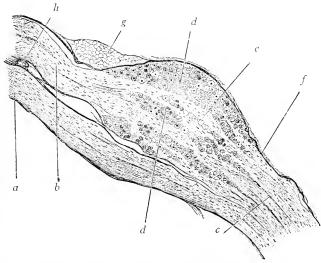
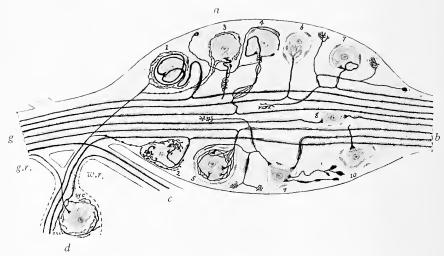


Fig. 263.—Longitudinal Section through a Spinal Ganglion.  $\times$  20. (Stöhr.) a, Ventral nerve root; b, dorsal nerve root; c, mixed spinal nerve; d, groups of ganglion cells; c, nerve fibres: f, perineurium; g, fat; h, blood-vessel.

vicinity of the point of origin of the main process of the cell. The majority of the cells of the spinal ganglia have one principal process which, at some distance from the cell body, divides into peripheral and central branches (p. 376). These cells are usually called unipolar cells. The principal process usually becomes medullated soon after emerging from the cell capsule (Fig. 264).

Among these cells a number of forms have been distinguished by Dogiel: (a) Cells with only a principal process. This process may pass almost directly from the capsule, but often takes several turns around the cell body, forming a "glomerulus," before emerging from the capsule (Fig. 264, 1 and Fig. 265, .1). This form is usually represented as the typical cerebro-spinal ganglion cell, but constitutes only a minority of these cells. (b) The principal process gives off collaterals. These lie within the capsule or are given off outside the capsule and terminate in other parts of the ganglion and its covering, either in terminal arborizations

or in terminal enlargements or bulbs. The collaterals may branch. Some of the terminations may be around the capsules of other cells. There may be one or several collaterals, sometimes a number of very short intracapsular collaterals. This last variety of cell may have more than one main process. (Fig. 264, 2 and 3, Fig. 265, B). (c) Cells with split processes. Here the main process divides into a number of fibres which reunite; this may be repeated. The splitting may be intracapsular or extracapsular. A variation of this is where there are two to six processes from the cell which form a complicated intracapsular network, finally uniting to form the single main process (Fig. 264, 4 and 5 and Fig. 265, C and D). (d) Cells with a number of dendrite-like processes which divide, forming an intra-



Ftg. 264.—Various Types of Cells and Nerve Terminations found in a Spinal Ganglion. Schematized from Dogiel. g.r., gray ramus communicans; sy.c., sympathetic cell; w.r., white ramus communicans. a. Spinal ganglion; b, dorsal or afferent root; c, ventral or efferent root; d, sympathetic ganglion; g, spinal nerve. For further explanation see text (pp. 383-385).

capsular network which finally fuses into the main process (Fig. 264, 6). (e) Cells whose principal process divides as usual, but the peripheral branch terminates by arborizations or bulbs in the ganglion and in its covering, or in the neighborhood of the dorsal root (Fig. 264, 7). (f) Bipolar cells (Fig. 264, 8). (g) Multipolar cells with a number of intracapsular dendrites and a main process (Fig. 264, 10; Fig. 265, E and F). (h) Cells with a principal process which probably enters the dorsal root and a number of processes which may be dendrite-like in character but also become medullated in places, and which branch and terminate in arborizations or bulbs in various parts of the ganglion. These latter apparently collectively represent the peripheral process which here ends in the ganglion (Fig. 264, 9).

The various endings in the ganglion of collaterals and other processes of ganglion cells often have capsules and resemble the terminations in receptors in other parts of the body (corpuscles of Pacini, end bulbs, etc.) and, together with their envelopes, may represent the receptors of the ganglion itself and of the connected nerves.

Sympathetic fibres enter the ganglion and form a plexus within it from which fibres pass and terminate within the capsules of the various ganglion cells.

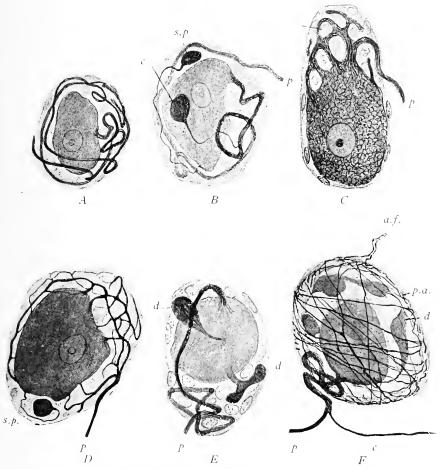


Fig. 265.—Cerebro-spinal Ganglion Cells and their Capsules. (Cajal.) A (adult man), Unipolar cell with single process forming a glomerulus; B (man), cell with short process ending in intracapsular bulb and main process giving off intracapsular collateral; C (dog), "fenestrated" cell with several processes uniting to form main process; D (ass), more complicated form of the same; E (man), cell with short bulbous dendrites; F (man), cell with bulbous dendrites and enveloped with pericellular arborizations (p,a.) of fibres (a,f.) terminating around cell; c, collateral; d, dendrite; p, principal process; s,p, short process. (Cajal's silver stain.)

The peripheral processes of the cerebro-spinal ganglion cells are the *afferent* fibres of the cerebro-spinal nerves (p. 381). The modes of termination of these peripheral processes are extremely varied

and complicated. These peripheral terminations are always free, in the sense that, while possibly sometimes penetrating cells, they probably never become directly continuous with their protoplasm.

In the skin, and in those mucous membranes which are covered with squamous epithelium, the nerve fibres lose their medullary sheaths in the subepithelial tissue, and, penetrating the epithelial layer, split up into minute fibrils which pass in between the cells and terminate there, often in little knob-like swellings (Fig. 266). In addition to such comparatively simple nerve endings, there are also found in the skin

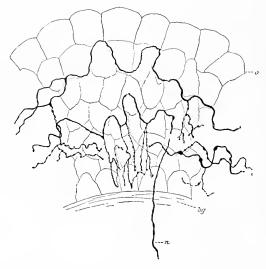


Fig. 266.—Free Endings of Afferent Nerve Fibres in Epithelium of Rabbit's Bladder. (Retzius.) o, Surface epithelium of bladder; bg, subepithelial connective tissue; n, nerve libre entering epithelium where it breaks up into numerous terminals among the epithelial cells.

and mucous membranes, especially where sensation is most acute, much more elaborate terminations. These may be classified as (r) tactile cells, (2) tactile corpuscles, and (3) end bulbs.

A simple tactile cell is a single epithelial cell, the centrally directed end of which is in contact with a leaf-like expansion of the nerve terminal, the tactile meniscus. In the corpuscles of Grandry, found in the skin of birds, and in Merkel's corpuscles, which occur in mammalian skin, several epithelial cells are grouped together to receive the nerve terminations. These are known as compound tactile cells, the axis cylinder ending in a flat tactile disc or discs between the cells.

Of the tactile corpuscles (Fig. 267) those of Meissner, which occur in the skin of the fingers and toes, are the best examples. These corpuscles lie in the papillæ of the derma. They are oval bodies, surrounded by a connective-tissue capsule and composed of flattened

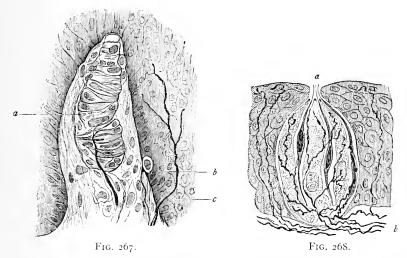


Fig. 267.—Tactile Corpuscle of Meissner, tactile cell and free nerve ending. (Merkel-Henle.) a, Corpuscle proper, outside of which is seen in the connective-tissue capsule. b, fibre ending on tactile cells c, fibre ending freely among epithelial cells.

b, fibre ending on tactile cell; c, fibre ending freely among epithelial cells.
Fig. 268.—Taste Bud from Circumvallate Papilla of Tongue. (Merkel-Henle.) a,
Taste pore; b, nerve fibres entering taste bud and ending upon neuro-epithelial cells. On either side fibres ending freely among epithelial cells.

cells. From one to four medullated nerve fibres are distributed to each corpuscle. As a fibre approaches a corpuscle, its neurilemma becomes continuous with the fibrous capsule, the medullary sheath disappears.

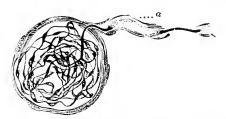


Fig. 269.—End Bulb from Conjunctiva. (Dogiel.) a, Medullated nerve fibre, axone of which passes over into dense end skein.

and the fibrillæ pass in a spiral manner in and out among the epithelial cells.

Of the so-called *end bulbs*, the simplest, which are found in the mucous membrane of the mouth and conjunctiva, consist of a central

core formed by the usually more or less expanded end of the axis cylinder, surrounded by a mass of finely granular, nucleated protoplasm—the inner bulb—the whole enclosed in a capsule of flattened connective-tissue cells. More complicated are the Pacinian bodies found in the subepithelial tissues of the skin and in many other or-

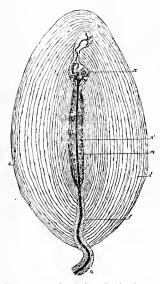


Fig. 270.—Pacinian Body from Mesentery of Cat. (Ranvier.) c, Lamina of capsule; d, epithelioid cells lying between laminæ of capsule; n, nerve fibre, consisting of axis cylinder surrounded by Henle's sheath, entering Pacinian body; f, perineural sheath; m, inner bulb; n, terminal fibre which breaks up at a into irregular bulbous terminal arborizations.

gans of mammalia. The Pacinian bodies (Fig. 270) are laminated, elliptical structures which differ from the more simple end bulbs already described, mainly in the greater development of the capsule. The capsule is formed by a large number of concentric lamellæ, each lamella consisting of connective-tissue fibres lined by a single laver of flat connective-tissue cells. lamellæ are separated from one another by a clear fluid or semifluid substance. As in the simpler end bulbs there is a cylindrical mass of protoplasm within the capsule known as the inner bulb. Extending lengthwise through the centre of the inner bulb, and often ending in a knob-like extremity, is the axis cylinder.

In voluntary muscle afferent nerves terminate in *Pacinian corpuscles*, in *end bulbs*, and in complicated end organs called *muscle spindles*, or neuromuscular bundles. The muscle spindle (Fig. 271) is an elongated cylindrical structure within which are muscle fibres, connective tissue, blood-vessels, and medullated nerves. The

whole is enclosed in a connective-tissue sheath which is pierced at various points by nerve fibres. A single spindle contains several muscle fibres and nerves. According to Ruffini, there are three modes of ultimate terminations of the nerve fibrils within the spindles: one in which the end fibrils form a series of rings which encircle the individual muscle fibre, termed annular terminations; a second in which the nerve fibrils wrap around the muscle fibres in a spiral manner—spiral terminations; a third in which the terminations take the form of delicate expansions on the muscle fibre—arborescent terminations. At the junction of muscle and tendon are found the

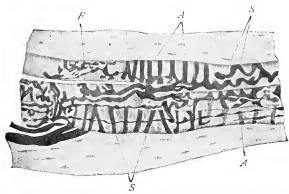


Fig. 271.—Middle Third of Muscle Spindle from Striated Voluntary Muscle Fibre of Cat. (From Barker, after Ruffini.) A, rings; S, spirals; F, arborescent branchings.

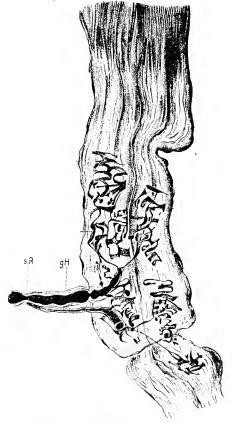


Fig. 272.—Tendon of Muscle of Eye of Ox. (Ciaccio.) Two muscle-tendon organs of Golgi, each showing ring-like and brush-like endings. gh, sheath of Henle; sr, node of Ranvier.

elaborate afferent terminal structures known as the muscle-tendon organs of Golgi (Fig. 272).

It is evident from the above that the nerve terminations are only stimulated through the intermediation of surrounding cells which may form quite elaborate structures. These cells constitute the receptors and probably render the various nerve terminations they envelop more or less inaccessible to all but one particular kind of stimulus. The above receptors are scattered throughout head and body (general or common senses) as distinguished from those which are concentrated into the organs of the special senses (smell, sight, hearing, taste) present only in the head (pp. 424, 425 and Chap. XII). The various stimuli received by them may give rise to sensations of light pressure or touch (tactile cells and corpuscles?), temperature and pain (diffuse terminations in epithelium and connective tissue?), muscle-tendon sense of movement and position (muscle spindles and possibly end bulbs, etc., in muscles, tendon organs of Golgi?). These may be roughly grouped into general cutaneous or superficial sensation and deep sensation (muscle-tendon and other bodily sensations). All receptors, both of general and special senses, may be classified (Sherrington) as those receiving stimuli from the external world (extero-ceptors, of superficial sensation, smell, sight, and hearing), those concerned with visceral reactions (intero-ceptors, including taste) and those giving information of bodily changes (proprio-ceptors, deep sensation).

THE CENTRAL PROCESSES OF THE CEREBRO-SPINAL GANGLION CELLS enter the central nervous system as the fibres of the afferent root, the entire bundle of afferent root fibres of a single nerve consisting of all the central processes of the corresponding ganglion. Having entered the central nervous system, the central processes divide into ascending and descending arms, as already mentioned (p. 376).

### THE SYMPATHETIC GANGLIA.

The sympathetic system of the neck and trunk consists of a series of *vertebral* or *chain ganglia*, lying ventro-lateral to the vertebræ and connected by longitudinal cords, and of gangliated *prevertebral plexuses* connected with the vertebral ganglia and also connected with ill-defined *peripheral ganglia* in the walls of the viscera (e.g., plexuses of Auerbach and Meissner). The sympathetic ganglia of the head are the *ciliary*, *sphenopalatine*, *otic*, and *submaxillary*.

The peripheral processes of certain spinal ganglion cells pass *via* the white rami communicantes to the vertebral ganglia and thence to visceral receptors. Axones of splanchnic efferent spinal neurones pass from the spinal cord *via* the ventral roots and white rami communicantes to the vertebral ganglia and terminate in various sympathetic ganglia. The first thoracic to the second lumbar spinal nerves

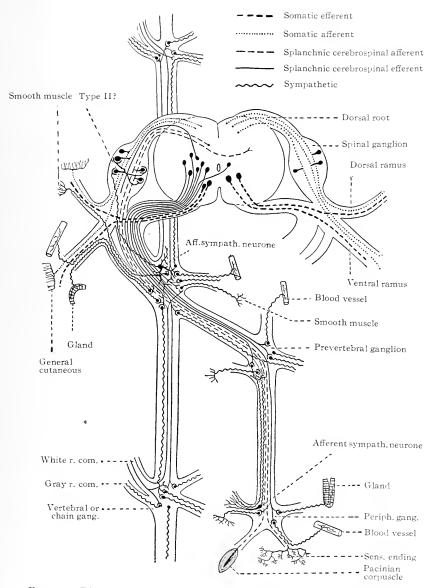


Fig. 273.—Diagram of the Sympathetic System and the Arrangement of its Neurones in a Mammal. On the left are shown the typical elements of a trunk segment including the sympathetic system. On the right are shown only the somatic afferent and efferent neurones of the spinal nerve. Of the sympathetic system are shown the white and gray rami, three ganglia of the chain, one prevertebral ganglion and one peripheral ganglion. The symbols used are explained in the figure. In most respects the diagram follows one of Huber's figures. (Johnston.)

It will be noted that the sympathetic outflow from any particular cord segment may

ultimately reach other segments of the body.

are thus connected with the sympathetic. The second, third, and fourth sacral nerves and visceral branches of the vagus, glossopharyngeus, and facialis have similar connections with the prevertebral plexuses. Some cerebro-spinal (especially vagus) fibres may pass directly to visceral structures. The sympathetic ganglia of the head are connected with certain of the cranial nerves (see p. 426).

Some of the sympathetic cells are probably afferent but the majority are efferent and send their axones via the gray ramus com-

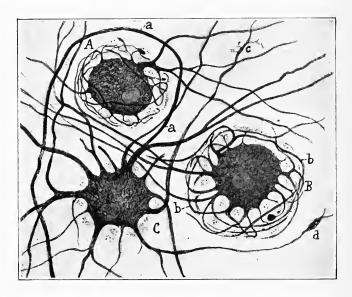


Fig. 274.—Sympathetic Nerve Cells (woman of 36 years). (Cajal.) A and B, cells whose dendrites (b) form a pericellular plexus. C, cell with long dendrites. a, axone; c and d, terminal part of a dendrite. The capsular cells are faintly indicated. (Cajal's silver stain.)

municans (to spinal nerves), longitudinal cords and efferent rami to the various visceral effectors (see below). The sympathetic is thus in the main composed of additional neurones intercalated in the visceral efferent path. The fibres of the white rami communicantes are mostly fine and medullated. The axones of the sympathetic cells are fine and non-medullated or thinly medullated. For further details see Fig. 273.

The larger ganglia resemble the spinal ganglia in having a connective-tissue capsule and framework. The cells are smaller and often densely pigmented. Each cell is surrounded by a capsule of cells similar to those surrounding the spinal ganglion cells. Often two or three

cells and their interlocked dendrites are enclosed within a common capsule (Fig. 275, A).

The typical sympathetic nerve cell is a multipolar cell with short branching dendrites confined to the capsule of the cell and often interlocked with the dendrites of adjacent cells, forming glomeruli. Sometimes a dendrite will pass some distance from the cell, arborize, and

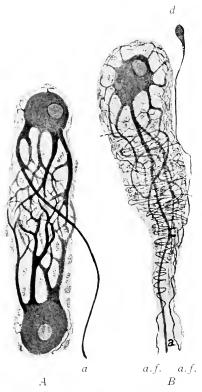


Fig. 275.—Sympathetic Nerve-Cells and their Capsules. (Cajal). .1. Two-celled glomerulus; B, cell surrounded with the pericellular terminal arborizations of two fibres (a.f.) passing to the cell; a, axones; d, fibre, probably dendritic, with bulbous termination. (Cajal's silver stain.)

interlock with a similar dendritic arborization of another cell. Another form of sympathetic cell has long slender dendrites often indistinguishable from axones. These cells are more frequent in the peripheral ganglia. Some of these cells have been considered to be afferent sympathetic cells. (Figs. 274 and 275.)

The sympathetic cells receive fibres which form arborizations around and within their capsules and also around the long dendrites.

Many of these are terminations of the visceral cerebro-spinal efferent neurones (Figs. 273 and 275, B).

The axones of the efferent sympathetic cells terminate in heart muscle, in smooth muscle of viscera (viscero-motor), of blood-vessels

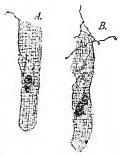


Fig. 276.—Nerve Endings on Heart Muscle Cells. (From Barker, after Huber and De Witt.)

(vaso-motor) and of hairs (pilo-motor), and in glandular epithelia (secretory). In heart muscle (Fig. 276) and in smooth muscle (Fig. 277) the nerves of the sympathetic system end in *fine feltworks of fibres*, which are in relation with the muscle cells. Satisfactory differentiation between efferent terminals and afferent terminals in heart and in smooth muscle has not yet been made.

In organs whose parenchyma is made up of so-called glandular epithelium, the sympathetic nerves terminate mainly in *free endings* 

which lie in the cement substance between the cells, thus coming in contact with, though not penetrating, the epithelial cells.

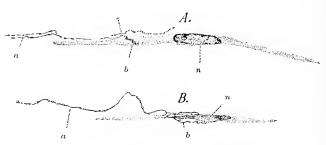


Fig. 277.—Nerve Endings on Smooth Muscle Cells. (From Barker, after Huber and De Witt.) a, Axis cylinder; b, its termination; n, nucleus of muscle cell.

#### TECHNIC.

- (1) Fix spinal and sympathetic ganglia in formalin-Müller's fluid (technic 5, p. 7). Stain sections with hæmatoxylin-eosin (technic 1, p. 18), or with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19).
- (2) Fix spinal and sympathetic ganglia in absolute alcohol or in 10-per-cent. formalin, and stain sections by Nissl's method (technic, p. 35).
  - (3) See also technic 1, p. 309.
- (4) Ganglia should also be prepared by Cajal's silver method, using the alcohol fixation (p. 34).

### EFFERENT PERIPHERAL CEREBRO-SPINAL NEURONES.

It has been seen that the bodies of these neurones lie in the ventral part of the neural tube where they form a part of the ventral gray column in the cord and the "motor" nuclei of cranial nerves in the segmental brain. The axones of these cell bodies emerge as the efferent roots and usually either pass (via the white ramus communicans, in spinal nerves) to various sympathetic ganglia to terminate there, or proceed as the efferent fibres of the peripheral nerves to terminate in the striated voluntary muscles of the body and head. In the

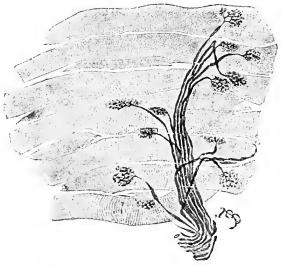


Fig. 278.—Motor nerve-endings in abdominal muscles of a rat. Gold preparation. X 170. (Szymonowicz).

spinal nerves these fibres pass beyond the spinal ganglia and then join the afferent fibers; in some cranial nerves they pass out with the afferent fibres. On their way to the muscles the motor axones may bifurcate several times, thus allowing one neurone to innervate more than one muscle fibre. In the perimysium the nerve fibres undergo further branching, after which the fibres lose their medullary sheaths and pass to the individual muscle fibres. Here each fibre breaks up into several club-like terminals which constitute the *motor end plate*. The location of the end plate, whether within or without the sarcolemma. has not been determined. As a rule each muscle fibre is supplied with a single end plate, though in large fibres there may be several. (Fig. 278.)

### THE SPINAL CORD.

The spinal cord encased in its membranes lies loosely in the vertebral canal, extending from the upper border of the first cervical vertebra to the middle or lower border of the first lumbar vertebra. It is cylindrical in shape and continuous above with the medulla oblongata, while below it terminates in a slender cord, the *filum terminale*. At two levels, one in its cervical and one in its lumbar region, the diameter of the cord is considerably increased. These are known, respectively, as the *cervical* and *lumbar enlargements*. The spinal nerve roots leave the cord at regular intervals, thus indicating a division of the cord into segments, each segment extending above and below its nerve roots one-half the distance to the next adjacent roots. There are 31 segments corresponding to the 31 spinal nerves; 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal.

# Origin of the Fibres which Make up the White Matter of the Cord.

It has already been observed that the white matter of the cord is composed mainly of medullated nerve fibres, most of which run in a longitudinal direction. From the study of the neurone it follows that each of these fibres must be the axone of some nerve cell. These cells, the medullated axones of which form the white matter of the cord, are situated as follows:

- A. Cells outside the spinal cord. (Extrinsic cells.)
- B. Cells situated in the gray matter of the cord. (*Intrinsic cells.*)
- (1) Cells outside the central nervous system (spinal ganglion cells).
- (2) Cells in other parts of the central nervous system (the brain).
- (3) Root cells, such as those of the anterior horn, whose axones form the ventral root (efferent peripheral neurones).
- (4) Intermediate neurones, whose axones enter into formation of the fibre columns of the cord (column cells.)
- (5) Cells of Golgi, type II, the axones of which ramify in the gray matter. (These cells do not give rise to fibres of the white matter, but are conveniently mentioned here among the other cord cells.)

# (1) THE SPINAL GANGLION CELL AND THE ORIGIN OF THE POSTERIOR COLUMNS.

It has already been seen that the central processes of these cells enter the cord as dorsal root fibres and split into ascending and descending longitudinal arms composing the greater part of the dorsal funiculus and the zone of Lissauer. They are described more in detail later (pp. 413 and 414).

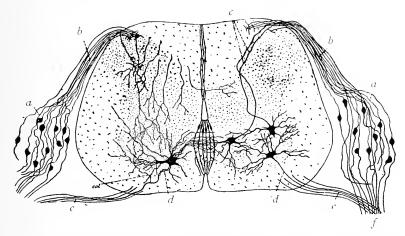


Fig. 279.—Transverse Section through Spinal Cord and Posterior Root Ganglia of an Embryo Chick. (Van Gehuchten.) a, Spinal ganglion, its bipolar cells sending their peripheral processes outward to become fibres of the mixed spinal nerve (f), their central processes into the dorsal columns of the cord as the dorsal root fibres (b); within the posterior columns these fibres can be seen bifurcating and sending collaterals into the gray matter of the posterior columns, one collateral passing to the gray matter of the opposite side. The few efferent fibres of the dorsal root (c) are disproportionately conspictions. The large multipolar cells of the ventral horns are seen sending their axones (d) out of the cord as the ventral root fibres (e) which join the peripheral processes of the spinal ganglion cells to form the mixed spinal nerve (f); col, collateral from axone of ventral horn cell. Dendrites of the anterior horn cells are seen crossing the median line in the anterior commissure. About the centre of the cord is seen the central canal; dorsal and ventral to the latter some ependymal cells stretching from the canal to the periphery of the cord. (Golgi Method.)

# (2) CELLS SITUATED IN OTHER PARTS OF THE CENTRAL NERVOUS SYSTEM WHICH CONTRIBUTE ANONES TO THE WHITE COLUMNS OF THE CORD.

These cells are situated in the motor areas of the cortex of the pallium, in the midbrain, cerebellum(?), and various parts of the segmental brain. The axones of these cells pass down the cord, forming the descending fibre tracts of the cord (p. 416). Collaterals and terminals of these fibres enter the gray matter of the cord to terminate there.

### (3) ROOT CELLS—MOTOR CELLS OF THE ANTERIOR HORN.

The course of the axones of these cells has been described (p. 395). The bodies are described on pp. 404 and 405.

# (4) COLUMN CELLS.

These are cells which lie in the gray matter of the cord and send their axones into the white columns or funiculi (see p. 403) where they either bifurcate or turn up or down, becoming longitudinal fibres. Some of the cells send their axones into the white matter of the same

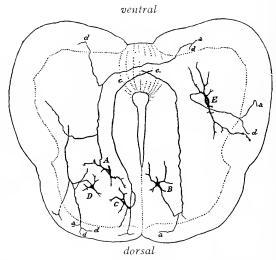


Fig. 280.—Cross Section through Spinal Cord of Embryo Chick of Eight Days' Incubation. (Cajal, Golgi's method.) A, Hecateromeric cell with axone sending off side fibril to gray matter and then dividing, one branch passing to the white matter of the same side, d, the other through the ventral commissure to the white matter of the opposite side, a and d. B and C, Hecateromeric cells of the dorsal gray matter; the axones divided, one branch, a, passing to the dorsal white columns of the same side, the other, c, through the anterior commissure to the opposite side of the cord. D, Tautomeric cell, the axones branching, but all branches passing to the gray matter or white matter of the same side of the cord. E, Tautomeric cell of the ventral horn with axone dividing into two branches, a and d, in the white matter of the same side. The importance of the hecateromeric cells is exaggerated in the figure. A, B and C without side processes a and d give a good representation of heteromeric cells.

side of the cord. These are known as *lautomeric cells* (Fig. 280, D, E). Others send their axones as fibres of the anterior commissure to the white matter of the opposite side of the cord—heteromeric cells. The axones of a few cross in the dorsal white commissure. In a few others the axone divides, one branch going to the white matter of the same side, the other to the white matter of the opposite side—hecateromeric cells (Fig. 280, A, B, C).

The axones of many of these cells are short, constituting the *short* fibre tracts (fundamental columns—ground bundles) of the cord (see

page 419; others are long, passing up through the cord to the brain (see page 413). Terminals and collateral branches of these longitudinal axones, especially of the short ones are constantly re-entering the gray matter to end in arborizations around the nerve cells (Fig. 281).

### (5) CELLS OF GOLGI TYPE II.

The axones of these cells do not leave the gray matter, but divide rapidly and terminate in the gray matter near their cells of origin, some crossing to terminate in the gray matter of the opposite side.

#### TECHNIC.

- (1) For the purpose of studying the spinal ganglion cell with its processes and their relations to the peripheral nerves and to the cord, the most satisfactory material is the embryo chick of six days' incubation, treated by the rapid silver method of Golgi (technic b, p. 32). Rather thick (75µ) transverse and longitudinal sections are made and mounted in balsam without a cover-glass. Owing to the uncertainty of the Golgi reaction several attempts are frequently necessary before good sections are obtained.
- (2) The root cells of the anterior horn with their axones passing out of the cord and joining the peripheral processes of the spinal ganglion cells to form the spinal nerves, can usually be seen in the transverse sections of the six-day embryo chick cord prepared as above, technic (1).
- (3) For studying the column cells of the cord, embryo chicks of from five to six days' incubation should be treated as in technic  $(\tau)$ .

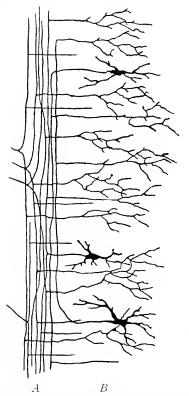


Fig. 281.—From Longitudinal Section of Spinal Cord of Embryo Chick. (Van Gehuchten.) A, White column of cord; B, gray matter. The cells of the gray matter (column cells) are seen sending their axones into the white matter, where they bifurcate, their ascending and descending arms becoming fibres of the white column. The dendrites of these cells are seen ramifying in the gray matter. To the left are seen fibres (posterior root fibres) entering the white matter and bifurcating, the ascending and descending arms becoming fibres of the white column. From the latter are seen fibres (collaterals and terminals) passing into the gray matter and ending in arborizations. (Golgi Method.)

incubation should be treated as in technic (1). Owing to the already mentioned uncertainty of the Golgi reaction, it is usually necessary to make a large number of

sections, mounting only those which are satisfactorily impregnated. It is rare for a single section to show all types of cells. Some sections contain tautomeric cells, some contain heteromeric, while in very few will the hecateromeric type be found.

Sections containing fewest impregnated cells frequently show collaterals to best advantage. These are seen as a fringe of fine fibers crossing the boundary line between gray matter and white matter.

(4) The silver method of Cajal, using the alcohol fixation (technic 2, p. 34), may also be advantageously used to display many of the above details of structure in embryo chicks. It is also capricious.

Whole neurones with long axones obviously cannot be directly demonstrated in single sections. To demonstrate these serial sections and indirect methods (degeneration, etc.) are used (see Fibre Tracts of Cord).

#### PRACTICAL STUDY.

Transverse Section of Six-day Chick Embryo (Technic 1, p. 399).—Using a low-power objective, first locate the cord and determine the outlines of gray matter and white matter. Observe the spinal ganglia lying one on either side of the cord (Fig. 270, a). One of the ganglia will probably show one or more bipolar cells, sending one process toward the periphery, the other toward the spinal cord. Note that the peripheral process is joined, beyond the ganglion, by fibres which come from the ventral region of the cord (fibres of the anterior root). In some specimens the latter can be traced to their origin in the cells of the anterior horn (Fig. 279, d). The union of the peripheral processes of the spinal ganglion cells and the anterior horn fibres is seen to make up the mixed spinal nerve (Fig. 279, f). Observe the central processes of the spinal ganglion cells entering the dorsal column of the cord and bifurcating (Fig. 270, b). As these branches pass up and down the cord, only a short portion of each can be seen in a transverse section. Note the fibres (collaterals) passing from the white matter into the gray matter. Note in some of the sections a little round mass just ventral and to the inner side of the spinal ganglion, in which nerve cells may be seen, and some fibres passing into or out of it. This represents the beginning of the sympathetic system with its chain of ganglia. Note the relation which this bears to the spinal cord and spinal ganglia.

In the same or other transverse sections study the column cells of the cord, carefully distinguishing between the dendrites and axone. This is not always easy, but the axone can usually be distinguished as being more slender, with smoother outline and more uniform size throughout its course. Axones may come off from dendrites as well as from the cell bodies. At least one tautomeric and one heteromeric column cell should be found and studied (Fig. 280). Study also the collaterals if they are stained. Remember that only a few of the elements present are stained in Golgi preparations and that there are apt to be present irregular silver precipitates without any significance. Capillaries often appear as a coarse brown-stained meshwork.

Study also any spongioblasts that may be stained. Those with nuclei near the central canal give a fair representation of the ependyma cells of the adult cord except the cell does not usually in the latter extend entirely through the wall of the neural tube.

Longitudinal Section of Six-day Chick Embryo (Technic 1, p. 399).— Using a low-power objective locate gray matter and white matter and identify plane of section relative to transverse section above described. Note in the white matter longitudinally-running fibres from which branches pass off into the gray matter (Fig. 281). Those of the posterior columns are the ascending and descending branches of the central processes of the spinal ganglion cells, and the branches passing into the gray matter are their collaterals and terminals. If the section happens to include the entering fibers of a posterior root, these can be seen branching in the posterior columns into ascending and descending arms (Fig. 281). The longitudinal fibres of the lateral and anterior columns are axones of column cells and of cells situated in higher centres (see pages 397 and 398). These also send collaterals and terminals into the gray matter.

# General Topography of the Cord, Cell Groupings, Arrangement of Fibres and Finer Structure.

The further description of the cord is best combined with the practical study of sections of the cord, taking sections through the lumbar enlargement as a type.

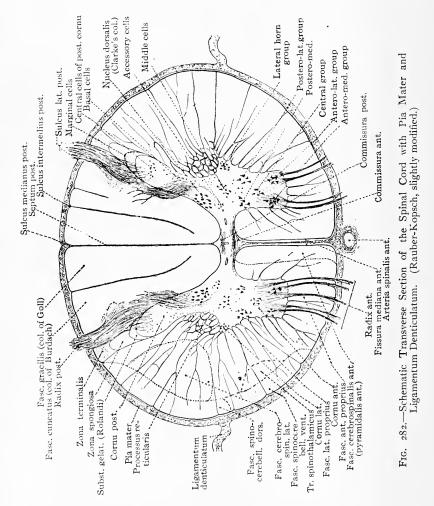
# PRACTICAL STUDY OF SECTIONS THROUGH LUMBAR ENLARGEMENT.

General Topography (Figs. 282 and 283).—The general features of the sections can be best seen with the naked eye or with a low-power dissecting lens.

Note the shape and size of the cord, and that it is surrounded by a thin membrane, the pia mater spinalis; the deep anterior median fissure, into which the pia mater extends; the posterior median septum consisting principally of neuroglia, over which the pia mater passes without entering; and the postero-lateral grooves or sulei at the entrance of the posterior root fibres. The gray matter is seen in the central part of the section (stained more lightly in the Weigert preparation, on account of the presence of numerous unstained cell bodies and dendrites) and arranged somewhat in the form of the letter H. Dorsally the gray matter extends almost to the surface of the cord as the dorsal gray columns (posterior horns or cornua). The ventral gray columns (anterior horns) are, on the other hand, short and broad, and do not approach the surface of the cord. Surrounding the gray matter is the white matter (stained deep blue in the Weigert preparation). This is divided by the posterior horn into two parts, one lying between the horn and the posterior median septum, the posterior funiculus (dorsal white column); the other comprising the remainder of the white matter, the antero-lateral funiculus (antero-lateral white column). This latter is again divided by the anterior horn and anterior nerve roots into a lateral juniculus (lateral white column) and an anterior juniculus (ventral white column). In the concavity between the anterior and posterior horns some processes of the gray matter extend out into the white matter where they interlace with the longitudinally running fibres of the latter to form the reticular process (not well marked in the lumbar cord).

For the study of further details the low-power objective should be used.

GRAY MATTER.—In the cross portion of the H is seen the *central canal*, usually obliterated in the adult and represented only by a group of epithelial cells. The central canal divides the gray matter connecting the two sides of the cord into a *ventral gray commissure* and a *dorsal gray commissure*. Immediately surrounding the epithelial cells is a light granular area composed mainly of neuroglia and known



as the central gelatinous substance. Toward the surface of the cord the posterior horn expands into a head or caput, external to which is an area similar in general appearance to that surrounding the central canal, the gelatinous substance of Rolando. The head is connected with the base of the dorsal horn by a narrower neck or cervix. External to the gelatinous substance of Rolando is a thin zone containing a plexus of fine medullated fibres (Weigert stain) known as the marginal zone or zona spon-

giosa, and external to this, occupying the space between it and the periphery, is a zone composed of fine longitudinal medullated fibres rather sparsely arranged and therefore staining more lightly with the Weigert method. This is the zona terminalis or zone of Lissauer. It belongs obviously to the white matter of the cord (see page 405). The portion of the gray matter connecting the dorsal and ventral horns may be termed the intermediate or middle gray. Note the well-defined groups of large nerve cells in the anterior horns and the fibres passing out from the anterior horns to the surface of the cord, ventral (anterior) nerve roots. (Figs. 282 and 283.)

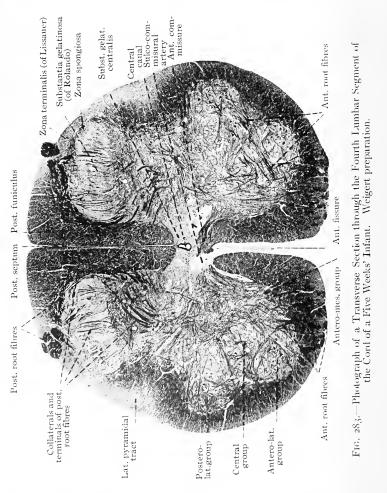
WHITE MATTER.—Note the general appearance of the white matter and the disposition of the supporting strands of neuroglia tissue (light in the Weigert, usually darker in other stains). The neuroglia is seen to form a fairly thick layer just beneath the pia mater from which trabeculæ pass in among the fibres, the broadest strand forming the posterior median septum. If the section has been cut through a dorsal (posterior) nerve root, a strong bundle of dorsal root fibres can be seen entering the white matter of the cord along the dorsal and mesial side of the posterior horn. Just ventral to the anterior gray commissure is a bundle of transversely-running medullated fibres—the anterior white commissure. (Fig. 283.) It is composed of the axones of various heteromeric column cells and of decussating terminals of various fibres. In the dorsal part of the dorsal gray commissure are also a few fine transversely-running medullated nerve fibres—the dorsal white commissure. It consists of collaterals of fibres in dorsal funiculi and axones of heteromeric column cells.

Cell Groupings.—The positions and groupings of the various cell bodies should now be studied. (Nissl, Hæmatoxylin-Eosin, Cajal, Figs. 282 and 283.) (For convenience, their general arrangement throughout the cord is here given; also the course of their axones, though this is usually only seen in Golgi preparations.)

- (A) Cells of the Dorsal Horn.—(a) Marginal cells arranged tangentially to the border of the gelatinous substance of Rolando. (b) Cells in the gelatinous substance of Rolando, arranged radially. The Golgi method indicates that the axones of (a) and (b) principally enter the adjoining lateral column. (c) Large stellate cells in the apex of the caput, most of the axones of which go to the lateral columns, but some cross in the ventral white commissure. (d) A central group in the central part of the dorsal cornu, some of the axones of which may cross in the ventral commissure. (e) Basal cells in the base of the horn and in the processus reticularis, the axones of which usually go to the lateral column but may cross. (f) Dorsal (thoracic) nucleus or cells of Clarke's column in the mesial part of the base of the dorsal horn. These are tautomeric cells, the axones of which form the dorsal spino-cerebellar tract (see page 415). Clarke's column is mainly confined to the dorsal or thoracic cord, but is also present in the first lumbar segment.
- (B) Cells of the Intermediate Gray.—(a) Middle nucleus whose cells may send their axones across in the ventral commissure or uncrossed to the lateral column; (b) various small cells including the accessory nucleus near Clarke's column; (c) intermedio-lateral group which in parts of the cord forms a projection of the gray known as the lateral horn. These are probably root cells whose axones pass into the sympathetic system. This nucleus is more conspicuous in the thoracic cord, but extends from the eighth cervical to about the third lumbar segment and is also present in the sacral cord (especially the third segment).

From the above it is seen that all the cells of the dorsal and intermediate gray, except the intermedio-lateral group, are column cells.

(C) Cells of the Ventral Horn.—These fall into two categories: (1) Tautomeric column cells, sending axones to the adjoining white matter, and heteromeric column cells, the axones of which cross in the ventral commissure. Among the latter may be a well-marked group in the dorso-mesial part of the horn (commissural



nucleus). (2) Root cells. Two main divisions may be distinguished: (a) Mesial group, present throughout the cord above the fifth sacral segment (Bruce). This group probably innervates the striated voluntary (somatic) muscles of the trunk. The mesial group is in part of the cord subdivided into a ventro-mesial and dorso-mesial group, the latter being present in the first, sixth and seventh cervical, thoracic (except first), and first lumbar segments. (b) Lateral group, present in the cervical, first thoracic, and lumbo-sacral regions. This group innervates the muscles of the

extremities and exhibits the following subdivisions: An antero-lateral (C4 to C8, L2 to S2), a postero-lateral (C4 to C8, L2 to S3) and a post-postero-lateral (C8 to Th1, S1 to S3). There is also a central group (L2 to S2) and a small anterior group (L1 to L4). The exact muscle groups innervated by these cell groups respectively have not yet been definitely determined. Other special cell groups are the *phrenic group* (C4), centrally located, *cilio-spinal* and other cells (C8 to Th2, *via* the sympathetic to dilator pupilke and blood-vessels of head), and the *spinal accessory* (C1 to C6). The latter is located laterally and innervates the sterno-mastoid and trapezius muscles.

For the determination of the destination of the axones of the efferent root cells the method of studying the changes in the cell body (Nissl stain) in definite lesions of the peripheral fibres (axonal degeneration) is used.

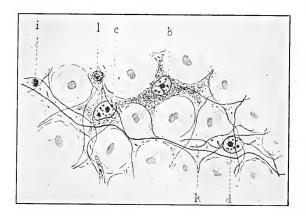
Arrangement of Fibres (Fig. 283).—With the low- and high-power objectives the course of the transverse (i.e., longitudinally cut) nerve fibres should be carefully studied in Weigert and Cajal preparations. These fibres pass from gray to white matter or vice versa, and are in general (a) root fibres entering or leaving the cord; (b) either axones of column cells in the gray passing out into the white there to become longitudinal fibres by turning or splitting, or they are the collaterals and terminals of the fibres of the white matter entering the gray to terminate there.

The arrangement of these fibres should be carefully studied in all parts of the section (Weigert and Cajal), taking one field at a time. In the dorsal part of the cord, the dorsal roots can be seen entering. From their lateral portion fine fibres detach themselves and enter the zone of Lissauer, the fibres of which are largely composed of their short ascending and descending arms. Most of the fibres of the root passes along the dorsal and mesial side of the dorsal horn forming the zone of entry of the dorsal roots. By bifurcating (not visible in the preparation) they become the longitudinal fibres of the dorsal funiculus. From the entering root fibres and fibres of the dorsal funiculus, bundles of fine fibres (collaterals and terminals) pass radially through the gelatinous substance of Rolando or sweep around its mesial side and enter the gray. Some of these terminate in the gelatinous substance of Rolando (Golgi preparations), some form part of the dense plexus of fibres in the caput and terminate there, others can be traced to the intermediate gray and, in some cases, some ("direct reflex collaterals") can be traced to the ventral horn. It will be noted that not many come from the mesial part of the dorsal funiculus. Collaterals from the zone of Lissauer enter the gelatinous substance of Rolando. In the middle part of the cord there is a similar interchange of fibres between the plexus in the gray and the adjoining white matter. In the ventral part of the cord a similar interchange takes place, but here besides these fine fibres are seen the coarse fibres of the ventral roots gathered from various parts of the ventral horn to form bundles which leave the ventral side of the horn, pass through the white matter and emerge as the ventral root fibres. The larger bundles of fibers in the ventral horn separate the cell groups, but between individual cells are seen numerous fine medullated fibres (principally terminals of fibres from the white funiculi). Trace as far as possible the course of the fibres of the ventral and dorsal white commissures.

Finer Structure.—Study with the high power the general histological structure of the gray and white matter. In the gray matter note (Cajal, Nissl, H.-E.), besides the nerve cells and their processes, the neuroglia nuclei. Note also the structure

and size of the medullated nerve fibres (Weigert). In the white matter note the appearance of the cross-cut medullated nerve fibres in Weigert, Cajal and H.–E. preparations. With the neuroglia stains study carefully the *neuroglia cells* and *neuroglia fibres*, including the neuroglia zone forming the margin of the cord. (Fig. 284.) Note also the pia mater and the connective-tissue septa entering the cord from the pia accompanied usually by a denser aggregation of glia fibres. Note carefully the number of neuroglia nuclei in some small field. Increase in neuroglia is characteristic of many pathological conditions. Study the *ependyma*. (Weigert, Nissl, Cajal, glia stain).

Study the internal structure of the nerve-cells of various sizes present, especially the amount and arrangement of the chromophilic substance (Nissl).



F16. 284.—From Transverse Section of Elephant's Cord. (Hardesty.) Benda's Neuroglia Stain. b, c, d and i, Four types of neuroglia cells; k, neuroglia fibre passing through several neuroglia cells; l, leucocyte.

The smallest nerve cells of the cord have a limited amount of chromophilic substance, usually either in the form of perinuclear caps or small bodies near the periphery of the cell. In the medium cells more chromophilic bodies are present. The cells of Clarke's column have a considerable number of chromophilic bodies arranged near the periphery of the cell. The root cells are richest in chromophilic substance (for further details see Chap. VI).

Blood-vessels (Fig. 285).—Study the arrangement and structure of the blood-vessels of the cord and pia. There are three principal longitudinal arteries, the anterior spinal artery given off from the vertebral arteries near their union into the basilar artery, and two posterior spinal arteries, given off from the inferior and superior cerebellar arteries. These arteries are reënforced by small arteries passing to the cord along the dorsal and ventral roots and form an arterial network in the pia mater. From the network terminal (i. e., non-anastomosing) branches enter the cord, supplying all parts except the ventral horn and column of Clarke. The latter are supplied by branches from the anterior spinal artery which pass dorsally in the ventral sulcus (sulco-commissural arteries) and enter the cord alternately to right and left. They then break up

into a rich capillary network in the ventral horn, supplying also a branch to the column of Clarke. The veins of the cord also form a plexus in the pia mater. Larger posterior median and anterior median veins can be distinguished. Portions of the above vessels can be seen, cut in various planes, in the pia and in the cord. The general appearance and structure of the blood-vessels, including capillaries, should be noted in the various methods of staining.

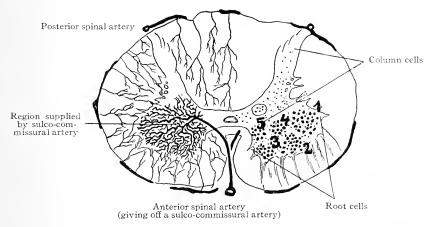


Fig. 285.—Schematic transverse section of Cord, Showing General Distribution of Blood-vessels (left) and Nerve-cells (right) (Bing). Root-cells; 1, postero-lateral group; 2, antero-lateral group; 3, antero-medial group; 4, central group; 5, postero-medial group. The broke 1 black lines on the surface of the cord are portions of the vascular network in the pia mater.

### Variations in Structure at Different Levels.

While the general structure above described obtains throughout the cord, the size and shape of the cord, the size and shape of the gray matter, and the relative proportion of gray matter and white matter, vary in different parts of the cord, which must therefore be separately considered. These variations are due to: (1) Variations in the size of the nerves entering and leaving, which cause corresponding variations in the gray matter which receives the afferent fibres and contains the cells of origin of the efferent fibres. Thus the larger nerves of the extremities cause the increase in size of the gray matter of the cervical and lumbo-sacral cord with which they are connected, and also an increase in the dorsal funiculi. (2) A gradual increase in the white matter of the cord, as higher levels are reached, due to an increase in the number of long ascending and descending fibres to and from the brain.

### PRACTICAL STUDY.

Section through the Twelfth Thoracic Segment (Fig. 287).—Note that the cord is smaller than in the lumbar enlargement and somewhat flattened dorsoventrally; that the amount of gray matter and white matter is diminished; that both anterior and posterior horns are more slender, the anterior horn containing comparatively few cells. At the inner side and base of the posterior horn may be seen the group of cells known as *Clarke's column* (p. 403). Medullated fibres can be seen passing from the dorsal funiculus into Clarke's column, where they interlace among the nerve cells. These fibres are collaterals of the dorsal root fibres terminating in the nucleus. From the nucleus coarser fibres can be seen gathering at its ventral side and thence passing outward to the periphery of the cord where they bend upward forming the beginning of the dorsal spino-cerebellar tract (see p. 415).

Section through the Mid-thoracic Region (Fig. 287).—Compare with the lumbar sections. Note the change in shape and size; that the cord is more nearly round and smaller; that while the reduction in size affects both gray matter and white matter, it is the former that shows the greater decrease. The horns are even more slender than in the twelfth thoracic section, and the anterior horn contains still fewer cells. Clarke's column is present, but not so large.

Section through the Cervical Enlargement (Fig. 286).—Note the marked increase in size of the cord, which affects both gray matter and white matter. Depending upon the exact level at which the section is taken, the cord may be nearly round or flattened dorso-ventrally. The posterior horns remain slender while the anterior are much broader than the posterior horns. The reticular process is more prominent than in any of the previous sections. As in the lumbar cord, the cell groups of the anterior horn are numerous and well defined. A more or less definite septum divides the posterior column into an inner part, the column of Goll, and an outer part, the column of Burdach.

For further variations and differences between the segments of the cord, compare Figs. 286, 287 and 288.

### Fibre Tracts of the Cord.

The determination of the fibre tracts of the cord has been accomplished principally by two methods: (1) The *myelogenetic* method, which is based upon the fact that the fibres of different systems acquire their myelin sheaths at different periods of embryonic development. Thus by examining cords from embryos of various ages and young specimens it is possible, using a myelin stain (e.g., Weigert), to distinguish different tracts by the presence or absence of myelinization of their fibres. (2) The method of *secondary* or *axonal degeneration*, based upon the fact that a fibre separated from its cell undergoes degenerative changes and ultimately disappears and that the cell body also usually shows certain changes (see page 124). The fibres distal to the injury can be distinguished during active degeneration by

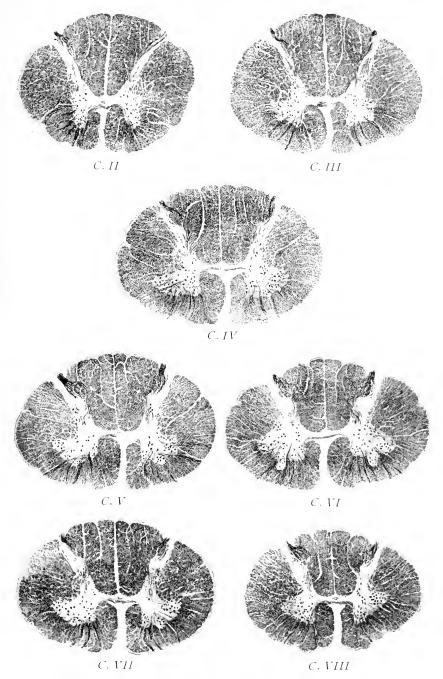
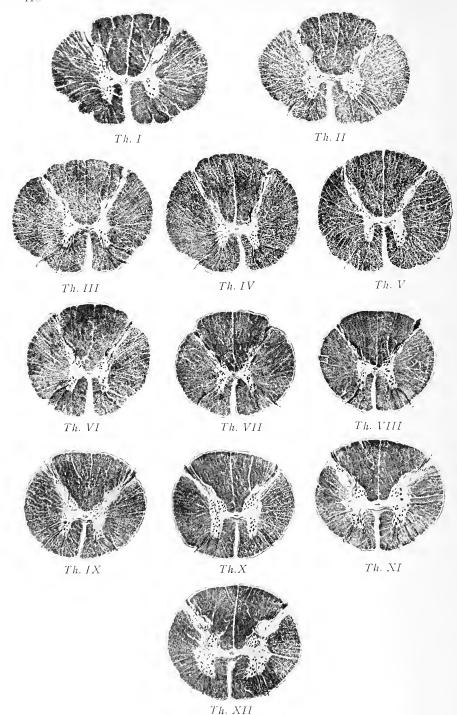


Fig. 286.—Transverse Sections through the Cervical (II-VIII) Segments of the Cord. Weigert preparations. (Rauber-Kopsch.)



 $\rm F_{IG.~287.}$  –Transverse Sections through the Thoracic (I–XII) Segments of the Cord. Weigert preparations. (Rauber-Kopsch.)

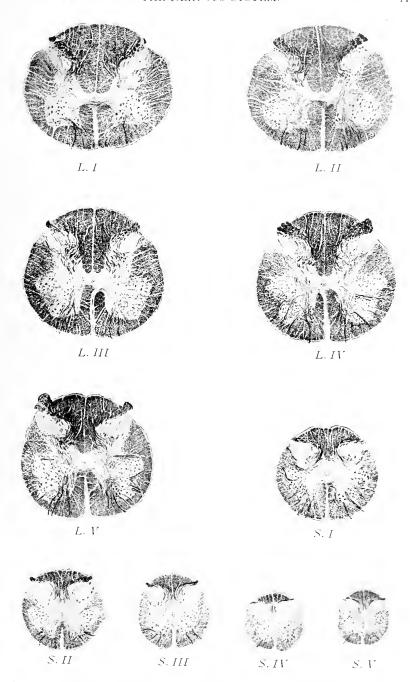
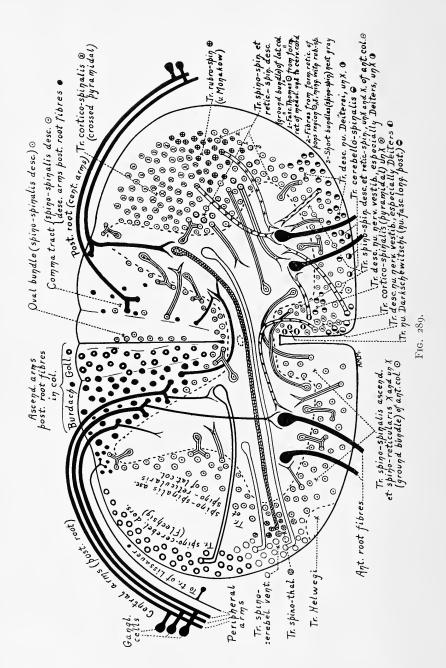


Fig. 288.—Transverse Sections through the Lumbar (I–V) and Sacral (I–V) Segments of the Cord. Weigert preparations. (Rauber-Kopsch.)



applying the Marchi stain (page 31). After their disappearance, however, a negative picture is obtained by staining the surrounding normal fibres (Weigert). The changes in the cell bodies whose axones are injured are distinguished by applying the Nissl stain (p. 35). Thus if the cord is cut at some particular level, at any level above the cut all fibres present which originate from cells below the cut will show degeneration ("ascending" degeneration), while the cell bodies of the cut fibres will show the axonal degeneration changes. On the other hand, at any level below the cut, fibres which originate from cells above the cut will show degeneration ("descending" degeneration), while the cell bodies of these fibres, located above the cut, will exhibit axonal degeneration. (3) Atrophy (von Gudden's method). This method is based upon the fact that extirpation of some part of the nervous system in a young animal is followed by an atrophy of parts in intimate relation therewith. This method only demonstrates grosser changes than the preceding, but on the other hand whole conduction paths involving more than one neurone relay may show changes. Other methods are the method of comparative anatomy, i.e., study of the simpler nervous systems of lower forms and the correlated development or absence of related parts of the nervous system, and the method of physiology, i.e., study of effects of stimulation or extirpation of various portions of the nervous system thereby indirectly demonstrating anatomical pathways.

### ASCENDING TRACTS.

- A. Tracts forming parts of afferent pallial paths.
- I. Long Ascending Arms of Dorsal Root Fibres. (Posterior Funiculi).—The origin of these tracts—central processes of the cells of the spinal ganglia—has been described (page 390). The distribution of the posterior root fibres to the gray matter of the cord was noted in connection with the study of the lumbar enlargement section (page 405). The general arrangement of these fibres in the dorsal funiculi remains to be noted.

FIG. 280—Diagram of the Tracts of the Cord (Cervical Region). Ascending tracts are shown on the left side, and descending tracts on the right. It will be noticed that the tracts of the cord are roughly divisible into three concentric zones: (1) A zone occupying most of the posterior columns and the peripheral part of the lateral columns. This zone comprises the principal long ascending tracts (beginnings of afferent suprasegmental paths). (2) The second zone lies immediately within the first in the lateral columns and also occupies the peripheral part of the anterior columns. It comprises the principal long descending tracts from various parts of the brain (terminal portions of efferent suprasegmental paths). (3) The third zone borders the gray matter and includes the ground or fundamental bundles of the cord (chiefly spinal intersegmental fibres).

In the figure, for nu, Darkschewitschi read interstitial nucleus of Cajal.

Each successive dorsal root sends its fibres into the cord next to the dorsal horn and therefore to the outer side of those from the next root below. Thus the fibres of the lower roots as they ascend the cord are gradually pushed inward toward the median line until they finally occupy that part of the posterior column lying near the posterior septum. The separation of the posterior column by a connective-tissue septum into the column of Goll and the column of Burdach occurs only in the cervical cord (Figs. 282 and 286). Here the most median fibres, i.e., those lying in the column of Goll, are the longest fibres of the posterior columns, having come from the lower spinal ganglia, while the column of Burdach (Fig. 282) consists of short and medium length fibres. The fibres of Goll's column end in the nucleus funiculi gracilis or nucleus of the column of Goll in the medulla (see p. 435 and Fig. 297). Those fibres of Burdach's which do not terminate in the spinal cord terminate in the medulla in the nucleus funiculi cuneati or nucleus of the column of Burdach (p. 435 and Fig. 297,). The nucleus gracilis and nucleus cuneatus—which will be seen in sections of the medulla (Fig. 297)—thus serve as terminal nuclei for the afferent root fibres in the columns of Goll and those of the column of Burdach which do not terminate within the cord. Inasmuch as many of the ascending arms are short, it is evident that only a fraction of the dorsal root fibres are represented at the higher levels. Those long arms which reach the medulla constitute the beginning of one of the principal afferent cerebral or pallial pathways. The axones of the neurones, whose bodies are the nuclei of Goll and Burdach, cross and form the tract known as the *medial fillet* (or *lemniscus*), composing the second system of this path. The fillet terminates in the thalamus and the path is completed by a third system of thalamo-cortical neurones to the cortex pallii. This path is, in brief, the long ascending arms of dorsal roots + fillet + thalamo-cortical path, decussating in the medulla (Fig. 203).

II. Spino-thalamic Tract.—This arises from heteromeric cells lying probably principally in the dorsal horn (groups c and d, p. 403). Their axones cross in the ventral commissure and reach the opposite lateral funiculus where they ascend in a position mesial to the ventral spino-cerebellar tract (see below). This tract terminates in the thalamus whence the path is completed by thalamo-cortical neurones. The path is thus: spinal ganglion (short arms and collaterals of dorsal roots) + spinothalamic + thalamo-cortical neurones, three systems of neurones. Its decussation takes place in the cord at about the level

of entry of the dorsal roots involved. Associated with this system may be some fibres to the tectum mesencephali (spino-tectal). (Figs. 289, 290 and 294).

B. Tracts forming part of paths to the cerebellum.

III. Dorsal Spino-cerebellar Tract (Tract of Flechsig, Direct or Uncrossed Cerebellar Tract).—This tract lies along the dorso-lateral periphery of the cord, being bounded internally by the crossed pyrami-

dal tract (Fig. 282, and Fig. 289). The fibres of the direct cerebellar tract are the axones of the cells of Clarke's column (Figs. 289, 290 and 204). These axones cross the intervening gray matter and white matter of the same side (tautomeric column cells) and turn upward as the direct cerebellar tract. In the medulla they form part of the restiform body or inferior cerebellar peduncle and pass to the cerebellum. Here they enter the gray matter of the vermis of the same or opposite side, ending in ramifications among the nerve cells. Some fibres either end in, or send off collaterals to, the cerebellar nuclei. The tract first appears in the upper lumbar cord, and increases in size until the upper limit of Clarke's column has been reached (page 403).

As already noted above, some fibres of the posterior root, or their collaterals, end in the column of Clarke. This path is composed then of two systems of neurones,

Fig. 290.—Diagram showing Beginnings of Principal Long Ascending Tracts of Cord and Termination of Lateral Pyramidal Tract. Each group of neurones is represented by one or two neurones. d.s-c.. Dorsal spino-cerebellar tract; p, lateral pyramidal tract; s-t., spino-thalamic tract; v.s-c., ventral spino-cerebellar tract; z,r., ventral root.

spinal ganglion cells and Clarke's column cells, and is uncrossed (with the exception that some fibres are interrupted in the nucleus lateralis of the medulla) (Fig. 308).

IV. Ventral Spino-cerebellar Tract.—This tract lies along the periphery of the cord, extending from the anterior limit of the direct

cerebellar to about the exit of the ventral roots (Fig. 282 and Fig. 289). It is probably formed by axones whose cell bodies are scattered through the intermediate gray matter, possibly group a (p. 403 and Fig. 282). Some fibres come from tautomeric, others from heteromeric cells, the axones of the latter crossing in the ventral commissure. The tract first appears in the upper lumbar cord and naturally increases in size as it passes upward. The fibres of this tract also end in the vermis of the cerebellum. They reach their destination in the cerebellum by a different route, ascending considerably farther than the dorsal spinocerebellar fibres and then turning back along the outer side of the superior cerebellar peduncle to the vermis. This path is thus also a two-neurone path, partly crossed and partly uncrossed. The ventral spino-cerebellar and spino-thalamic tracts are sometimes referred to as Gower's tract. (Figs. 294 and 308).

It seems probable that muscle-tendon sense passes up the cord by tract I (uncrossed in the cord), while pain and temperature pass up by the spinothalamic tract (crossed). The path pursued by touch is more doubtful but it may pass up partly by tract I and partly by ascending arms of varying lengths which end in the cord around heteromeric column cells (partly uncrossed and partly crossed in the cord). This path may join the fillet in the medulla. It would seem probable that the cerebellar tracts convey scimuli from muscletendon receptors.

#### Descending Tracts.

I. The Pyramidal Tracts (Tractus Cortico-spinalis, Cerebrospinalis or Pallio-spinalis).—The cell bodies of the neurones whose axones make up this system are situated in the cerebral cortex anterior to the fissure of Rolando (precentral area, Fig. 327). Their axones converge and pass downward through the internal capsule, pes pedunculi, pons, and medulla, sending off fibres to the efferent nuclei of the cranial nerves. In the medulla the tracts come to the surface as the anterior pyramids. At the junction of medulla and cord occurs what is known as the pyramidal decussation. Here most of the fibres of each tract cross to the opposite dorso-lateral region of the cord and continue downward as the crossed pyramidal tract. This lies in the dorsal part of the lateral column (Figs. 282 and 289). It extends to the lowermost part of the cord. In the cervical and dorsal regions it is separated from the surface of the cord by the direct cerebellar tract. In the lumbar region the latter tract is no longer present and the crossed pyramidal comes to the surface. The minority of the

fibres, instead of decussating, remain on the same side to pass down the cord along the anterior median fissure as the direct pyramidal tract, occupying a small oval area adjacent to the anterior sulcus (Fig. 280). It does not usually extend below the middle or lower dorsal region of the cord. As these tracts descend they decrease in size from loss of fibres which continually leave them to terminate in the ventral horns. The fibres of the crossed tract terminate mainly in the horn of the same side, while most of the fibres of the direct tract cross through the anterior commissure to the opposite side of the cord. These tracts are thus mainly crossed tracts, as the great majority of their fibres cross to the opposite side of the cord. There are, however, some homo-lateral (uncrossed) fibres in the lateral pyramidal tract. The tracts are apt to differ in size on the two sides of the cord, owing to the fact that the proportion of fibres which decussate is not constant. The axones terminate in arborizations around the motor cells of the ventral horns. The pyramidal tracts or pallio-spinal system together with the spinal efferent peripheral neurone system constitutes the pallio-spino-peripheral efferent conduction path. According to some authorities the pyramidal fibres terminate around cells in the intermediate gray matter whose axones in turn terminate around the efferent root cells. (Figs. 293 and 294.)

The pyramidal tracts convey to the cord the impulses which result in voluntary movements, especially, probably, individual movements of parts of the limbs (foot, hand, finger, etc.).

- II. The tecto-spinal tract originates in the midbrain roof, decussates and descends to the cord where it lies near the ventral sulcus. Its presence in the cord has been disputed. (Fig. 320.)
- III. Tract from the interstitial nucleus of Cajal (located in the reticular formation of the tegmentum of the midbrain cephalad to the nucleus of the III nerve). It is uncrossed and lies also near the ventral sulcus. Its fibres terminate in the ventral horn. Some fibres have been traced into the lumbar cord. (Figs. 289 and 320.)
- IV. The Rubro-spinal Tract (von Monakow's Tract).—This consists of axones of the red nucleus (nucleus ruber) located in the tegmentum of the midbrain. These axones cross and descend to the cord, being joined by axones of the other cells in the reticular forma-

<sup>&</sup>lt;sup>1</sup> The fibres in question have been variously stated to originate from the nucleus of Darkschewitsch, the nucleus of the posterior longitudinal fasciculus and the nucleus of the posterior commissure. Whether any of these nuclei is the same as the interstitial nucleus of Cajal, or the nucleus of van Gehuchten in fishes, is uncertain.

tion in the region of the pons. In the cord the tract lies mingled with and ventral to the lateral pyramidal tract. Its fibres terminate in the dorsal part of the ventral horn. This tract is a lower link in a three-neurone path from the cerebellum composed as follows: (a) Cells in cerebellar cortex to nucleus dentatus in cerebellum; (b) cells in dentatus via superior peduncle to the red nucleus; (c) rubro-spinal tract to (d) efferent peripheral neurones of cord. (Figs. 289, 294 and 308.)

V. Tract from Deiters' Nucleus (a terminal nucleus of the vestibular nerve in the medulla) or vestibulo-spinal tract.—This tract occupies the ventral and mesial periphery of the cord. The more lateral fibres are uncrossed, those near the ventral sulcus come from the nuclei of both sides. Descending with these fibres are probably axones of other vestibular nuclei, and of other nuclei in the gray reticular formation (reticulo-spinal fibres) of the medulla. These fibres all terminate in the ventral horn. Some fibres have been traced to the sacral cord. Deiters' nucleus receives fibres from the cerebellum, and thus this tract is a segment of a second efferent cerebellar pathway: (a) Cells in cerebellar cortex to nucleus fastigii in cerebellum; (b) cells of nucleus fastigii to Deiters' nucleus; (c) cells of Deiters' nucleus to (d) efferent peripheral neurones of cord. According to some authorities some fibres proceed from cerebellum to cord without interruption in Deiters' nucleus. (Figs. 289 and 294.)

All the fibres of V are sometimes collectively called the antero-lateral descending tract or marginal bundle of Löwenthal.

Tract III and the mesial part of V constitute the major portion of the descending fibres of an important bundle in the segmental brain known as the *medial longitudinal fasciculus*.

- VI. Fasciculus of Thomas.—Besides the reticulo-spinal fibres already mentioned are fibres in the lateral column which originate in the reticular formation of the medulla and terminate in the gray of the cervical cord. These are known as the tract of Thomas. (Fig. 289.)
- VII. Helweg's tract is a small triangular bundle of fibres lying along the ventro-lateral margin of the cord, and is traceable upward as far as the olives (Fig. 289). The origin and destination of its fibres are not definitely known.
- VIII. Septo-marginal Tract.—This is a small bundle of fibres lying next the posterior septum. It appears to change its location in different levels, e.g., in the sacral cord it occupies a small dorso-median triangle, in the lumbar region it forms an oval bundle (of Flechsig) at the middle of the septum and a superficial bundle, in the thoracic and

cervical cord its fibres are more scattered. It is probably composed of descending axones of cells in the cord. (Fig. 289).

IX. The so-called "comma" tract of Schultze is a small commashaped bundle of descending fibres lying about the middle of the posterior column (Fig. 289). It is most prominent in the dorsal cord. Its fibres are believed by some to be descending branches of spinal ganglion cells, by others to be descending axones from cells situated in the gray matter of the cord (column cells).

In general the descending tracts fall into two categories: (1) descending suprasegmental tracts which originate in the cortex of the pallium (Tract I), or of the midbrain (Tract II), and (2) descending intersegmental tracts. Of the latter some originate in nuclei lying in the segmental brain (interstitial nucleus of Cajal, nucleus ruber, nucleus of Deiters) which receive efferent suprasegmental fibres, and thus form links of descending suprasegmental paths. Other reticulo-spinal fibres come from other cells in the gray reticular formation. Other still shorter tracts (spino-spinal), from cells in the cord, form the descending fibres in the ground bundles (see below). Tracts VIII and possibly IX, are in this category.

Many tracts contain fibres proceeding in a direction opposite to that of most of the fibres.

## FUNDAMENTAL COLUMNS OR GROUND BUNDLES.

The ascending and descending tracts above described are known as the long-fibre tracts of the cord. If the area which these tracts occupy be subtracted from the total area of white matter, it is seen that a considerable area still remains unaccounted for. This area is especially large in the antero-lateral region, and extends up along the lateral side of the posterior horn between the latter and the crossed pyramidal tract (Figs. 282 and 289). A small area in the posterior column just dorsal to the posterior commissure, and extending up a short distance along the medial aspect of the horn, should also be included. These areas are occupied by the fundamental columns or short-fibre (spino-spinal or proprio-spinal) systems of the cord. The fibres serve as longitudinal commissural fibres to bring the different segments of the cord into communication (Fig. 292). The shorter fibres lie nearest the gray matter and link together adjacent segments. The longer fibres lie farther from the gray matter and continue through several segments. The origin of these fibres as axones of cells of the gray matter, and the manner in which they re-enter the gray matter as terminals and collaterals have been considered (pp. 398 and 399).

The fact, alluded to above, that the shorter fibres lie nearest, or mingled with the gray is, in a general way, true throughout the central nervous system. A result of this in the cord is the superficial position of many of the longest tracts.

Attention has already been called to the concept of neural arcs which may traverse the cord or both cord and suprasegmental structures (page 378).

It must be kept in mind that there are probably no *isolated* neural arcs and that every neural reaction involving any given arc always influences and is influenced by other parts of the nervous system.

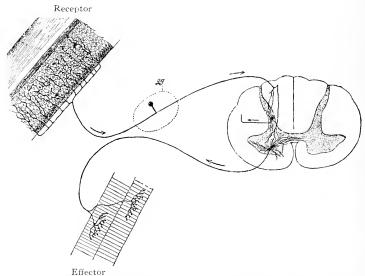


Fig. 201—Diagram illustrating a Two-neurone Spinal Reflex Arc. Groups of neurones are represented by one neurone. gg, Spinal ganglion. (Van Gehuchten).

From the neurones thus far studied and the tracts which their axones form, the following neural arcs may be constructed:

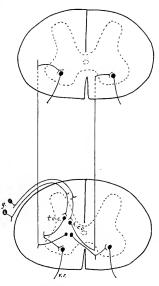
(1) A Two-neurone Spinal Reflex Arc (Fig. 291).—(a) Peripheral afferent neurones; their peripheral processes and receptor, the spinal ganglion cells, their central processes with collaterals terminating around motor cells of anterior horn; (b) peripheral efferent neurones, i.e., motor cells of anterior horn with axones passing to effector. Such a two-neurone reflex arc is chiefly uncrossed and in most cases involves only one segment or closely adjacent segments. As it involves only one synapsis (see chapter VI) (in the ventral gray) it is sometimes termed a monosynaptic arc.

(2) A Three-neurone Spinal Reflex Arc (Fig. 292).—(a) Peripheral afferent neurones as in (1), but terminating around column cells of the cord. (b) Cord neurones (column cells)—axones in the fundamental columns with collaterals and terminals to anterior horn cells of different levels. (c) Peripheral efferent neurones as in the two-neurone reflex.

Such a three-neurone or disynaptic reflex arc may involve segments above or below the segment of entrance of the stimulus and is uncrossed or crossed according as the cord neurones are tautomeric heteromeric.

The independence of the cord as a reflex mechanism is much diminished in man.

(3) A cerebellar Arc may be constituted as follows: (a) Peripheral afferent neurones to (b) column cells in cord (e.g., Clarke's column) via spino-cerebellar tracts to cerebellar cortex; (c) various associative cortical neurones; (d) axones of cortical cells to (e) dentate nucleus the axones of which (superior peduncle) pass to (f) nucleus ruber via rubro-spinal tract to (g) efferent Fig. 202.—Diagram illustrating peripheral neurones in cord. Another arc would consist of (a), (b) and (c) the same, (d) cerebellar cortex to nucleus fastigii in cerebellum to (e) nucleus of Deiters to (f) efferent peripheral neurones to effector (Figs. 294 and 308).



Three-neurone Spinal Reflex Arcs of one segment and more than one segment. Groups of neurones are represented by one neurone. g, Spinal ganglion cells: h.c.c., heteromeric column cell; t.c.c., tautomeric column cell; v.r., ventral root.

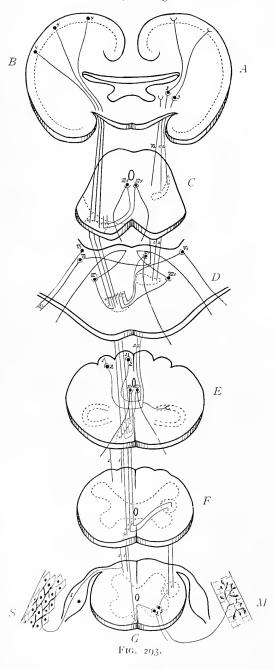
(4) A Cerebral or Pallial Arc: (a) Peripheral afferent neurones, via long ascending arms to (b) nucleus gracilis or cuneatus, thence as medial lemniscus to (c) thalamus to cortex pallii; (d) associative neurones of cortex; (e) cortical precentral neurones via pyramid to (f) efferent peripheral neurones to effector. Another arc would involve the spino-thalamic tract instead of the lemniscus. (Figs. 203 and 204.)

Similar arcs may include efferent sympathetic neurones.

#### TECHNIC.

(1) Carefully remove the cord (human if possible; if not, that of a large dog) with its membranes, cut into two or three pieces if necessary, and lay on sheet cork. Slit the dura along one side of the cord, lay the folds back, and pin the

dura to the cork. Care must be taken to leave the dura very loose, otherwise it will flatten the cord as it shrinks in hardening. With a sharp razor now cut the cord, but not the dura, into segments about 1 cm. thick. Fix in Orth's fluid (p. 7).



Pieces of the cord may be cut out as wanted and embedded in celloidin. Sections should be cut about  $15\mu$  in thickness.

(2) For the study of the general internal structure of the cord, stain a section through the lumbar enlargement of a cord prepared according to the preceding technic (1) in hæmatoxylinpicro-acid-fuchsin (technic 3, p. 19) and another section through the same level in Weigert's hæmatoxylin (technic p. Mount 29). both in balsam. For Weigert staining, material fixed in formalin or in Orth's fluid should be further hardened in Müller's fluid for at least a month, changing the fluid frequently at first to remove the formalin. Mallory's glia stain should also be used with material fixed in Zenker's fluid (technic, p. 27). The silver method of Cajal (alcohol-fixation) should also be used (technic, p. 34) and that of Nissl.

(3) From a cord prepared according to technic 1, remove small segments from each of the following levels:
(1) the twelfth dorsal, (2) the mid-dorsal, and (3) the cervical enlargement. The segments are embedded in celloidin, sections cut 15 to 20 \mu thick, stained by Weigert's method (page 29), and mounted in

balsam. Medullated sheaths alone are stained by this method and appear dark blue or black.

- (4) A human cord from a case in which death has occurred some time after fracture of the vertebræ with resulting crushing of the cord, furnishes valuable but of course rarely available material. If death occur within a few weeks after the injury, the method of Marchi should be used; if after several weeks, the method of Weigert (page 29). The picture in the cord is dependent upon the fact that axones cut off from their cells of origin degenerate and disappear. After a complete transverse lesion of the cord, therefore, all ascending tracts are found degenerated above the lesion, all descending tracts below the lesion. The method of Marchi gives a positive picture of osmic-acid-stained degenerated myelin in the affected tracts. The method of Weigert gives a negative picture, the neuroglia tissue which has replaced the degenerated tracts being unstained in contrast with the normal tracts, the myelin sheaths of whose fibers stain, as usual, dark blue or black.
- (5) Human cords from cases which have lived some time after the destruction of the motor cortex, or after interruption of the motor tract in any part of its course, may also be used for studying the descending fibre tracts.
- (6) The cord of an animal may be cut or crushed, the animal kept alive for from two weeks to several months, and the cord then treated as in technic (4). The most satisfactory animal material may be obtained from a large dog by cutting the cord half-way across, the danger of too early death from shock or complications being much less than after complete section.

Fig. 293.—Diagram showing the Most Important Direct Paths which an Impulse follows in passing from a Receptor (S) to the Cerebral Cortex and from the latter back to an Effector (M) (e.g., muscle), also some of the cranial-nerve connections with the cerebral cortex. Groups of neurones are represented by one or several individual neurones. A, Sensory cortex: B, motor cortex: C, level of third nerve nucleus; D, level of sixth and seventh nerve nuclei; E, level of sensory decussation; F, level of pyramidal decussation; G, spinal cord.

#### From Periphery to Cortex.

Neurone No. 1.—The Peripheral afferent Neurone: 1, Spinal, cell bodies in spinal ganglia; receptor, S, peripheral arm of spinal ganglion cell; central arm of spinal ganglion cell as fibre of dorsal root to column of Goll or of Burdach, thence to nucleus of one of these columns in the medulla.  $V_1$ , Cranial (example, fifth cranial nerve, trigeminus; cell bodies in Gasserian ganglion); receptor; peripheral arm of Gasserian ganglion cell; central arm of Gasserian ganglion cell to medulla as afferent root of fifth nerve, thence to terminal nuclei in medulla.

Neurone No. 2.—2, Spinal connection—cell body in nucleus of Goll or of Burdach; axone passing as fibre of fillet to thalamus.  $V_2$ , Cranial nerve connection (trigeminal), cell body in one of trigeminal nuclei in medulla, axone as fibre of secondary trigeminal tract to thalamus

Neurone No. 3.—3, Cell body in thalamus, axone passing through internal capsule to termination in cortex. (Various association neurones in cortex omitted.)

#### From Cortex to Periphery.

Neurone No. 4.—4, Cell body in motor cerebral cortex; axone through internal capsule and pes to (a) motor nuclei of cranial nerves, (b) by means of pyramidal tracts to ventral gray of spinal cord.

Neurone No. 5.—5, Spinal, cell body in ventral gray of cord; axone as motor fibre of ventral root through mixed spinal nerve to effector (muscle).

Neurone No. 5.—Cranial—V<sub>5</sub>, Cell body in motor nucleus of trigeminus; axone passing to muscle as motor fibre of fifth nerve.

 $III_5$ , Peripheral efferent neurone of third nerve—oculomotor.  $VI_5$ , Peripheral efferent neurone of sixth nerve—abducens.  $VII_5$ , Peripheral efferent neurone of seventh nerve—facial.  $XII_5$ , Peripheral efferent neurone of twelfth nerve—hypoglossal.

- (7) The cord of a human feetus from the sixth month to term furnishes good material for the study of the anterior and posterior root fibres, the plexus of fine fibres in the gray matter, the groupings of the anterior horn cells, etc. The pyramidal tracts are at this age non-medullated and are consequently unstained in Weigert preparations. The Weigert-Pal method gives the best results.
- (8) For the study of the course of the posterior root fibres within the cord, cut any desired number of posterior roots between the ganglia and the cord and treat material by the Marchi or the Weigert method, according to the time elapsed between the operation and the death of the animal.

## BRAIN.

## General Structure.

The principal peculiarities of the brain as distinguished from the cord depend upon two factors: certain peculiarities of the receptors and effectors of the head and the development of higher coördinating apparatus in the central nervous system of the head.

Besides the receptors of the general senses (p. 390), there are in the head the highly specialized receptors of smell, sight, hearing and position (semi-circular canals), which are respectively concentrated into certain localities and form, together with certain accessory structures, the organs known as the nose, eye and ear. Each of these groups of receptors has its own special connection with the brain (nerves I, II and VIII) and its own paths within the latter (see below). The special receptors of taste show a less degree of aggregation into an organ and, together with other visceral receptors, are innervated by afferent portions of a group of nerves (VII, IX and X) which have a common continuation within the brain. The remaining somatic receptors of the general senses, scattered over the anterior part of the head, are innervated by one nerve (V) having its own central continuations. The striated voluntary muscles of the head fall into four groups; those of the eye, of the mouth, of the face, pharynx and larynx (modified branchial musculature) and of the tongue. The oral and branchial musculatures are usually regarded as visceral and those of the eye and tongue as somatic, a distinction shown by differences of grouping in the brain of their efferent peripheral neurones. The nose and ear have practically no voluntary motor apparatus.

The higher coördinating apparatus or suprasegmental structures (p. 377) of the brain are essentially expansions of the dorsal walls of parts of the brain having manifold connections with the rest of the nervous system which are complexly interrelated by enormous num-

bers of association neurones. The presence of these latter has probably necessitated the extensive layers of externally placed neurone bodies (cortex) characteristic of suprasegmental structures.

The structure of the basal part of the brain, connected with the cranial nerves (segmental brain, p. 377), is affected by both the peculiarities of peripheral structures mentioned above and by the presence of bundles of fibres and masses of gray forming portions of paths to and from suprasegmental structures (see below).

The following summary embodies the resulting general structural features of the brain:

## SEGMENTAL BRAIN AND NERVES.

Afferent Peripheral (Segmental) Neurones.—(I) Visceral group comprising nerves VII (geniculate ganglion), IX (superior and petrosal ganglia) and X (jugular and nodose ganglia). The nerves of taste probably belong entirely to this group. The peripheral arms of these ganglia innervate visceral receptors and the central arms form a descending tract in the medulla, the fasciculus solitarius which has its terminal nucleus giving rise to secondary tracts.

- (2) General Somatic Group (common sensibility).—Semilunar ganglion of V. Peripheral arms to skin of anterior part of head, to mouth and probably to muscle tendon receptors. Central arms form descending tract in medulla, the radix spinalis V. Terminal nucleus the continuation in medulla of dorsal horn. Secondary tract to thalamus and thence to cortex cerebri.
- (3) Semicircular Canal Group.—Ganglion of Scarpa of VIII. Peripheral arms to semicircular canals. Central arms constituting vestibular portion of VIII, forming descending tracts in medulla and terminating in several vestibular terminal nuclei (including Deiters).
- (4) Acoustic Group.—Ganglion spirale of VIII. Peripheral arms to cochlea. Central arms forming cochlear part of VIII and terminating in medulla in various nuclei with secondary tract (lateral fillet) to midbrain. Thence by third system of neurones to medial geniculate body and by fourth system of neurones to cortex cerebri.
- (5) Visual Group.—Ganglion in retina. Second neurone system beginning in retina and forming the optic tract (optic "nerve") to lateral geniculate body and by third neurone system to cortex cerebri.
- (6) Olfactory Group.—"Ganglion" cells in olfactory mucous membrane forming olfactory nerve (fila olfactoria). Secondary tracts

from olfactory bulb (and tertiary tracts) to parts of diencephalon and hippocampus.

Efferent Peripheral (Segmental) Neurones.—(1) Visceral.—(a) Bodies more laterally placed in gray matter of hindbrain. Axones to striated voluntary muscles of jaw (V), face (VII), pharynx and larynx (IX and X). (b) Bodies more deeply placed in gray of mid- and hindbrain. Axones to glands, smooth and heart muscle, either directly or via sympathetic ganglia of head and body.

- (2) Somatic.—Bodies located near median line in gray matter of hindbrain (XII and VI), and midbrain (IV and III), to muscles of tongue (XII) and eye (VI, IV and III). Nerve III also contains neurones whose axones pass to sympathetic ganglia (ciliary).
- (3) Sympathetic.—Bodies compose the sympathetic ganglia of the head (ciliary, sphenopalatine, submaxillary and otic). These ganglia are connected with afferent and efferent portions of cranial nerves (III, V, VII, IX and X), in a manner similar to the connections between sympathetic ganglia of body and spinal nerves. They are also connected with sympathetic fibres from the body.

Intersegmental Neurones.—These are represented principally by the gray reticular formation of the hindbrain and midbrain and long descending tracts external to it. The gray reticular formation is composed of neurone bodies and short intersegmental tracts intermingled. Among the former are certain well differentiated nuclei (e.g., nucleus ruber, nucleus of Deiters and interstitial nucleus of Cajal) the axones of which form long, principally descending, intersegmental tracts external to the gray reticular formation. Other cells in the gray reticular formation form the shorter tracts within it. The reticular formation may also contain the motor nuclei of the cranial nerves and is traversed by various fibers passing to tracts and by terminals from tracts.

Afferent and Efferent Suprasegmental Paths.—The afferent paths consist of the ascending tracts and nuclei already mentioned (spino-cerebellar, nuclei gracilis and cuneatus and medial lemniscus, terminal nuclei of the afferent cranial nerves and their secondary tracts and further continuations). The tracts occupy, in general, positions external to the reticular formation and long intersegmental tracts. The efferent suprasegmental paths consist either of descending suprasegmental tracts which proceed without interruption to the efferent peripheral neurones, or of descending suprasegmental and short or long intersegmental tracts in whose nuclei the suprasegmental

tracts terminate and which in turn terminate around the efferent peripheral neurones. The large descending tracts from the pallium markedly affect the configuration of the brain. There are two such principal descending pallial paths; one to the nuclei of the pons Varolii and thence across to the opposite cerebellar hemisphere and one continuing down to the medulla and cord as the pyramids. These two paths are added ventrally to the segmental and intersegmenta-apparatus and form the pes pedunculi (added ventrally to the tegmenl tum of the midbrain), the pons Varolii (ventral to the tegmentum of part of the midbrain, to the isthmus and part of the hindbrain) and the pyramids (ventral to the hindbrain).

## SUPRASEGMENTAL STRUCTURES.

These are the pallium or cerebral hemispheres, the corpora quadrigemina and the cerebelium. They consist essentially of the endings and beginnings of their respective afferent and efferent paths and of their own association neurones, the bodies of which lie in their respective cortices.

The corpora quadrigemina are relatively of much less importance in the human brain.

In accordance with the above there are usually to be distinguished in transverse sections of the brain at various levels the following:

- A. Peripheral (segmental) neurones. (1) Efferent ("motor" nuclei and root fibres).
- (2) Central continuations of afferent neurones (afferent roots). (a) Those entering at and therefore belonging to the segment involved.
- (b) Those entering above or below the segment and represented in the segment by descending or ascending (overlapping) tracts.
- B. Terminal nuclei of (2) and the secondary tracts originating from them. These may fall under category C or D (below).
- C. Intersegmental nuclei and tracts of the segmental brain, consisting principally of the gray reticular formation and long descending tracts (arrangement much modified in forebrain).
- D. Nuclei and tracts forming afferent and efferent suprasegmental paths.
  - E. Suprasegmental structures (not present in many transections).

The afferent paths include some of the nuclei and tracts under B, and their continuations, and the efferent include some of the longer systems under C, together with efferent suprasegmental tracts to them.

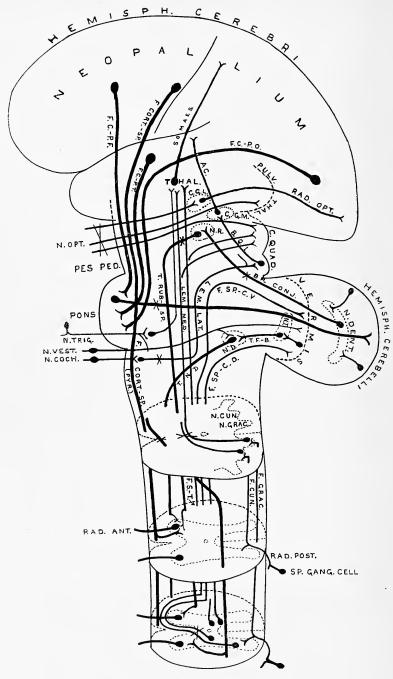


FIG. 294.

The general histology of the brain is similar to that of the cord. The largest nerve-cells (large cells of efferent or motor nuclei, cells in motor cerebral cortex and certain cells in the reticular formation) usually present a chromophilic substance similar in arrangement, etc.. to the efferent nerve cells of the cord. The Purkinje cells, however, differ from these (see cerebellum). The chromophilic substance of medium and small cells presents an appearance in general similar to corresponding cells of the cord. Many minor differences may, however, obtain between various neurone groups. The neuroglia cells and fibres also present the same general characteristics as those in the cord, with variations peculiar to certain localities (e.g., parts of the cerebellum).

## Hindbrain or Rhombencephalon.

This includes the medulla, cerebellum, and part of the tegmentum and pons. Its peripheral nerves are the V, VI, VII, VIII, IX, X, and XII. <sup>1</sup>

The *medulla oblongata* or *bulb* is the continuation upward of the spinal cord and extends from the lower limit of the pyramidal decussation below to the lower margin of the pons above.<sup>2</sup>

Fig. 294.—Principal afferent and efferent suprasegmental pathways (excepting the rhinopallial connections, the efferent connections of the midbrain roof and the olivo-cerebellar connections). Efferent peripheral neurones of cranial nerves are omitted. Each neurone group (nucleus and fasciculus) is indicated by one or several individual neurones. Decussations of tracts are indicated by an X. ac, Acoustic radiation, from medial geniculate body to temporal lobe; br. conj, brachium conjunctivum (superior cerebellar peduncle): brachium pontis, from pons to cerebellum (not labeled); b.q.i, brachium quadrigeminum inferius; c.g.l, lateral or external geniculate body; c.g.m, medial or internal geniculate body; c.quad, corpora quadrigemina; f.cort.-sp, cortico-spinal fasciculus (pyramidal tract): f. c.-p.f, frontal cortico-pontile fasciculus (from frontal lobe); f.c.-p.t, temporal corticopontile fasciculus (from temporal lobe); f.c.-p.o, occipital cortico-pontile fasciculus (from occipital lobe); f.cun, fasciculus cuneatus (column of Burdach); t.f.-b, fastigio-bulbar tract; f.grac, fasciculus gracilis (column of Goll); f.s.-t, spino-thalamic fasciculus; f.sp.-c.d. dorsal spino-cerebellar fasciculus (tract of Flechsig); f.sp.-c.v, ventral spino-cerebellar fasciculus; lem. lat, lateral lemniscus or lateral fillet: lem. med, medial lemniscus or fillet: n.coch, cochlear nerve; n.cun. (terminal) nucleus of the column of Burdach: n.d, nucleus of Deiters; *n.dent*, nucleus dentatus; *n.grac*, nucleus of the column of Goll; *n.opt*, optic nerve; *n.r.*, nucleus ruber; *n.t.*, nucleus tecti (or fastigii); *n.trig*, trigeminal nerve; *n.v.est*. vestibular nerve; pes. ped, pes pedunculi (crusta); pulv. thal, pulvinar thalami; pyr, pyramid; rad. ant, ventral spinal root; rad. post, dorsal spinal root; rad. opt, optic radiation (from lateral geniculate body to calcarine region); somæs, bundles from thalamus to postcentral region of neopallium; sp. gang, spinal ganglion; t.f.-b., tractus fastigio-bulbaris; thal. thalamus; t.n.d, tract from the nucleus of Deiters; t. rub.-sp, rubro-spinal tract (von Monakow). (Lateral view of brain.)

<sup>&</sup>lt;sup>1</sup> It is better probably to reckon the so-called medullary part of the XI with the X.
<sup>2</sup> It would be better to include in the term medulla oblongata what here falls under pontile tegmentum of the hindbrain.

Externally, the medulla shows the continuation upward of the anterior fissure and posterior septum of the cord. On either side of the anterior fissure is a prominence caused by the anterior pyramid, and to the outer side of the pyramid the bulging of the olivary body may be seen. The antero-lateral surface of the medulla is also marked by the exit of the fifth to the twelfth (inclusive) cranial nerves. The posterior surface shows two prominences on either side. The more median of these, known as the clava, is caused by the nucleus

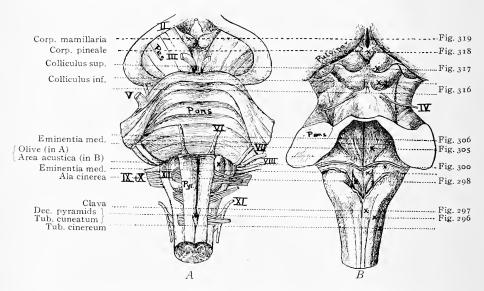


Fig. 295.—Ventral (A) and dorsal (B) views of part of Brain Stem (cerebellum removed). Structures named at the left are indicated by their reference lines running to an X. On the right are named the figures showing transverse sections through the brain at the levels indicated by the reference lines. The level for Fig. 319 is not accurately indicated.

gracilis, or nucleus of the column of Goll; the other, lying just to the outer side of the clava, is due to the nucleus cuneatus or nucleus of the column of Burdach. Lateral to this is a third eminence, the tuberculum cinereum, due in part to the descending root of the V, merging anteriorly with the eminence of the restiform body. The central canal of the cord continues into the medulla, where it gradually approaches the dorsal surface and opens into the cavity of the fourth ventricle. The floor of the fourth ventricle exhibits a medial eminence occupied caudally by the nucleus hypoglossi. Lateral to this is a triangular area, the ala cinerea, surrounded by furrows. This is partly occupied by nuclei of the vagus. Forward and laterally a broader

triangular area with an angle directed into the lateral recess marks the area occupied by the nuclei of the acoustic nerve. Still further forward near the median line are eminences indicating the positions of the nucleus abducentis and genu facialis. The roof of the fourth ventricle is formed by the thin plexus chorioideus and the cerebellum. (Fig. 295.)

The *pons* is a mass of fibres and gray matter extending across the ventral surface of portions of mid- and hindbrain. The term is often used to include the whole of the basal part of the brain thus covered by the pons. It is better, however, to restrict it to the pons itself. The part of the hindbrain dorsal to the pons, which is the continuation forward of the medulla, may be included in the term *tegmentum* of the hindbrain.

The cerebellum is described on p. 455.

#### TECHNIC.

The technic of the medulla (and the rest of the segmental brain) is the same as that of the cord (page 421). Transverse sections should be cut through the following typical levels, stained by Weigert's method (page 29), and mounted in balsam:

- 1. Through the pyramidal decussation.
- 2. Through the sensory decussation.
- 3. Through the lower part of the olivary nucleus.
- 4. Through the middle of the olivary nucleus.
- 5. Through the entrance of the cochlear nerve.
- 6. Through the entrance of the vestibular nerve.
- 7. Through the roots of the sixth and seventh cranial nerves.
- 8. Through the root of the fifth cranial nerve.

The methods of Nissl, Cajal and glia stains should also be used when practicable.

#### PRACTICAL STUDY.

## Transverse Section of the Medulla through the Decussation of the Pyramidal Tracts (Motor Decussation) (Figs. 205 and 206).

The most conspicuous features of this section are the decussation of the pyramids, the larger size of the dorsal horn and the beginning of the gray reticular formation. Surrounding the central canal is the *central gray*.

Efferent Peripheral Neurones.—Nuclei of first cervical spinal nerve in ventral gray, and root fibres passing out to emerge on ventral aspect. Nuclei of XI, in mesial position in central gray, or in ventral gray. Axones pass out laterally from latter and emerge on the lateral surface. The mesial or deep nuclei are best reckoned with nerve X.

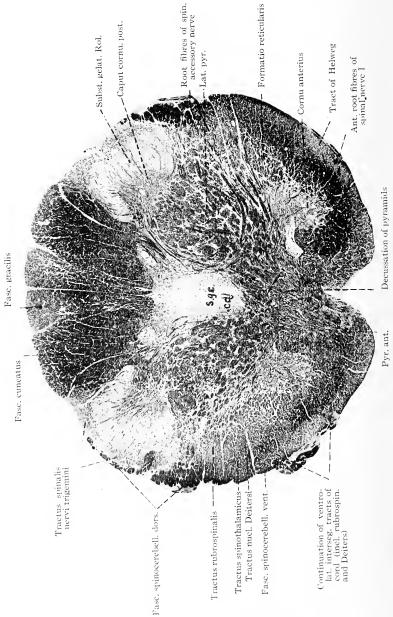


Fig. 296.—Transverse Section of the Medulla of a Five Weeks' Infant through the Decussation of the Pyramidal Tracts. Photograph. Weigert preparation. c.c., central canal; s.g.c., central gelatinous substance. (X 14).

Afferent Roots, their Terminal Nuclei and Secondary Tracts.—Some afferent fibres of the first cervical spinal nerve are still entering at this level.

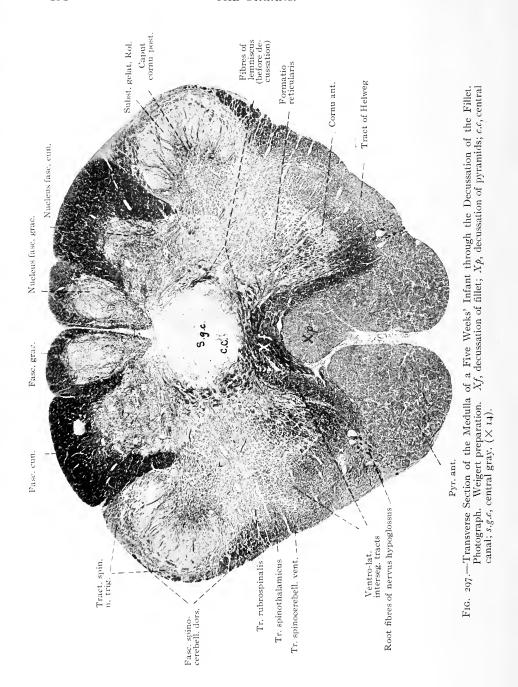
Ascending afferent roots: The dorsal funiculus comprising the fasciculus cuneatus and fasciculus gracilis remain as in the cord. Collaterals and terminals from them can be seen entering the subjacent gray.

Descending afferent roots: Some of the fine fibres between the enlarged dorsal horn and the periphery, occupying the position of the zone of Lissauer in the cord, are descending afferent root fibers of the V-cranial nerve or tractus spinalis trigemini (spinal V). Collaterals and terminals from these fibres terminate in the gelatinous substance of Rolando and also traverse it to form a plexus of medullated fibres in its inner side very similar to the cord. The axones of the dorsal horn cells (or terminal nucleus of the V) form the secondary tracts of the V, which cannot be distinguished (p. 452 and Fig. 307).

Secondary tracts, forming parts of afferent suprasegmental paths: These form a mass of fibres along the lateral periphery of the medulla which consists of (a) the dorsal spino-cerebellar, (b) the ventral spino-cerebellar and (c) the spino-thalamic tracts.

Intersegmental Neurones.—The neurone bodies are, as in the cord, scattered throughout the gray. The continuation of the ventro-lateral intersegmental tracts of the cord (and the tecto-spinal tract) is the U-shaped mass of fibres around the ventral gray. This mass consists of the long descending, the shorter ascending and descending intersegmental tracts, and the tecto-spinal; *i.e.*, (a) rubro-spinal (in lateral arm of U), (b) vestibulo-spinal (lateral and mesial), (c) tract from interstitial nucleus of Cajal (mesial), (d) tecto-spinal (mesial), (e) shorter descending and ascending tracts which may be regarded as the equivalent of the ground bundles of the cord comprising shorter reticulo-spinal and spino-reticular fibres. The shortest of these fibres, which in the cord were next the lateral gray, are now mingled with the gray, the combination constituting the gray reticular formation. Other short intersegmental tracts lie in and adjoining the dorsal horn, as in the cord.

Descending suprasegmental paths include certain of the long descending intersegmental tracts as previously explained. Besides these there are efferent suprasegmental neurones known as the pallio-spinal or pyramidal tracts and the tecto-spinal tracts. Bundles of fibres are seen crossing (pyramidal decussation) from the anterior pyramid of one side to the opposite dorso-lateral column, where they turn downward as the crossed pyramidal tract. In their passage through the gray matter, they cut off the ventral horn from the rest of the gray matter. These fibres, as already noted in the cord, are descending axones from motor cells situated in the precentral cerebral cortex. In the pyramidal decussation most of these fibres cross to the opposite dorso-lateral region to pass down the cord as the crossed pyramidal tract (p. 416, and Fig. 289; Fig. 293, F). A few remain in their original anterior position to continue down the cord as the direct pyramidal tract (p. 417, and Fig. 289; Fig. 293, F). A few pass to the ventral tract in the same side, thus being uncrossed fibres in the lateral tract. The bundles of fibres do not cross in a transverse plane, but take a downward direction at the same time. For this reason transverse sections show these fibres cut rather obliquely. Because of the fact that the fibres cross in alternate bundles, the number of decussating fibres seen in any one section is greater on one side than on the other (Fig. 205).



# 2. Transverse Section of the Medulla through the Decussation of the Fillet or Lemniscus (Sensory Decussation) (Figs. 295 and 297).

The most conspicuous features are the appearance of the nuclei cuneatus and gracilis, the decussation and formation of the medial lemniscus or fillet, and the increase of the gray reticular formation.

**Peripheral Efferent Neurones.**—In the lateral part of the central gray is the dorsal nucleus of the X (nucleus alæ cinereæ). In the ventral part of the central gray is the nucleus hypoglossi and, passing ventrally and emerging lateral to the pyramids, may be seen the axones of its cells—the root fibres of the XII.

In the nucleus XII can be distinguished (Weigert stain) coarse fibres which are the root fibres, and fine fibres which are terminals of other fibres ending in the nucleus. Among these have been distinguished collaterals from secondary vagoglossopharyngeal and trigeminal tracts (three-neurone reflex). Whether pyramidal fibres reach the nucleus directly or *via* intercalated neurones is uncertain.

Afferent Roots, their Terminal Nuclei and Secondary Tracts.—Entering afferent root fibres are usually not present.

The funiculi or fasciculi cuneatus and gracilis have diminished, and internal to them have appeared large masses of gray. These are the nuclei of the columns, and are known, respectively, as the nucleus of the column of Goll or the nucleus gracilis, and the nucleus of the column of Burdach or the nucleus cuneatus. In the higher sensory decussation levels there is usually an accessory cuneate nucleus.

These nuclei serve as nuclei of termination for the fibres of the posterior funiculi. Their termination in these nuclei is the ending of that system of fibres which has been traced upward from their origin in the cells of the spinal ganglia; the completion of the course of the spinal peripheral afferent neurones. As the fibres of the posterior columns are constantly terminating in these nuclei, there is, in passing from below upward, a constant increase in the size of the nuclei and a corresponding decrease in the size of the posterior columns, until, just below the olive, the whole of the column of Goll and most of the column of Burdach are replaced by their respective nuclei. (Pp. 413, 414.)

Study the plexus of fine fibres in these nuclei, formed by the terminals of the column fibres, also the coarser fibres (axones of the cells of the nuclei) gathered in the ventral part of the nuclei, whence they emerge and curve<sup>1</sup> around the central gray, cross to the opposite side ventral to it and dorsal to the pyramids, and then turn brainward forming the bundle of fibres known as the *medial lemniscus* or *fillet*.

The spinal V has increased and also its terminal nucleus, the dorsal horn. The spino-cerebellar and spino-thalamic tracts occupy about the same positions.

In the central gray dorsal to the central canal is a nucleus representing a union of the caudal ends of the terminal nuclei of the fasciculi solitarii (see next section)—the *nucleus commissuralis*. Fibres of the fasciculi solitarii also decussate here.

Intersegmental Neurones.—The rubro-spinal tract, tracts from Deiters' nucleus and interstitial nucleus of Cajal occupy about the same positions. The

<sup>&</sup>lt;sup>1</sup>Fibres having a transverse curved or arched course are in general termed arcuate fibres. If they are deeply located, they are internal arcuate fibres, if near the periphery, they are superficial or external arcuate fibres. Obviously the same fibre may be, in different parts of its course, internal arcuate, external arcuate, and longitudinal.

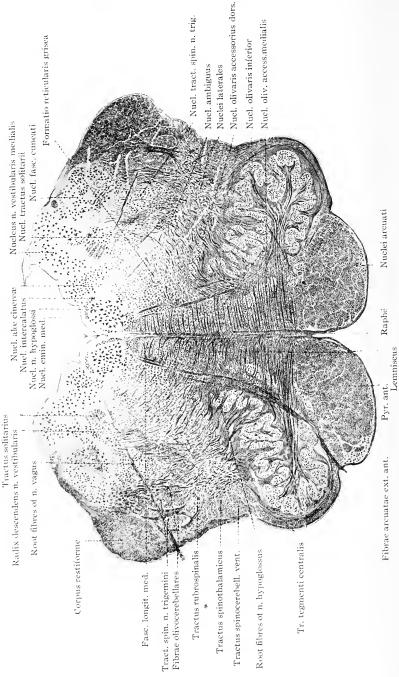


Fig. 298.—Transverse Section of the Medulla through the Lower Middle Part of the Inferior Olivary Nucleus. Weigert preparation. (Rauber-Kopsch.) The arrow indicates the median sulcus of the rhomboid fossa.

reticular formation has increased, the whole of the ventral horn and intermediate gray containing bundles of longitudinal fibres. The formation is also traversed by transverse fibres, representing the beginnings or terminations of various longitudinal fibres.

Efferent Suprasegmental Neurones.—The decussation of the pyramids has now nearly or entirely ceased. The lateral pyramidal tracts are no longer in the lateral columns but are part of the anterior pyramidal tract which forms two large masses of fibres on each side of the ventral sulcus. The tecto-spinal tract occupies the same position.

## Transverse Section of the Medulla through the Lower Part of the Inferior Olivary Nucleus (Figs. 295 and 298).

The central canal has opened into the *fourth ventricle*, the central gray (including the central gelatinous substance) now being spread out on its floor. The roof

of the ventricle is formed by its *chorioid plexus*. The most conspicuous new feature is the *olive*.

## Efferent Peripheral Neurones.

—The nucleus of the XII is large and occupies a swelling in the floor of the ventricle each side of the median line, known as the "eminentia" hypoglossi. The root fibres of the XII pass lateral to the medial lemniscus, between the olive and pyramid, and then emerge at the groove between olive and pyramid.

The dorsal nucleus of the X occupies a swelling lateral to the preceding and known as the ala cinerea. Some of the root fibres of the X are axones from this nucleus. They probably innervate (via the sympathetic) some, at least, of the smooth muscles, heart and glands, innervated by the vagus (X).

The bodies of another group of peripheral efferent neurones form the *nucleus ambiguus*, often difficult to distinguish, in the reticular g. f.s.n. d.n.x
f.s. d.n.x
n.amb
n.amb
pyr.

Fig. 290.—Diagram of Origin of Cranial Nerves X and XII. (Schäfer.) pyr, Pyramid: o, olivary nucleus; r, restiform body; d. V., spinal root of fifth nerve; n.XII, nucleus of hypoglossal; XII, hypoglossal nerve; d.n.X.XI, dorsal nucleus of vagus; n.amb, nucleus ambiguus; f.s., solitary fasciculus (descending root of vagus and glossopharyngeal); f.s.n, nucleus of solitary fasciculus; X, motor fibre of vagus from nucleus ambiguus; g, ganglion cell of sensory root of vagus sending central arm into solitary fasciculus (f.s.) and collateral to its nucleus (f.s.n.); f.s.n, cell of nucleus of solitary fasciculus sending axone as internal arcuate fibre to opposite side of cord (secondary vagus and glosso-pharyngeal tract.) This course of the secondary tract is doubtful.

formation. Their axones pass obliquely, dorsally and mesially, join the other root fibres of the X, and then bending abruptly, pass with them to the lateral surface of the medulla. Some of them probably innervate the striated muscles of the larynx. (Fig. 290).

Afferent Peripheral Roots, their Terminal Nuclei and Secondary Tracts.—Other root fibres are the afferent fibres of the X which form a common root with the preceding. Sometimes they can be seen joining the fasciculus solitarius of which they form a part. Some fibres or collaterals may enter the adjacent gray (terminal nucleus of the X) (see page 437, Fig. 299).

If the roots of the X do not show well in the section, defer their study until the following section where the IX shows similar relations.

The spinal V is partly pierced and partly covered by transverse fibres, principally olivo-cerebellar fibres (see below). Its terminal nucleus is less conspicuous. Two new bundles of descending root fibers have appeared; one is the fasciculus solitarius composed of the afferent root fibres of the X, IX (including gustatory fibres), and, higher up, of the VII. A small mass of gray of a gelatinous appearance near it is its terminal nucleus. The course of the secondary tract cannot be made out and is not accurately known. The other bundle is the descending vestibular root. It lies lateral to the fasciculus solitarius. Accompanying it are cells which constitute its terminal nucleus. Occupying the floor of the ventricle lateral to the dorsal nucleus of the X is another terminal nucleus of the vestibular nerve, the nucleus medialis (triangular or chief nucleus). Internal arcuate fibres emerging from these regions may represent secondary tracts (probably reflex) from these nuclei. (P. 441; Fig. 302.)

The nucleus gracilis has disappeared. The nucleus cuneatus may be present, much diminished, and give rise to some internal arcuate fibres to the medial lemniscus. The lemniscus is now a tract which has become built up on each side of the median line. This latter is known as the raphé (*i.e.*, "seam," stitched by the decussating fibres).

The ventral spino-cerebellar tract and spino-thalamic tract are in about the same lateral position, but the dorsal spino-cerebellar tract has moved dorsally and together with olivo-cerebellar fibres (see below) begins to form the *restiform body* (see below).

In the lateral part of the reticular formation, between spinal V and olive are seen the *nuclei laterales*. In these nuclei some of the spino-cerebellar fibres end. The axones of these nuclei partly enter the restiform body on the same side and partly cross to the opposite restiform body (p. 455; Fig. 308). They form some of the *ventral external arcuate fibres* seen in the section. The lateral nuclei are thus partial interruptions in the spino-cerebellar path. The *nuclei arcuati* are well marked.

Other Afferent Cerebellar Neurones.—A new and important convoluted mass of gray is the *inferior olivary nucleus*, forming a bulging in the lateral surface of the medulla known as the olive. Near it are the *dorsal* and *medial accessory olives*. The axones of the olivary cells are the *olivo-cerebellar fibres*. They cross through the fillets, pass through or around the opposite olivary nucleus, thence proceed dorsolaterally, being gathered into more compact bundles, traverse or surround the spinal V and dorsal to it bend longitudinally, forming a great part of the restiform body. The latter produces an eminence on the dorso-lateral surface of the medulla. The restiform body, thus formed by these spino-cerebellar and olivo-cerebellar fibres, together with certain others, passes into the cerebellum higher up, forming the major part of the inferior cerebellar arm or peduncle. (Comp. p. 455.)

Fibres appearing on the external surface of the olivary nucleus are the termina-

tion of a large tract descending to the olivary nucleus, the *central tegmental tract*. Its origin in higher levels is not accurately known, but is possibly the nucleus lenticularis of the endbrain.

**Intersegmental Neurones.**—The reticular formation is now still more extensive.

The original U-shaped mass of intersegmental tracts (and the tecto-spinal tract) has now become widely separated into two parts. The lateral part consisting principally of the rubro-spinal tract and uncrossed fibres from Deiters' nucleus lies mesial to, or partly mingled with, the spino-thalamic and ventral spino-cerebellar tracts. The mesial part of the U, consisting principally of crossed and uncrossed fibres from Deiters' nucleus and other nuclei in the reticular formation, and of fibres from the interstitial nucleus of Cajal, now forms the medial longitudinal fasciculus dorsal to the fillet. Near this bundle or united with it, is the tecto-spinal tract (predorsal tract). When these tracts have passed down to below the formation of the fillet and the olives, they assume the positions noted in the lower levels of the medulla.

Efferent Suprasegmental Neurones.—The pyramids are the same. Small bundles of more lightly stained fibres present in the fillet here and in higher levels (Weigert stain, not indicated in the figures) are efferent pallial fibres detached from pes or pyramids. They are aberrant fibres which rejoin the pyramids or are fibres innervating motor cranial nuclei. The tecto-spinal tract (see above).

## 4. Transverse Section of the Medulla through the Middle of the Olivary Nucleus.

Such a section is so similar to 3 and 5 that its detailed description may be omitted. The nucleus cuneatus has disappeared; the fillet increased somewhat; fasciculus solitarius and descending vestibular root have increased; also their terminal nuclei. The olivary nucleus, olivo-cerebellar fibres, and the restiform body have greatly increased. The formatio reticularis has increased in extent.

## Transverse Section of the Medulla through the Entrance of the Cochlear Root of Nerve VIII. (Figs. 295 and 300.)

Efferent Peripheral Neurones.—The dorsal vagus nucleus is not present, but the nucleus ambiguus is usually present and probably sends some axones to nerve IX, passing out with the afferent fibres (see below). The nucleus XII has disappeared and also its root fibres.

Afferent Roots, their Terminal Nuclei and Secondary Tracts.—Usually the afferent root fibres of nerve IX are present. They enter on the lateral aspect of the medulla ventral to the restiform body, traverse the spinal V, and pass to the fasciculus solitarius or its terminal nucleus. The fasciculus solitarius is smaller, and just above the entrance of the IX consists of only a comparatively few descending afferent root fibres of the VII.

The fibres of the *cochlear nerve* enter the extreme lateral angle of the medulla, where many. or, according to some, all of them terminate in two masses of cells enveloping externally the restiform body and known as the *ventral* (or *accessory*) and

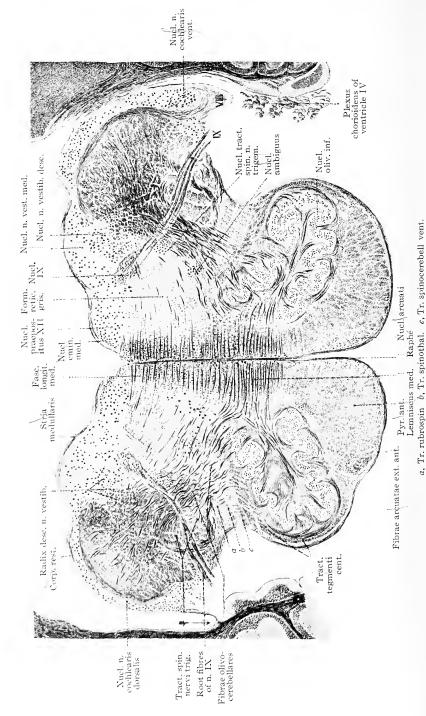


Fig. 300.—Transverse Section of the Medulla through the Entrance of the Cochlear Nerve. Weigert preparation. (Rauber-Kopsch.) The arrow on the left is directed into the lateral recess of the fourth ventricle.

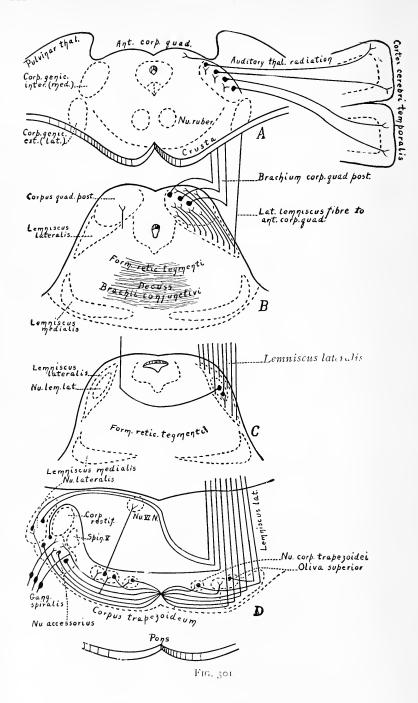
dorsal (or lateral) cochlear nuclei. Most of the axones of the dorsal nucleus pass across in the floor of the ventricle (striæ medullares) to form a part of the opposite secondary tract (lateral lemniscus) of the cochlear nerve. The axones of the ventral nucleus also decussate, but by a more ventral route, and also form a part of the lateral lemniscus. This latter decussation takes place at a higher level (see next section).

The auditory nerve is divided into two parts: the cochlear nerve (ganglion spirale) and the vestibular nerve (ganglion of Scarpa). The fibres of the cochlear root enter at a lower level than those of the vestibular. Some of them enter the ventral cochlear nucleus; the remainder pass dorsalward to the dorsal cochlear nucleus, or nucleus of the acoustic tubercle. According to some authorities, some root fibres pass to the superior olivary and trapezoid nuclei. The axones of the cells of the ventral and dorsal nuclei form the secondary cochlear tract (lateral fillet). These fibres decussate (trapezius) and send collaterals to, or are partially interrupted in, the nucleus olivaris superior, trapezoideus, nucleus of lateral fillet and posterior corpus quadrigeminum. According to some authorities all the fibres of the lateral lemniscus terminate in the posterior corpus quadrigeminum. From the posterior corpus quadrigeminum, the path is formed by the arm or brachium of the latter to the medial geniculate body and thence to the temporal cortex cerebri. It is thus not possible to state definitely how many neurone systems are involved, but the principal ones are: (1) ganglion spirale, (2) dorsal and ventral nuclei and (decussation) lateral lemniscus, (3) posterior corpus quadrigeminum and its brachium, (4) medial geniculate body of the thalamus and geniculo-cortical fibres. If the lateral lemniscus fibres be regarded as simply passing by the posterior corpus quadrigeminum, giving collaterals to it (Cajal), the path might in part consist of three neurone systems analogous to those of the paths from the cord, trigeminus and eye. (Figs. 294, 301.)

The fibres of the vestibular root enter higher and mesial to those of the cochlear root, passing dorsally along the inner side of the restiform body to four terminal nuclei, which cannot all be clearly seen in any one section; (a) Deiters' nucleus (lateral vestibular nucleus) situated at the end of the main bundle of root fibres, just internal to the restiform body; (b) you Bechterew's nucleus (superior vestibular nucleus) situated somewhat dorsal to Deiters' nucleus in the lateral wall of the fourth ventricle; (c) the median or principal nucleus of the vestibular division—a large triangular nucleus, occupying a considerable part of the floor of the fourth ventricle; (d) the descending vestibular nucleus which accompanies the descending fibres of the vestibular root (spinal eighth). Fibres also pass to the cerebellum. The axones of the cells of the terminal vestibular nuclei form the secondary vestibular tracts, some axones going to (a) the cerebellum (?), (b) the midbrain, especially to the nuclei of nerves III and IV (via Deiters and von Bechterew, the former by the medial longitudinal fasciculus), (c) the medulla and cord, probably to various motor nuclei, via the medial longitudinal fasciculus, lateral tract from Deiters' nucleus and other tracts in the reticular formation. (Figs. 294, 302 and 308.)

The descending vestibular root is large, as is also its terminal nucleus and the medial terminal vestibular nucleus, in the present section.

The spinal V is unchanged, its terminal nucleus being rather indistinct. Secondary trigeminal tracts cannot be distinguished—such fibres probably either join the



## EXPLANATION OF FIG. 301

Fig. 301.—Diagram showing Connections of the Cochlear Portion of the Auditory (VIII) Nerve. A, Section at level of anterior corpora quadrigemina and red nucleus; B, through level of posterior corpora quadrigemina; C, through level of nucleus of lateral lemniscus (Nu. lem. lat.); D, through pons at level of VIII nerve. Spacing between the different levels is not proportionate. In B and C the basis pedunculi is omitted. Each neurone group is indicated by one or several individual neurones.

Neurone No. 1.—Cell bodies in spiral ganglion (gang. spiralis); peripheral processes end in organ of Corti; central processes terminate principally in ventral or accessory nucleus (Nu. accessorius) and lateral nucleus (Nu. lateralis) or tuberculum acusticum; some also terminate in superior olives (Oliva superior), and nuclei of trapezoid body (Nu.

corp. trapezoidei) of same and opposite sides.

Neurone No. 2. (or 3?).—Axones of cells in accessory nucleus, in superior olives, and in nuclei of trapezoid body, constitute a ventral path in the lower border of the tegmentum, and form the lateral part of the lateral lemniscus (Lemniscus lateralis) or lateral fillet on the opposite side. Axones of cells in the lateral nucleus traverse the floor of the fourth ventricle as the striæ medullares, forming a dorsal pathway, decussate and then turn ventrally to a point dorsal to the superior olive and join the lateral lemniscus as its mesial part. Some axones also of cells in the accessory and lateral nuclei pass dorsally, looping around the restiform body, and then proceed ventrally (bundle of Held) to join the opposite lemniscus. The lateral lemniscus passes upward to the posterior corpus quadrigeminum, some of the axones terminating en route in the nucleus of the lateral lemniscus. From cells in this nucleus some axones again join the lateral lemniscus, and a few decussate and then pass upward to the posterior corp. quad. The axones of the lateral lemniscus terminate in the posterior corp. quad. The axones of the lateral lemniscus terminate in the posterior corp. quad. Some fibres of the lateral lemniscus probably go to the ant. corp. quad.

Neurone No. 3 (or 4?).—Axones of cells in the gray matter of the posterior corp. quad. form its brachium (Brachium corp. quad. post.) and ascend to terminate in the internal

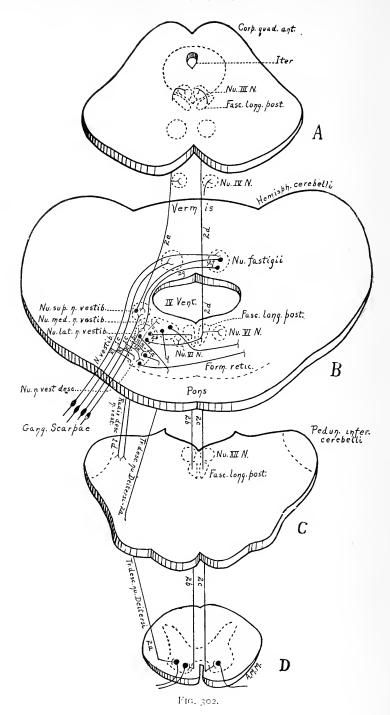
or medial geniculate body (Corp. genic. inter.).

Neurone No. 4 (or 5?).—Axones of cells in the internal geniculate body pass as a part of the thalamic radiation via the posterior part of the internal capsule to the cortex of the

temporal lobe of the cerebrum.

The axones which constitute the ventral path (Neurones 1 and 2) form a bundle of fibres known as the trapezoid body (Corpus trapezoideum). The decussation of these is peculiar in that the dorsal axones of the bundle on one side become the ventral ones on the opposite side; this accounts for the convergence of the axones at the median raphé.

Axones of cells in the superior olive pass to the nucleus of VI nerve (reflex). There is possibly also a descending path from the lateral nucleus to the spinal cord (not indicated).



### EXPLANATION OF FIG. 302.

Fig. 302.—Principal Connections of the Vestibular Portion of the Auditory (VIII) Nerve. A, Section at level of oculomotor (III) nerve; B, section through pons and cerebellum; C, through inferior olives; D, through spinal cord. Each neurone group is indicated by one or several individual neurones.

Neurone No. 1.—Cell bodies in ganglion of Scarpa: peripheral processes end in semicircular canals; central processes bifurcate, and ascending arms go to Deiters' nucleus (Nu. lat. n. vestib.) (t a), to von Bechterew's nucleus (Nu. sup. n. vestib.) (t b), and to nuclei fastigii and cortex of vermis of cerebellum (t c); descending arms go to nucleus of descending root (Nu. n. vestib. desc.) (t d) and (collaterals?) to principal or median nucleus

(Nu. med. n. vestib.) (1 e).

Neurone No. 2.—Axones of some cells in Deiters' nucleus descend ( $2\,a$ , Tr. desc. nu. Deitersi) uncrossed to antero-lateral column of the cord, axones of other cells enter the posterior longitudinal fasciculus (Fasc. long. post.,  $2\,b$ ) of same side and descend to anterior column of the cord, others pass to the posterior longitudinal fasciculus of opposite side whence some ( $2\,c$ ) descend to anterior column of the cord, occupying a position near the anterior median fissure, while some ( $2\,d$ ) ascend in the posterior longitudinal fasciculus and terminate principally in the nuclei of VI, IV, and III nerves. Axones of cells in von Bechterew's nucleus ascend ( $2\,e$ ), joining lateral part of posterior longitudinal fasciculus of same side, and terminate in nuclei of IV and III nerves. Axones of cells in the nucleus of the descending root probably pass in part to lateral part of reticular formation of same and opposite sides, ascending and descending (to other motor nuclei?). Axones of cells in the median nucleus probably pass largely into the reticular formation, possibly also to the posterior longitudinal fasciculus (not indicated). Axones of cells in the nuclei fastigii of the cerebellum pass to von Bechterew's nucleus ( $2\,f$ ) and to Deiters' nucleus'( $2\,g$ ). The cerebellum ( $1\,c$ ) are not known. [It is evident that impulses other than vestibular ones entering the cerebellum may also by  $2\,f$  and  $2\,g$  act indirectly upon the motor nuclei inervated by axones of the cells in Deiters' and von Bechterew's nuclei. Compare Figs. 204 and 308.]

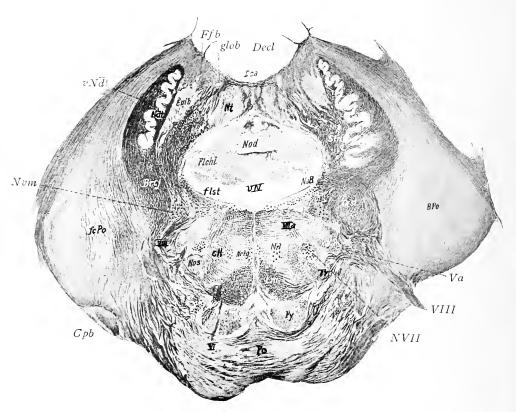


Fig. 303.—Section through the Hindbrain at the Level of the Junction of Pons and Cerebellum and the Entrance of the Vestibular Part of the Eighth Nerve. Weigert preparation. (Marburg.) Va, Radix spinalis trigemini (spinal root of the fifth); VI, nervus abducens (external eye muscle nerve); VIIa, pars nuclearis nervi facialis (pars prima, crus of origin or ascending facial root); VIII, nervus acusticus (eighth, vestibular part); BPo, brachium pontis (middle cerebellar peduncle); Brcj, brachium conjunctivum (superior cerebellar peduncle); cH, fasciculus tegmenti centralis; Cpb, corpus pontobulbare (Essick); Crst, corpus restiforme; Dca, decussatio cerebelli anterior; Decl, declive; Emb, embolus (nucleus emboliformis); fc Po, fibræ pontocerebellares; Ffb, fasciculus fastigiobulbaris (uncinate bundle of Russell); flst, pedunculus flocculi; glob, nucleus globosus; Lm, Lemniscus medialis (mesial fillet tract); NVII, nucleus facialis (motor nucleus of facial nerve); NaB, nucleus angularis, or superior, vestibularis (Bechterew); Ntl, nucleus dentatus cerebelli; Nod, nodulus cerebelli; Nos, nucleus olivaris superior; Ntl, nucleus reticularis lateralis (nucleus of the lateral column); Ntlg, nucleus reticularis regmenti; Nt, nucleus tecti (nucleus fastigii); Nvm, nucleus vestibularis magnocellularis or lateralis (Deiters) (large-celled nucleus of vestibular nerve); Plchl, plexus chorioideus lateralis; Po, pons; Py, pyramid; Stri, stratum intermedium (pedunculi); Tr, corpus trapezoides; vIV, ventriculus quartus; vNdt, vellus nuclei dentati cerebelli (fleece of the cerebellar olive).

medial lemniscus or form an independent ascending tract in the reticular formation. The fillet is about the same. The ventral spino-cerebellar and spino-thalamic tracts are in the same positions.

Other Afferent Cerebellar Neurones.—The olives are still larger and send many bundles of olivo-cerebellar fibres to the opposite restiform body which has still further increased in size. External arcuate fibres may be present and probably contain fibres to the restiform body and possibly fibres from the cerebellum, which end in the reticular formation. The arcuate nuclei are present. The central tegmental tract is larger.

Intersegmental Neurones.—The reticular formation is very extended. Its composition (longitudinal and transverse fibres, and cells) should be examined carefully. The rubro-spinal tract is in the same position, but the lateral tract from Deiters' nucleus is now more internally located. Its fibres cannot usually be distinguished, but are bending inward and toward its nucleus of origin (located somewhat higher). The medial longitudinal fasciculus may be partially separated from the medial lemniscus. It is a complex bundle and contains at various levels (a) descending and ascending fibres from Deiters' nucleus and other cells scattered in the reticular formation, (b) descending fibres from the interstitial nucleus of Cajal in the tegmentum of the midbrain, (c) according to some recent observations, descending fibres from the thalamus which end in the nuclei of cranial nerves V, VI, VIII and X. The fibres of this fasciculus probably terminate in many nuclei, especially those of eye-muscle nerves (III, IV and VI) (comp. Figs. 302, 308 and 320).

Efferent Suprasegmental Neurones.—The pyramids and tecto-spinal tracts are in the same positions. The aberrant efferent pallial fibres already noted (p. 439) may be seen in the lemniscus.

# 6. Section through the Hindbrain at Level of Junction of Pons and Cerebellum and Entrance of Vestibular Nerve. (Figs. 295 and 303.)

The most conspicuous features are the nuclei and fibres of the *pons*, added ventrally to the preceding structures, which are now collectively known as the *tegmentum*; the *cerebellum*, enclosing dorsally the *fourth ventricle*; and the connections (*inferior* and *middle peduncles*, *arms*, or *brachia*) of the cerebellum with the rest of the brain. The greater part (restiform body) of the inferior peduncle represents ascending cerebellar connections from all parts below the level, the middle peduncle (from the pons) represents a descending connection from the pallium to the cerebellum. The superior peduncle (efferent cerebellar) is not fully formed at this level. (Comp. p. 455.)

Efferent Peripheral Neurones.—In this level and that of the next section are present the *nuclei* and *root fibres* of *nerves VII and VI*.

The nucleus of nerve VII, or *nucleus facialis* is seen occupying a lateral position in the reticular formation similar to that of the nucleus ambiguus. In it may be made out the usual plexus of fine terminals and the coarser root fibres which proceed dorso-mesially to the floor of the ventricle, where they partially envelop the nucleus of the VI (usually not present in this level). They then turn brainward, forming a compact longitudinal bundle (next section) and finally turn ventro-

laterally and caudally to emerge on the lateral aspect. This latter part is the second part as distinguished from the first part of the connection. The bend is known as the *genu facialis*.

Four groups of cells composing the nucleus facialis have been distinguished: three ventral groups which, passing from the most mesial to the most lateral group, innervate respectively the muscles of tympanum, of pinna and of mouth and face. The dorsal group (to superior branch of facial) innervates the frontalis,

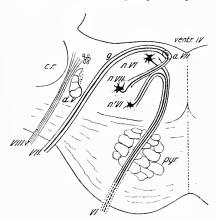


Fig. 304.—Diagram of Origin of Sixth and Seventh Cranial Nerves. (Schäfer.) pyr, Pyramid; cr, restiform body; dV, spinal root of fifth nerve; Ventr. IV, fourth ventricle; VIII.v, vestibular root of eighth nerve; n.VI, chief nucleus of sixth nerve; n'VI, accessory nucleus of sixth nerve; VI, sixth nerve; n.VII, nucleus of seventh nerve; from which the axones pass dorso-mesially to the floor of the ventricle, where they turn brainward, appearing as a bundle of transversely cut fibres, aVII, and ascend to the "genu," g, where they turn and pass ventro-laterally and somewhat caudally to the surface as the seventh nerve, VII.

corrugator supercilii and orbicularis palpebrarum. Among the terminals in the nucleus have been distinguished collaterals (reflex) from the fillet, secondary acoustic and trigeminal tracts and other adjacent fibres; also terminals of the tecto-spinal tract. Whether the nucleus receives direct terminals from the pyramids or whether fibres of the latter are only connected with it via intercalated neurones is uncertain.

Some of the *root fibres of the VI* are usually seen passing to the surface. For nucleus see next section.

Afferent Roots, their Terminal Nuclei and Secondary Tracts.—The afferent vestibular root fibres enter at the lower border of the pons and pass lateral to the spinal V, mesial to the ventral cochlear nucleus and restiform body, and enter the field previously occupied by the descending vestibular root, the fibres of which are a continuation of the root. Scattered large cells in this region form the nucleus of Deiters. Dorso-mesial to this is still

the medial vestibular terminal nucleus and dorsal to Deiters' at the external angle of the fourth ventricle is the *superior vestibular terminal nucleus* (von Bechterew). Fibres seen passing from the vestibular region to the cerebellum and lying near the ventricle are partly vestibular root fibres to the cerebellum (especially to the nucleus tecti, or fastigii, see below), and partly descending fibres from cerebellar nuclei (especially from the nuclei fastigii, forming *fastigio-bulbar* fibres) to Deiters' nucleus, other vestibular nuclei, and other cells in the reticular formation. It is thus evident that such nuclei as Deiters' may act as parts of vestibular bulbospinal reflex arcs and also as parts of efferent cerebellar paths. Internal arcuate fibres from the vestibular area are probably principally fibres (secondary tracts) from the various vestibular nuclei to the medial longitudinal fasciculus and other tracts in the reticular formation. (Comp. pp. 441, 449, 455, Figs. 302, 308.)

The nucleus olivaris superior lies ventral to the nucleus facialis and lateral

to the central tegmental tract. This nucleus together with several other small nuclei in its immediate vicinity (preolivary nucleus, semilunar nucleus, trapezoid nucleus) is one of the nuclei intercalated in the cochlear path (Fig. 301). Lateral to it is seen a mass of fibres which pass by it toward the median line through the medial lemniscus, and decussate, finally turning longitudinally dorso-lateral to the opposite superior olive. These are fibres of the *trapezius*, and together with the more dorsal secondary cochlear fibres (p. 441) form the *lateral lemniscus* (See Fig. 301 and page 441). The lateral lemniscus is thus one of the links in the cochlear or auditory pathway. Fibres pass from superior olive to nucleus of nerve VI (reflex). (For the afferent part of VII, see Table of Cranial Nerves.)

The spinal V occupies the same position though separated from the surface by the pontile fibres; internal to it is its terminal nucleus. Note the change in the shape of the lemniscus. The ventral spino-cerebellar and spino-thalamic tracts are in the same position though separated from the surface by the mass of pontile fibres.

Other Afferent Cerebellar Neurones.—The inferior olives are not present, and the olivo-cerebellar fibres are here entering the cerebellum as a part of the restiform body. The central tegmental tract (to the olives) occupies the ventral part of the reticular formation. The restiform body is entering the white matter of the cerebellum. It has been seen to be composed of the dorsal spino-cerebellar tract, olivo-cerebellar fibres and fibres from the lateral and possibly other nuclei in the reticular formation. The dorsal spino-cerebellar tract terminates in the cortex of the vermis or middle lobe of the cerebellum, the olivo-cerebellar fibres terminate in all parts of the cerebellar cortex. The fibres mesial to the restiform body, consisting of ascending vestibular fibres to the cerebellum and descending fibres to vestibular and other nuclei (see cerebellum), are sometimes called the internal or juxta-restiform body. This and the restiform body proper constitute the inferior cerebellar peduncle. The pons consists of gray matter—the pontile nuclei—and of transverse and longitudinal fibres. The longitudinal fibres include the pyramids which pass through to the medulla and cord, and other fibres from the pallium (pallio-pontile or cerebro-pontile) which terminate in the pontile nuclei. The axones of the latter form the transverse pontile fibres (ponto-cerebellar fibres) which cross and pass to the cortex of the opposite cerebellar hemisphere. They constitute the *middle cerebellar peduncle* or *brachium pontis*. (Comp. p. 455.)

This whole pontile system may be termed the pallio-cerebellar path or connection. It is principally, or entirely, a crossed connection. There are probably also transverse fibres in the pons connecting cerebellum and reticular formation. Fibres passing vertically in the raphé from pons to reticular formation (perpendicular fibres of pons) may be in part continuations of these and in part efferent pallial fibres from pes to tegmentum. The latter are either aberrant fibres or fibres innervating directly or indirectly motor cranial nuclei.

Intersegmental Neurones.—The reticular formation is extensive. In it there may be distinguished, besides the nuclei already mentioned, various more or less well-defined reticular nuclei (see Fig. 303). The fibres of the lateral tract from Deiters' nucleus (not distinguishable) are here emerging from Deiters' nucleus. The medial longitudinal fasciculus occupies the same position, but is here well separated from the fillet. Some of the internal arcuate fibres in the dorsal part of

the reticular formation may be fibres from Deiters' nucleus to this bundle. They may be crossed or uncrossed, and may descend in it as already mentioned (page 418) or ascend (see Fig. 302). Other internal arcuate fibres here, as elsewhere, pass from the various terminal nuclei to form secondary tracts. Other transverse fibres are axones of cells of reticular nuclei or collaterals and terminals ending in them.

Efferent Suprasegmental Neurones.—The spino-tectal tract lies ventral to the medial longitudinal fasciculus. The pyramids are in the same position, but are partly surrounded by pontile fibres and nuclei. (See also pons, above.)

The Cerebellum.—In the gray matter there is to be distinguished the external gray or cortex, and internal nuclei forming interruptions or relays in paths to and from the cortex. The white matter consists of the fibres of various afferent and efferent cerebellar paths and association fibres of the cerebellum. The cortex is studied elsewhere. The internal nuclei can usually be distinguished. the nucleus dentatus cerebelli (corpus dentatum), a convoluted mass of gray resembling the inferior olives (and sometimes called the cerebellar olives), and mesial to this the nucleus globosus, nucleus emboliformis and the nucleus tecti or fastigii. The nucleus tecti receives fibres from various parts of the cerebellar cortex and also vestibular root fibres (p. 445). Its axones, in part at least, pass to Deiters' nucleus and other nuclei in the reticular formation (fastigio-bulbar tract). The corpus dentatum, nucleus globosus, and nucleus emboliformis also receive fibres from the cerebellar cortex. Their axones form the superior cerebellar peduncle (brachium conjunctivum), cross and pass to the red nucleus, reticular formation, nucleus of nerve III, and thalamus. At the level of the section the superior peduncle is not vet fully formed. (See also p. 445.)

Note where possible the structure of the *plexus chorioideus* of the fourth ventricle. It consists of a layer of flattened cells next the ventricle which are ectodermic, and an outer mesodermic part consisting of connective tissue and blood-vessels.

## 7. Transverse Section of the Hindbrain through the Roots of Nerves VI (Abducens) and VII (Facial). (Figs. 295 and 305.)

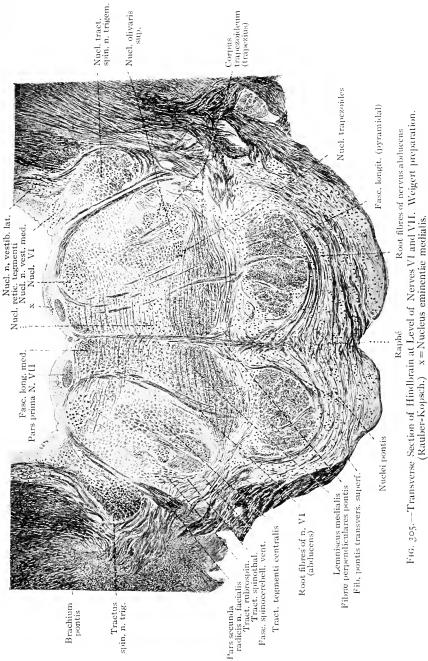
Efferent Peripheral Neurones.—The nucleus facialis is usually not present but various portions of the root fibres may be present (see preceding section), especially the longitudinal part.

The nucleus of the VI or nucleus abducentis is present in about the middle of the floor of the ventricle and just beneath the central gray or partly within it. Its fibres, the root fibres of the abducens, are seen passing ventrally.

Afferent Roots, Their Terminal Nuclei and Secondary Tracts.—The lateral (Deiters') and medial vestibular nuclei are usually still present, also possibly fastigio-bulbar fibres. The ventral cochlear nucleus has disappeared, but other cochlear nuclei (superior olivary and trapezoid) are usually present. Often fibres can be seen passing from the superior olive to the nucleus VI.

Fibres of the secondary cochlear tract (corpus trapezoideum) are still traversing the medial lemniscus, and decussating. The tract they are forming (lateral lemniscus) is not yet very distinct.

The spinal V is in the same position, but it and its terminal nucleus tend to separate into groups of fibres and cells, and to change their relative positions. The



medial lemniscus is more flattened in cross section, extending transversely instead of dorso-ventrally. The ventral spino-cerebellar tract and spino-thalamic tract are in the same positions in the external part of the tegmentum ventral to the spinal V and external to the superior olive.

Other Afferent Cerebellar Connections.—The restiform body has now merged with the white matter of the cerebellum. The nuclei and transverse fibres of the pons (ponto-cerebellar neurones) have increased. The longitudinal fibres in the pons at this level are principally the pyramids, but some are pallio-pontile fibres which terminate in the nuclei pontis. Perpendicular fibres are present.

Intersegmental Neurones.—The reticular formation is practically unchanged. One of its nuclei (nucleus reticularis tegmenti) can be seen as a lighter area (Weigert) in the medial part, dorsal to the medial lemniscus. The rubro-spinal tract is in the same position near or mingled with the spino-thalamic and ventral spino-cerebellar tracts. These fibres are not easily distinguished among the various fibres of the cochlear tract which cross them. The medial longitudinal fasciculus is now a well-marked tract occupying the same position. From now on, it contains ascending fibres from Deiters' nucleus and perhaps other reticular nuclei besides the descending fibres from the interstitial nucleus of Cajal.

Efferent Suprasegmental Neurones.—The pyramids and tecto-spinal tract (predorsal fasciculus) occupy the same positions. The fastigio-bulbar fibres have been mentioned. The superior cerebellar peduncle is now more distinct as it is being formed by fibres from the dentate nucleus. It lies near the dorso-lateral part of the ventricle.

# 8. Transverse Section of the Hindbrain Through the Roots of Nerve V (Trigeminus). (Figs. 295 and 306)

Efferent Peripheral Neurones.—Motor nucleus of V. This is mesial to the terminal nucleus of the V and its coarse efferent root fibres may be seen, in favorable levels, passing out with the entering afferent fibres. Some of the finer terminal fibres present in the nucleus are afferent root fibres of the V (two-neurone arc) and collaterals of secondary tracts of V (three-neurone arc) The nature of its connections with efferent pallial fibres is not known. Collaterals are also received from the mesencephalic root. (Fig. 307.)

Afferent Roots, their Terminal Nuclei and Secondary Tracts.—The afferent fibres of the V pass through the pons and enter the tegmentum where they divide into short ascending and long descending arms. The former, together with collaterals, terminate in the cephalic end of the terminal nucleus of the V. This is broken up into groups of cells which lie dorso-lateral to the entering fibres. The long descending arms pass down to the cord as the spinal V, giving off collaterals and terminals to the terminal nucleus en route. (Fig. 307). A third source of fibres of the V is a series of cells extending upward into the roof of the mesencephalon. The axones of these cells form the mesencephalic root of the V. There is reason to suppose, from their peculiar location and for other reasons, that these are afferent peripheral neurones which have remained within the neural tube. From the region of the terminal nucleus of the V, a transverse bundle passes to the opposite side in the floor of the fourth ventricle. This is considered a secondary

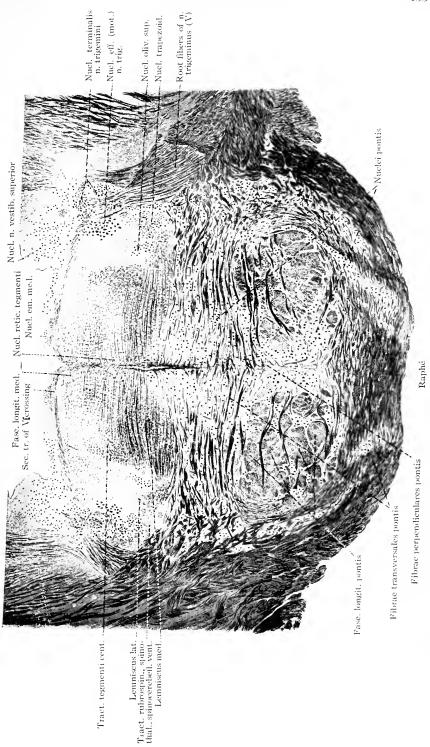


Fig. 306.—Section through Hindbrain at about the Exit of Nerve V. Weigert preparation (Rauber-Kopsch.)

decussating trigeminal tract which forms an ascending tract in the dorsal part of the reticular formation. Fibres of secondary tracts give off collaterals to various efferent nuclei and probably axones of some cells of the terminal nuclei become intersegmental fibres in the reticular formation. Secondary tracts to the thalamus (via fillet and also in reticular formation?) form part of the trigeminal afferent pallial path.

The superior terminal vestibular nucleus (of von Bechterew) may still be present. The superior olivary and trapezoid nuclei may be present. The secondary (and

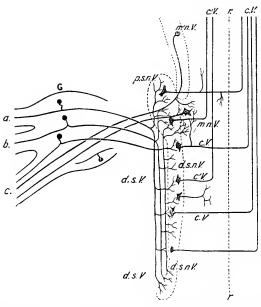


Fig. 307.—Diagram of Origin of Fifth Cranial Nerve. (Schäfer.) G, Gasserian ganglion; a,b,c, the three divisions of the nerve; m.n.V, principal motor nucleus; p.s.n.V, principal terminal "sensory" nucleus; d.s.n.V, terminal nucleus of spinal root; d.s.V, descending or spinal root; c.V and c'.V, secondary trigeminal tracts (axones of cells in terminal nuclei); r, median raphé; m'.n.V, mesencephalic nucleus.

tertiary (?), see Fig. 301) cochlear tract or lateral lemniscus is now well formed and may be seen lying dorso-lateral to the superior olivary and trapezoid nuclei.

The medial lemniscus is still more flattened. The spino-thalamic and ventral spino-cerebellar tracts occupy the same positions.

Other Afferent Cerebellar Neurones.—The transverse pons fibres are the same, but the longitudinal fibres have increased owing to the presence of more palliopontile fibres. The perpendicular pontile fibres are seen passing dorsally in the raphé into the tegmentum.

The central tegmental tract is in nearly the same position.

Intersegmental Neurones.—The reticular formation is somewhat diminished. In it is the nucleus reticularis tegmenti. The rubro-spinal tract is in the same position, mingled with the spino-thalamic and ventral spino-cerebellar. The medial longitudinal fasciculus is unchanged.

Efferent Suprasegmental Neurones.—The pyramids now occupy the central part of the pons, and are broken up into a number of bundles. In the dorsal part of the pons fibres pass obliquely dorsally. These are probably efferent pallial fibres which act directly or indirectly on some of the efferent nuclei of cranial nerves (motor path to cranial nerves). The pallio-pontile fibres have been mentioned.

The superior peduncle is now a large bundle of fibres flattened against the inner surface of the dorso-lateral brain wall.

The tecto-spinal tract is in the same position.

### CEREBELLUM.

The cerebellum, connected with the rest of the brain by its three peduncles, consists of two lateral lobes or hemispheres connected by a median lobe, the vermis. These are divided into various lobules, the surfaces of which are marked by parallel transverse folds or laminæ. When these are cut across it is seen that they give off secondary or tertiary laminæ, the whole producing the appearance known as the arbor vitæ. The surface of the cerebellum is composed of gray matter, the cortex, enveloping the white matter. Besides this there are masses of gray within, the internal nuclei of the cerebellum (dentatus, globosus emboliformis, and fastigii), embedded in its white matter. Fibres entering the cortex are the terminations of the fibres of the restiform body (dorsal spino-cerebellar tract to the cortex of the vermis, olivo-cerebellar fibres to the whole cortex, fibres from the lateral nucleus and possibly other nuclei in the reticular formation), vestibular root fibres to the vermis, the ventral spino-cerebellar tract to the vermis, and the pontile fibres to the cortex of the hemispheres. The cortical cells do not send axones outside the cerebellum, all efferent fibres being interrupted in the internal nuclei. The dentate nucleus receives fibres from the cortex of the hemispheres; the globose and emboliform nuclei receive fibres from the cortex of the vermis; and the nucleus fastigii receives fibres from various parts. The axones of the first three form the superior peduncle; the axones of the nucleus fastigii are fastigio-bulbar fibres, principally crossed, to vestibular nuclei and possibly other reticular formation nuclei. There may be some efferent fibres in the middle peduncle to reticular formation nuclei, but the major part, at least, of this peduncle consists of the ponto-cerebellar fibres already described. The inferior and middle peduncles are thus largely afferent and the superior peduncle is efferent, to red nucleus, thalamus and nucleus of nerve III. (Figs. 294 and 308.)

In the **cortex** can be distinguished an outer or *molecular layer* with few cells and few medullated fibres, an inner, *granular* or *nuclear layer*,

and between the two a single row of large flask-shaped cells, the *cells* of *Purkinje* (Figs. 309, 310). These latter give off several main dendrites, which enter the molecular layer and form a remarkably rich arborization extending to the surface. The Golgi method shows the larger and medium branches smooth, but the terminal branches thickly beset with "gemmules." The dendritic arborization is flattened, extending at right angles to the laminæ. The axone is given off from the end opposite to the dendrites and passes through the granular layer

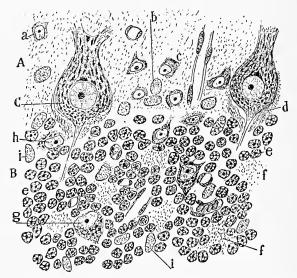


Fig. 309.—Part of a Vertical Section through the Adult Human Cerebellar Cortex. Nissl Method. (Cajal). A, Inner portion of the molecular layer; B, granular layer; C, body of a Purkinje cell; a, stellate cell of the molecular layer; b, nuclei of the epithelial-like neuroglia cells (cells of the fibres of Bergmann); c, stellate cell with marginal chromophilic substance; d, fibrillar mass corresponding to the baskets; e, nuclei of the granule cells; f, islands or glomeruli in the granular layer; g, h, Golgi cells in the granular layer; i, nuclei of neuroglia cells.

into the white matter, either to one of the internal cerebellar nuclei where it terminates, or to some other part of the cortex. The Purkinje cells are almost the only cells, the axones of which enter the white matter. It is evident that all intracortical connections must ultimately converge on these cells to reach the efferent cerebellar paths. The axones of the Purkinje cells give off collaterals not far from their origin, which pass into the molecular layer and appear to terminate there in end "buttons" upon the bodies of adjacent Purkinje cells. The medullated axones form the coarser fibres traversing the granular layer. The cell body is fairly well filled with small chromophilic bodies of

uniform size, often showing a slightly concentric arrangement (Fig. 309).

The cells in the molecular layer (stellate cells) are either superficial stellate cells with irregular branching dendrites and a short axone or deep stellate (basket) cells. These latter are cells the axones of which (apparently non-medullated) have a narrow neck and unusual thickening beyond the neck. They extend at right angles to the laminæ for a distance of several Purkinje cells, giving off to each Purkinje cell one or more collaterals which pass toward the granular layer and envelop.

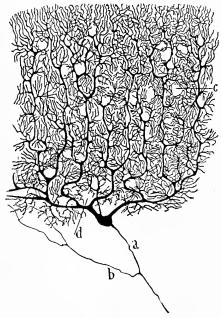


Fig. 310.—Purkinje Cell of Adult Human Cerebellum. Golgi preparation. (Cajal.) a, Axone; b, recurrent collateral; d, spaces occupied by basket cells; c, spaces occupied by blood-vessels.

with their terminal arborizations, the body and proximal, non-medullated portion of the axone of the Purkinje cell. Collaterals of other basket cell axones may terminate around the same Purkinje cell, forming the "basket." The dendrites of the basket cells ramify throughout the molecular layer. Besides the cells contained in it, and the dendritic arborizations of the Purkinje cells, the molecular layer contains the axones of the granule cells and the terminations of the climbing fibres (see below). In ordinary stains it presents a general punctate appearance, with the scattered nuclei of the short axone and basket

cells, and the coarser dendrites of the Purkinje cells distinguishable. (Figs. 300 and 311.)

The granular layer with ordinary stains presents the appearance of closely packed nuclei with clear spaces here and there ("islands" or "glomeruli") and also a few larger cells (Fig. 309). Most of these nuclei belong to the granule cells, which are caryochrome cells. The granule cells are small and possess three to six dendrites which are comparatively short and terminate in the glomeruli with a compact arborization, each branch of which ends in a small varicosity. The

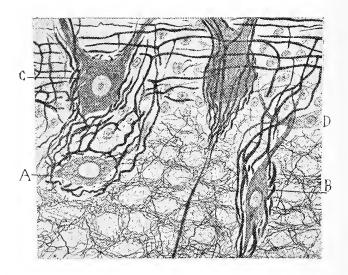


Fig. 311.—Section of Adult Human Cerebellum. Silver Method of Cajal. (Cajal.) A, B, Cells in the granular layer enveloped by basket fibres; C, cell of Purkinje. The axone of one of the cells of Purkinje is shown.

axones of the granule cells, which are non-medullated, ascend into the molecular layer where each divides into two branches running longitudinally along the laminæ, and terminating in varicosities (Figs. 312, 314). These are the *parallel fibres* of the molecular layer. They thus run at right angles to and through the dendritic expansions of the Purkinje cells and their cross sections together with the terminal dendritic arborizations of the Purkinje cells give the molecular layer its punctate appearance. The scattered larger cells in the granular layer are principally *short axone* or *Golgi cells*, whose main dendrites usually penetrate and branch within the molecular layer. Their axones often form very extensive and complicated arborizations in the granular layer, the terminations of which are concentrated in the glomeruli.

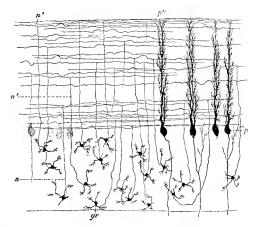


Fig. 312.—Diagram of Longitudinal Section of Cerebellar Lamina. Golgi method. (Kölliker.) gr, Cell of the granular layer; n, axone of granule cell; n', the same in molecular layer where it branches and runs in long axis of lamina; p, Purkinje cell showing how much less extensively its dendrites (p') branch in long axis of lamina. (Compare Fig. 314.)

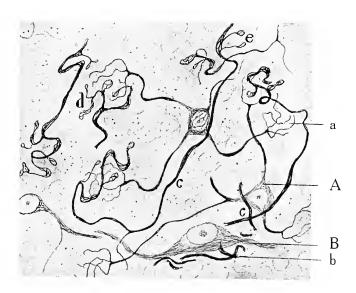


Fig. 313.—Granule Cells and Mossy Fibres in the Cerebellum of Adult Cat. Silver method of Cajal. (Cajal.) A, Granule cell; B, Golgi cell; a, dendritic arborization of granule cell; b, mossy fibres passing by Golgi cell; c, mossy fibre; d, termination of a mossy fibre; e, terminal processes given off from a thickening in a mossy fibre.

Dislocated cells of this type may have their cell bodies in the molecular layer.

In the cortex there are also the terminations of the afferent cerebellar fibres already mentioned (p. 455). These are of two types, *mossy fibres* and *climbing fibres*. The mossy fibres, so called from the appearance of their terminations in embryos, are the coarsest fibres of the white matter. While in the latter they bifurcate, branches going to

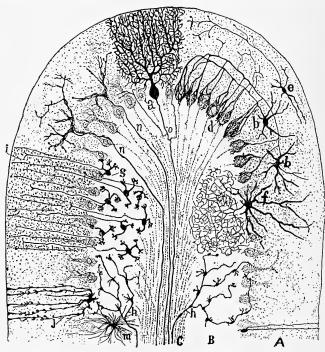


Fig. 314.—Semi-diagrammatic transverse Section of a Cerebellar Lamina of a Mammal, as shown by the Golgi Method. (Cajal.) A, Molecular layer; B, granular layer; C, white matter; a, Purkinje cell, seen flat; b, basket cells of the molecular layer; d, their terminal arborizations which envelop the bodies of the Purkinje cells; e, superficial stellate cells; f, Golgi cell; g, granule cells with their axis-cylinders ascending and bifurcating at i; h, mossy fibres; j, neuroglia cell; m, neuroglia cell in granular layer; n, climbing fibres.

different laminæ. These main branches give off secondary branches which enter the granular layer and there arborize. During their course, and also at their terminations, these branches are thickened in places and there give off short, thick, terminal branches which end in varicosities. These terminal branches are located within the glomeruli. The glomeruli thus contain the dendritic terminations of the granule cells, the axonal terminations of the Golgi cells, and the terminations of the mossy fibres. (Fig. 313.)

The climbing fibres pass from the white matter, through the granular layer to the cells of Purkinje. Passing by the bodies of the latter they arborize into terminals which envelop the smooth dendritic branches of the Purkinje cells; *i.e.*, all but the terminal dendritic arborizations. Three kinds of fibres thus terminate around the Purkinje cells; the granule axones, probably in contact with its terminal dendritic arborizations; the climbing fibres around its coarser dendritic branches; and the basket fibres around its body. The respective sources of the mossy and climbing fibres are unknown.

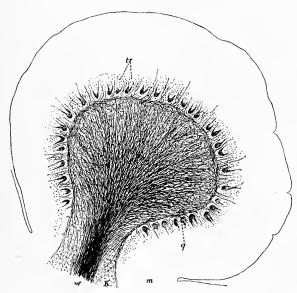


Fig. 315.—Cross Section of a Cerebellar Convolution Stained by Weigert's Method. (Kölliker.) m, Molecular layer; K, granular layer; w, white matter; q, fine fibres passing from white matter into the molecular layer; tr, dots represent longitudinal fibres of molecular layer among bodies of Purkinje cells.

It is evident from the above that all of the cells of the cerebellar cortex except the Purkinje cells are association cells of the cortex.

The medullated fibres of the cerebellum (Weigert) (Fig. 315) pass from the white matter into the granular layer and ramify throughout the latter, forming quite a dense plexus separating groups of granule cells. Sometimes straight fibres can be seen passing through toward the molecular layer which are probably either the climbing fibres or axones of the Purkinje cells. Beneath and between the bodies of the Purkinje cells is a plexus of fibres extending into the deeper part of the molecular layer, the remainder of this layer containing few or no

medullated fibres. These fibres in the vicinity of the Purkinje cells are probably principally formed by the recurrent collaterals of the Purkinje cells already mentioned. The remaining fibres of the granular plexus would apparently consist of the arborizations of mossy fibres and of the Golgi cells. Whether the former are medullated is, however, somewhat uncertain.

Most of the neuroglia cells in the cerebellum are of the same general type as seen elsewhere, but in the Purkinje cell layer are apparently epithelial-like cells which send vertical processes to the periphery. Some of these processes, as seen in the Golgi method, are rough and branched, others are smooth. In ordinary stains these processes are sometimes visible and are known as the *fibres of Bergmann*. (Figs. 309, 314.)

### Isthmus.

### PRACTICAL STUDY.

## 9. Transverse Section through the Isthmus at the Exit of Nerve IV (Trochlearis). (Figs. 295 and 316.)

In this there are to be distinguished three parts, the thin *roof* (superior medullary velum), the *tegmentum* and, ventral to the latter, the *pons*. The tegmentum consists essentially of the reticular formation, efferent cerebellar and midbrain connections, and externally the afferent pallial connections. The pons contains the efferent pallial paths to the cerebellum and parts of the nervous system caudal to it. The cavity is the *iter* or *aqueductus Sylvii*. Next to this is the *central gray* of the brain wall.

Efferent Peripheral Neurones.—The root fibres of the IV are seen in the roof. They originate from nuclei lying further forward in the ventral part of the central gray. The fibres pass from the nuclei dorsally and caudally in the outer part of the central gray and finally decussate in the roof and emerge. It is only the latter part of this course which is seen in this level.

Afferent Roots, their Terminal Nuclei and Secondary Tracts.—The mesencephalic root of the V lies in the lateral part of the central gray. Mingled with its fibres may be seen the rounded cells, the axones of which form these fibres.

The lateral lemniscus occupies part of the lateral swelling on the surface of the tegmentum. Groups of cells among its fibres constitute the *dorsal nucleus* of the lateral lemniscus. The medial lemniscus is now still more flattened. The spinothalamic tract is in about the same position, between the two lemnisci. At this level, the principal afferent suprasegmental paths form an L-shaped mass, enveloping the rest of the tegmentum and representing general bodily sensation and hearing. There are also cranial nerve ascending paths lying probably within the reticular formation and fillet (secondary vago-glossopharyngeal and trigeminal tracts, representing visceral, taste, and general head sensation). These cannot be distinguished in the section.

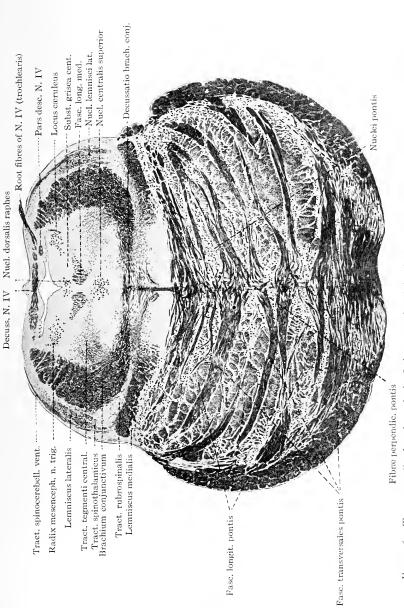


Fig. 316.—Transverse Section through the Isthmus at the Exit of Nerve IV. Weigert preparation. (Rauber-Kopsch.)

The ventral spino-cerebellar tract is on the surface, and now comes to lie external to the superior cerebellar peduncle. At about this point it turns caudally, and passes back into the cerebellum, accompanying the superior peduncle.

Other Afferent Cerebellar Connections.—The central tegmental tract occupies the same position. (For the pallio-cerebellar connection see "Efferent Suprasegmental Neurones" below.)

Intersegmental Neurones.—The reticular formation is diminished in extent. One of its nuclei, the *nucleus centralis superior*, lies near the raphé. The rubrospinal tract has moved somewhat mesially. It is dorsal to the medial lemniscus. The medial longitudinal fasciculus is in the same position, and is a well-marked bundle lying at the boundary between the ventral part of the central gray and the reticular formation.

Efferent Suprasegmental Neurones.—The pyramids are now broken up into bundles which may show a tendency to gather in the ventral part of the pons (distinguishable in one-month infant, where they are medullated while the pontile system is not). Bundles apparently forming lateral and mesial portions of the medial lemniscus (not indicated in the figure) are aberrant efferent pallial fibres. Such bundles have been seen passing from pons to tegmentum and also imbedded in the medial lemniscus in lower levels (pp. 449, 439). Some of these fibres are possibly fibres acting directly or indirectly on the efferent peripheral neurones or motor nuclei of the cranial nerves.

The pallio-pontile fibres are still more numerous. The gray matter in the pons (nuclei pontis) is very extensive. The transverse fibres of the pons no longer pass at this level into the cerebellum, but are collected at the sides of the pons to pass backward to the cerebellum (compare with an external view of the brain).

The superior cerebellar peduncles or brachia conjunctiva are two large crescentic bundles of fibres in the lateral part of the reticular formation. Some of their fibres have begun to decussate in the ventral part of the reticular formation.

The tecto-spinal tract or predorsal fasciculus lies ventral to the medial longitudinal fasciculus.

### Midbrain or Mesencephalon.

The dorsal surface of the midbrain presents four rounded prominences, the two posterior and the two anterior corpora quadrigemina or the inferior and superior colliculi. Ventrally are seen two diverging masses of longitudinal fibres, the pes pedunculi, separated by a deep groove or sulcus. In the midbrain are to be distinguished, (a) the expanded roof, the corpora quadrigemina, (b) the legmentum containing the segmental (cranial nerves IV and III) and intersegmental apparatus and the afferent suprasegmental paths, and (c) the basis pedunculi, ventral to the tegmentum and comprising the principal efferent pallial paths (pes pedunculi) and the substantia nigra.

The cavity of the midbrain is the aqueductus Sylvii or iter.

### PRACTICAL STUDY.

10. Transverse Section through Midbrain at Level of Anterior Corpora Quadrigemina and Exit of Nerve III (Oculomotor). (Figs. 295 and 317).

Compared with the preceding section, the following are the most conspicuous changes: The roof has now enlarged into the anterior corpora quadrigemina (or superior colliculi); the tegmentum now contains the nuclei and roots of nerve III and the red nucleus; instead of the pons, the ventral part of the brain is now composed of the basis pedunculi, consisting of a mass of efferent pallial fibres and the substantia nigra. The term crura cerebri or cerebral peduncles is loosely used to include all except the roof of the brain at this level.

Efferent Peripheral Neurones.—The nucleus of nerve III or oculomotor nucleus is located in the ventral part of the central gray in a V-shaped trough formed by the fibres of the medial longitudinal fasciculus. The nucleus is divided into large and small-celled groups. The large-celled groups are two lateral groups subdivided into anterior and posterior dorso-lateral and anterior and posterior ventro-mesial, and a central or median group-nine in all. Between the cephalic or anterior groups are on each side a small-celled group known as the Edinger-Westphal nucleus, and still further forward are two small-celled anterior median nuclei. The connections of these groups with the extrinsic muscles of the eye innervated by nerve III (internal, superior and inferior recti, and inferior oblique) and the levator palpebræ superioris and intrinsic eye muscles (ciliary and sphincter pupillæ, via ciliary sympathetic ganglion) are uncertain. From a priori grounds, the innervation of the intrinsic muscles by the small-celled groups and the other muscles by the large-celled groups would seem probable. Some of the fibres, usually stated to be from the posterior dorso-lateral group, decussate. Recent observations (Cajal) would indicate that the decussating fibres come from the ventro-mesial lateral groups. The various fibres pass ventrally in a number of bundles, some passing mesial to, some traversing, and some passing lateral to the superior cerebellar peduncle and red nucleus. Ventral to these the root fibres come together and emerge on the ventral aspect of the midbrain. (Figs. 317 and 318.)

Immediately caudal to the nucleus of nerve III (not in the plane of the section) is the nucleus of the nerve IV occupying a position similar to the lateral groups of the nerve III nucleus. The course of the root fibres of the IV has been mentioned (preceding section).

Afferent Roots, their Terminal Nuclei and Secondary Tracts.—The mesencephalic trigeminal root is sometimes distinguishable on the lateral border of the central gray.

The lateral lemniscus has partly or wholly terminated in the posterior corpus quadrigeminum (inferior colliculus) at a lower level. Fibres from the latter form its arm or brachium, representing another link of the cochlear path. In the present section the fibres of the brachium of the posterior corpus quadrigeminum are seen entering the medial geniculate body (which is a part of the thalamus). Axones of the cells of this body constitute the last relay of the cochlear path to the temporal cortex cerebri (not present in this section).

The medial lemniscus is now a laterally placed, curved bundle, displaced laterally by the red nucleus. According to some authorities, some of its fibres terminate in the anterior corpus quadrigeminum. The spino-thalamic tract is plainly distin-

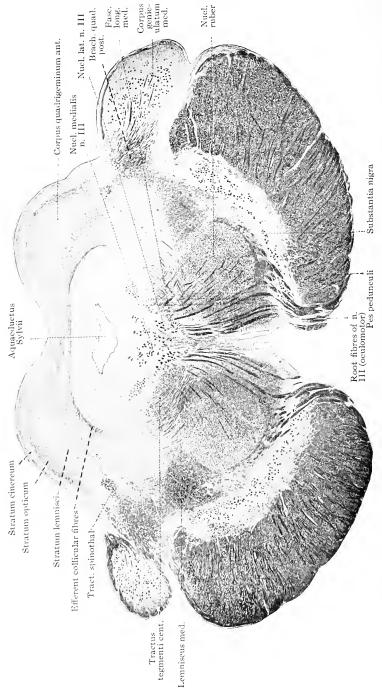


Fig. 317.—Transverse Section through Midbrain at Level of Anterior Corpora Quadrigemina and Exit of Nerve III.
Weigert preparation. (Rauber-Kopsch.)

guishable as a bundle dorsal to the dorsal edge of the medial lemniscus. At this level, then, the afferent paths from cord to pallium have practically united.

In the anterior corpus quadrigeminum are terminations of the optic tract (so-called optic nerve) (see below).

The central tegmental tract is displaced dorsally by the red nucleus.

Intersegmental Neurones.—The reticular formation is smaller. The rubrospinal tract (not distinguishable) is emerging from its nucleus of origin, the nucleus ruber. Just below this level its fibres decussate (ventral decussation of Forel) and pass to the location they have been seen to occupy in preceding levels. The nucleus ruber or red nucleus is very conspicuous, occupying a large part of the reticular formation. It gives rise to rubro-bulbar as well as rubro-spinal fibres.

The medial longitudinal fasciculus is diminished, some of its descending fibres having been formed from reticular formation nuclei below this level. Many of its fibres, both ascending and descending, send collaterals and terminals to the cells of the oculomotor nucleus.

Efferent Suprasegmental Neurones.—The ventral part of the brain is composed of a mass of efferent pallial fibres, the pes pedunculi. The pyramidal fibres from the precentral areas of the cerebral hemisphere (pallio-spinal and some pallio-bulbar fibres) occupy about the middle three-fifths, but are also scattered through other parts of the pes, especially the mesial part. The leg fibres are probably more numerous laterally, the arm fibres in the middle, and the face fibres mesially. In the lateral part of the pes are pallio-pontile fibres from the occipital and temporal lobes of the cerebral hemispheres (occipito-temporal pallio-pontile fibres). In the mesial part are efferent pallial fibres from the frontal lobe, in part to the pons nuclei (frontal pallio-pontile) and in part possibly from the lower frontal region to the motor nuclei of cranial nerves VII and XII. There is also the bundle already referred to (p. 464) which in its downward course passes from the lateral part of the pes to the mesial part of the medial lemniscus and is variously stated to contain fibres from cortex cerebri or from thalamus to the medulla (p. 470).

Dorsal to the pes and constituting the remainder of the basis pedunculi is a mass of gray matter which, on account of the pigmentation of its cells, is known as the *substantia nigra*. This receives many collaterals and terminals of efferent pallial fibres and possibly of fillet fibres. The destinations of the axones of its cells are not definitely known. They are stated to join the pes.

The superior cerebellar peduncle has completed its decussation below this level and its fibres are seen surrounding or within the nucleus ruber which is their terminal nucleus, as well as the nucleus of origin of the rubro-spinal tract.

Internal arcuate fibres from the gray matter of the anterior corpus quadrigeminum pass through the reticular formation, and form an oblique decussation. This decussation is the *dorsal*, or *fountain-like decussation of Meynert*. The fibres originate from cells in the anterior corpus quadrigeminum (tectum opticum), and after decussation form the descending *tecto-spinal* (*predorsal*) tract or ventral longitudinal fasciculus (see also below).

The Anterior Corpus Quadrigeminum or Superior Colliculus.—In this four principal layers may be distinguished besides the usual covering of neuroglia cells and fibres: (1) An outer white layer, *stratum zonale*. This consists of fine nerve fibres coming from the superior brachium, possibly fibres from the optic

tract and cerebral cortex. Among them are small nerve cells, mostly horizontal and with tangential or centrally directed axones. (2) A gray layer, the stratum cinereum. This consists of radially arranged nerve cells with their larger dendrites proceeding outward, and their axones inward. The largest cells lie deepest. In this layer the optic fibres principally terminate. (3) The stratum opticum consists principally of optic fibres which send their terminals mostly into the preceding layer, but also into the deeper layers. It also contains cells whose axones pass into the next layer. (4) Deep gray-white layer, or stratum lemnisci, because it is stated to contain fibres from the medial lemniscus which terminate in the superior colliculus (denied by some). This layer contains large and medium stellate cells whose axones, together with axones from cells in the more superficial layers, either pass across to the opposite colliculus or sweep ventrally around the central gray, decussate in the raphé and proceed caudally as the tecto-spinal tract. The above relations have been principally ascertained by the Golgi method. The superior colliculus also possibly receives fibres from the lateral lemniscus and spino-thalamic tract. It also receives fibres from the occipital and temporal cortex cerebri.

Belonging to the midbrain is the posterior commissure (not in the section) the fibres of which cross in the roof just anterior to the superior colliculus. Its fibres originate from collicular cells (in turn receiving optic fibres), decussate and terminate in the interstitial nucleus and other nuclei in the reticular formation.

The colliculus thus consists essentially of (a) afferent fibres from the retina (optic tract), the pallium and possibly other parts of the nervous system, and (b) efferent neurones to other parts of the brain and cord brought into various relations with each other in the colliculus either directly or by (c) the association cells of the colliculus, the axones of which do not leave the latter.

### Forebrain or Prosencephalon.

Interbrain (diencephalon or thalamencephalon).

In the interbrain or diencephalon, three parts may be distinguished; the *thalamus*, *epithalamus*, and *hypothalamus*. The epithalamus consists principally of the pineal body, the habenuke, and strike thalami. The hypothalamus consists mainly of the structures in the ventral expansion of the interbrain, such as the corpora mamillaria, tuber cinereum, infundibulum and posterior lobe of the hypophysis. The epithalamus and hypothalamus are principally connected with olfactory paths (see p. 477 and Fig. 321). Certain extensions forward of the tegmentum are also termed subthalamic (*e.g.*, corpus subthalamicum or corpus Luysii).

The **thalamus** comprises the great bulk of the interbrain. It consists of a number of nuclei forming links in afferent and efferent pallial paths and of other nuclei connected with the corpora striata. There is much difference of opinion both as to the number of the nuclei and

their connections. According to some authorities the thalamus may be regarded as divided into internal and external segments (usually separated by the lamina medullaris medialis). The internal segment consists of an anterior nucleus, median nucleus, the "median center" or nucleus of Luys, and a nucleus arcuatus. The external segment consists of a dorso-lateral, an external ventro-lateral, an internal ventrolateral, and a ventral nucleus. To the external segment should be added the pulvinar and lateral and medial geniculate bodies (metathalamus). The various nuclei of this external segment receive the fibres of the afferent pallial paths and complete the paths by sending fibres to the cortex pallii. These paths are (1) the medial lemniscus, spinothalamic, and secondary trigeminal tracts (general sensory from body and face) to the ventro-lateral nuclei and thence to the cortex of the central region of the pallium; (2) the lateral fillet or brachium of inferior colliculus (hearing) to the medial geniculate body, and thence to the temporal region of the pallium; (3) the optic tract to the lateral geniculate body and thence to the occipital pallial cortex; (4) part of the superior cerebellar peduncle (also said to be distributed to nuclei of inner segment). The visceral (including gustatory) and vestibular paths to the pallium are not definitely known. As the olfactory nerve belongs to the endbrain, its path to the pallium does not traverse the thalamus. Besides giving rise to the above thalamo-cortical fibres, the external thalamic segment in all probability receives many descending fibres from the cortex pallii. The various fibres connecting thalamus and cortex constitute the thalamic radiations. In general the anterior parts of the cortex are connected with the anterior part of the external thalamic segment, the middle with the middle, and the posterior with the posterior. It is also probable that the thalamo-cortical fibres from the various lateral nuclei are arranged dorso-ventrally, so that the fibres from the ventral parts pass to the ventral part of the central region of the pallium, dorsal to dorsal, etc. (E. Sachs.)

The nuclei of the internal segment of the thalamus do not appear, according to some recent researches, to have direct connections with the cortex pallii. The anterior nucleus receives the bundle of Vicq d' Azyr (mamillo-thalamic tract) and probably sends fibres to the nucleus caudatus (see p. 478). It thus belongs to the olfactory apparatus. The median nucleus is also probably connected with the nucleus caudatus. The median center of Luys and the nucleus arcuatus send fibres to adjoining thalamic nuclei, especially the lateral nuclei, and appear to be thus association nuclei. Other authorities affirm that

ascending tracts are received by some of these internal nuclei and that they have direct cortical connections.

Descending tracts coming directly from the thalamus have not been definitely demonstrated. The ventral nucleus appears to send fibres to the nuclei of the cranial nerves V, VI, VIII, and X, via the medial longitudinal fasciculus. (E. Sachs.)

#### PRACTICAL STUDY.

11. Transverse Section through the Junction of Midbrain and Thalamus. (Figs. 205 and 318.)

The most conspicuous change from the last section is the appearance, or increase, of the geniculate bodies and pulvinar, and the thalamic radiations.

Efferent Peripheral Neurones.—The nuclei and root fibres of the III nerve are still present.

Afferent Roots, their Terminal Nuclei, Secondary Tracts, and Tertiary Neurones.—The fibres of the *optic tract* (optic "nerve") are seen entering the ventral surface of one of their terminal nuclei, the *lateral* or *external geniculate body*. Other optic fibres (not entirely traceable) enter the pulvinar thalami and the superior colliculus (*Stro*) (see also preceding section). On the dorso-lateral surface of the lateral geniculate body, a bundle of fibres accumulates which represents the beginning of the geniculo-calcarine tract to the occipital cortex, thereby completing the *visual path*.

Internal to the lateral geniculate body is the medial (internal) geniculate body which now contains the terminals of the brachium of the inferior colliculus. Fibres from its cells gather on its lateral surface. These represent the beginning of the geniculo-temporal tract to the temporal cortex, thereby completing the auditory path.

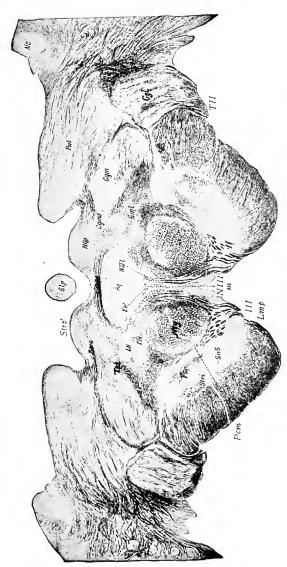
Internal and ventral to the medial geniculate body are the medial lemniscus (bulbo-thalamic) and spino-thalamic tracts about to terminate in the ventro-lateral thalamic nuclei whose axones complete the *general sensory path* by passing to the central cortex.

The central tegmental tract can hardly be distinguished.

Intersegmental Neurones.—The nucleus ruber is still large, but the remainder of the reticular formation has nearly disappeared. The medial longitudinal fasciculus is much diminished as its ascending fibres terminate in the nucleus of nerve III and many of its descending fibres originate from cells below this level.

Efferent Suprasegmental Neurones.—The pes pedunculi occupies the same position, and dorsal to it is the diminished substantia nigra. Along the ventromesial border of the pes a bundle of fibres can sometimes be distinguished (Fig. 318, Lmp), which at lower levels comes to lie mesial to the medial lemniscus (aberrant peduncular fibres, comp. p. 467). Descending pallial fibres (not distinguishable) also probably form part of the thalamic radiations (pp. 469, 472).

Fibres of the superior cerebellar peduncle may be seen within and around the nucleus ruber. Some of these terminate in the latter, some pass further forward to end in the thalamus (compare pp. 455, 469).



laterale; III, fasciculus tegmenti lateralis; Lm, lemniscus medialis; LmP, fasciculus lemnisci ad pedunculum; NG, nucleus NIIII, nucleus oculomotorii lateralis; NIIIm, nucleus oculomotorii medialis (centralis); NQa, nucleus corporis quadrigemini anterioris; NIg, Nucleus ruber tegmenti; Peni; pedunculus corporis mammillaris; Pp, pes pedunculi; Pul, pulvinar (thalami); Sn.S, substantia nigra; Stri, stratum intermedium (pedunculi): Stro, stratum 'gm, corpus geniculatum mediale (or internum); Ugma, ganglion accessorium corp genicul. med.: Url, pars retrolenticularis capsulæ internæ; EIF, Edinger-Westphal nucleus; FII, fasciculi tegmenti of Forel; FIp, fasciculus longitudinalis medialis (posterior); G/p, glandula pincalis; Gmd, ganglion mesencephali dorsale; Gml, ganglion mesencephali opticum; Strz', stratum zonale corp. quadrigemini; TII, tractus opticus; T3t, Tractus spinothalamicus; Fsp. fasciculus III, Nervus oculomotorius. Aq, Aquæductus Sylvii; Cgl, corpus geniculatum laterale (or externum) Section through the Junction of Midbrain and Thalamus. 318.—Transverse subthalamico-peduncularis. caudatus. Marburg.)

The Anterior Corpus Quadrigeminum is somewhat diminished. The *posterior commissure* passes across in the roof dorsal to the central gray (see preceding section).

The Thalamus (can hardly be included under the preceding structures).— The corpora geniculata have been mentioned. The *pulvinar* thalami is a large gray mass dorsal to the medial geniculate body. Fibres passing laterally from it contribute to the *retrolenticular portion of the internal capsule (Cirl)*. These fibres are a part of the *thalamic radiations*.

The nucleus caudatus (a portion of the corpus striatum of the endbrain) is present.

12. Section through the Interbrain at the Level of the Optic Chiasma. (Figs. 295 and 319.)

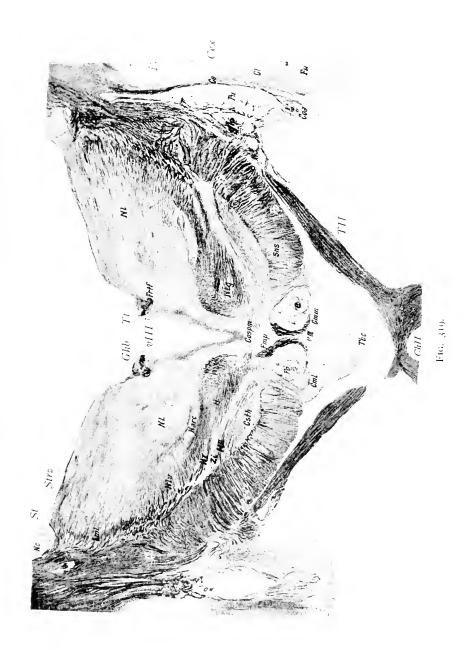
Efferent Peripheral Neurones.—None present.

Afferent Roots, their Terminal Nuclei, Secondary Tracts, and Tertiary Neurones.—Fibres of the optic nerve are seen decussating and forming the *optic chiasma*. The further continuation of the optic fibres to their termination is called the *optic tract*. Both nerve and tract constitute the secondary optic tract, the optic chiasma being analogous to the decussation of the medial lemniscus and of the lateral lemniscus (trapezius). (For further description of optic paths see Fig. 320.)

The medial lemniscus, spino-thalamic, and secondary trigeminal tracts are now lost in the ventro-lateral thalamic nuclei, cells of which constitute the tertiary neurones of the various afferent pallial paths (see pp. 469 and 470).

Intersegmental Neurones.—The cephalic end of the nucleus ruber is still present on the right (Ntg). On the left are seen some fibres in its place, lateral to which are two transverse bundles enclosing a strip of gray matter. These are known as the area tegmenti or field of Forel and represent a subthalamic forward extension of the tegmentum. The gray or zona incerta may be regarded as representing a continuation of part of the reticular formation. The ventral bundle of fibres (HII) are probably fibres from the red nucleus passing through the pes as perforating fibres (fp) on right) to the globus pallidus (glp), right). The dorsal bundle (HI) probably represents fibres connecting red nucleus and pallium, probably from pallium to red nucleus. Other fibres in this region are probably fibres of the superior cerebellar peduncle which have passed by the nucleus ruber to the

F16. 310.—Section through the Interbrain at the Level of the Optic Chiasma. (The chorioid plexus of the third ventricle has been removed.) Weigert preparation. (Marburg.) Ce, Capsula externa; Cex, capsula extrema; ChII, chiasma nervorum opticorum (or optic chiasma); Ci, capsula interna; Cl, claustrum; Cml, ganglion laterale corp. mammillaris; Cmm, ganglion mediale corp. mammill.; Coa, commissura anterior; Cospm, commissura supramammillaris; Csth, corpus subthalamicum; e, nucleus externus gangl. med. corpor. mammillaris; Fmp, fasciculus mammillaris princeps; Fo, fornix; Fp, fibra perforantes (pedunculi); frtf, fasciculus retroflexus (Meynert); Fsp, fasciculus subthalamico-peduncularis; Fu, fasciculus uncinatus; Ghb, ganglion habenulæ; glp, globus pallidus; II, area tegmenti Forel; III, pars dorsalis area tegmenti; HII, pars ventralis area tegmenti; I, insula Reillii; i, nucleus internus gangl. mdial. corp. mammillaris; Lml, lamina medullaris lateralis; Nare, nucleus arcuatus thalami; Ne, nucleus caudatus; NL, nucleus Luysii (nucleus centralis, or median centre, thalami; Nl, nucleus lateralis thalami; Nlv, nucleus lateralis ventralis thalami; Nlg, nucleus ruber tegmenti; Pp, pes pedunculi; Pu, putamen; SnS, substantia nigra; St, stria cornea; Strz, stratum zonale thalami; TII, tractus opticus; Tbc, tuber cincreum; Tt, tenia thalami; VIII, ventriculus tertius; Zi, zona incerta.



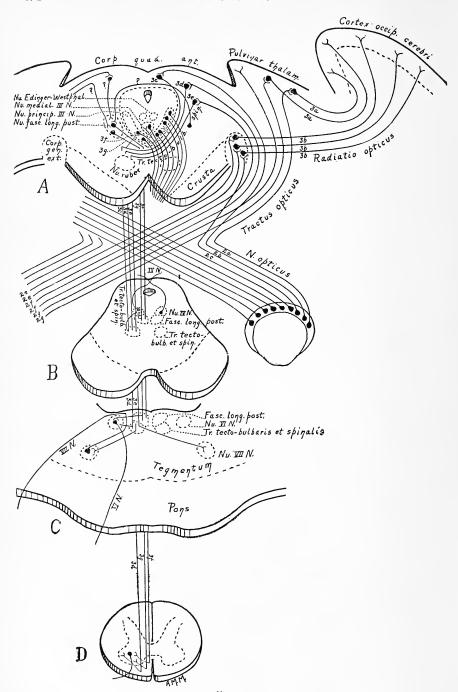


FIG. 320.

### EXPLANATION OF FIG. 320.

Fig. 320.—Diagram of the Optic (II) Nerve and some of its Principal Connections. A, Level of nerves II and III; B, level of nerve IV; C, level of nerves VI and VII; D, spinal cord. Neurone groups are represented by one or several individual neurones.

The rods and cones (receptors) and the bipolar cells (=Neurone No. 1) of the

retina are not indicated.

Neurone No. 2.—2 a, Axones of ganglion cells in temporal part of retina pass to pulvinar of thalamus of same side; 2b, axones of ganglion cells in temporal retina pass to anterior corpus quadrigeminum of same side; 2c, axones of ganglion cells in temporal retina pass to external geniculate body of same side; 2c, axones of ganglion cells in nasal side of retina cross in optic chiasma and pass to external geniculate body of opposite side; 2f. axones of ganglion cells in nasal side of retina cross in optic chiasma and pass to anterior corpus quadrigeminum of opposite side; 2g, axones of ganglion cells in nasal side of retina cross in optic chiasma and pass to anterior corpus quadrigeminum of opposite side; 2g, axones of ganglion cells in nasal side of retina cross in optic chiasma and pass to pulvinar of thalamus of opposite side. Macular fibres

are partly crossed and partly uncrossed.

Neurone No. 3.—3 a, Axones of cells in pulvinar to cortex of occipital lobe of cerebrum (this connection is disputed); 3 b, axones of cells in external geniculate body to cortex of occipital lobe of cerebrum; 3 a and 3b constitute the primary optic radiation; 3 c, 3 d and 3 e, axones of cells in middle layer of tectum (roof) of anterior corpus quadrigeminum decussate ventral to medial longitudinal fasciculus (dorsal tegmental decussation or decussation of Meynert) and form the tractus tecto-bulbaris et spinalis or predorsal bundle. (Tr. tectobulb. et spin.) to bulb (medulla) and anterior column of cord, innervating by collaterals and terminals, directly or indirectly, chiefly the nuclei of III, IV, VI, and VII cranial nerves and motor nuclei of spinal nerves. 3 f and 3 g (possibly another neurone intercalated between these and optic terminals), axones of cells in interstitial nucleus of Cajal (Nu. fasc. long. post.) form part of medial longitudinal fasciculus and descend on same side to anterior column of cord next to anterior median fissure, innervating nuclei of III, IV, and VI cranial nerves and motor nuclei of spinal nerves.

Neurone No. 4.—Axones of cells in above-mentioned motor nuclei. Axones from cells in median nucleus of nerve III (Nu. med. III N.) and possibly in Edinger-Westphal nucleus, probably innervate the intrinsic muscle of eyeball (ciliary and pupillary reflex path).

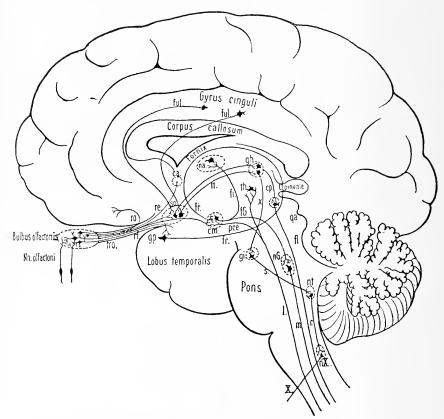
Pallio-tectal fibres, by means of which the quadrigeminal reflex centre is brought

under the control of the cerebral cortex, are not indicated.

It is evident from the diagram that the cerebral pathway of the optic nerve is via the external geniculate body (and pulvinar of thalamus?), and the reflex pathway is via the superior colliculus (anterior corpus quadrigeminum).

lateral nucleus and median center of the thalamus (see also p. 469). The interstitial nucleus of Cajal falls in the level between this and the preceding section.

Efferent Suprasegmental Neurones.—The pes pedunculi now lies partly between the thalamus and nucleus lenticularis (see p. 478) constituting the greater part of the *internal capsule*. The parts of the internal capsule as shown in horizontal sections of the hemispheres are shown in figure 322. The most dorsal part is here passing into the corona radiata (p. 478) of the cerebral hemispheres (not included in the section). The part present in this level is the most posterior part of the capsule (occipito-temporal pallio-pontile fibres (see p. 479).



F16. 321.—Diagram of Olfactory Paths (von Bechterew.) X, Root fibres of vagus;  $\epsilon a$ , commisura anterior;  $\epsilon m$ , corpus mammillare;  $\epsilon p$ , fibres from nucleus habenulæ to posterior commissure; fG, tract from corpus mammillare to Gudden's nucleus; fh, fasciculus mammillo-thalamicus; fh, fasciculus longitudinalis medialis; fr, fornix; ful, fibres of fornix longus; gh, nucleus habenulæ; gi, ganglion interpedunculare; gp, gyrus pyriformis; l, lemniscus medialis; m, fibres from Gudden's nucleus to substantia reticularis grisea; n, nucleus anterior thalami; nG, Gudden's nucleus; n, nucleus tegmenti (v. Gudden); nX, nucleus motorius nervi vagi; peE, pedunculus corporis mammillaris from fillet; qa, corpora quadrigemina; r, fibres from nucleus tegmenti (v. Gudden) to nuclei of cranial nerves; re, radix lateralis tractus olfactorii; rf, fibres of tractus olfactorius to trigonum olfactorium; ro, radix medialis tractus olfactorii; s, fibres from ganglion interpedunculare to nucleus tegmenti; so, area of trigonum olfactorium; th, thalamus; tro, tractus olfactorius; tt, tænia thalami; x, fasciculus retroflexus.

Dorsal to the mesial part of the pes is the *corpus subthalamicum* which has replaced the substantia nigra. It receives collaterals from the pes and is said to contribute fibres to the latter. Superior cerebellar peduncle (see Intersegmental Neurones above).

**Thalamus.**—At this level the *ventro-lateral nucleus*, the *nucleus arcuatus*, and the *median center of Luys* can usually be distinguished. At the outer border of the thalamus, fibres accumulate forming the *lateral medullary lamina*. These fibres continue outward as *thalamic radiations*, entering the internal capsule which they may follow a distance, or cross obliquely and enter the corona radiata.

Epithalamic and Hypothalamic Structures and their Connections.— The ganglia habenulæ are two small masses of gray matter occupying eminences on the mesial walls of the thalamus. A bundle of fibres near each is the stria medullaris (near the tænia thalami) consisting of fibres from the olfactory bulb and trigonum and representing afferent olfactory connections (p. 478). The ganglion habenulæ contains a mesial small-celled and a lateral large-celled nucleus. Their axones form the fasciculus retroflexus of Meynert to the interpeduncular ganglion, situated more caudally (Fig. 321). There is also a commissura habenularis connecting the two ganglia. The stria terminalis (stria cornea), another olfactory connection, lies in the groove between the ventricular surfaces of nucleus caudatus and thalamus. The tuber cinercum is seen projecting ventrally. Dorsal to this are seen the corpora mammillaria containing lateral and mesial nuclei. The mammillary body receives the fibres of the *fornix* (from the rhinopallial cortex, see below) and also fibres from the medial fillet. It gives rise to the bundle of Vicq d'Azvr (mammillo-thalamic tract) to the thalamus, and mammillo-tegmental fibres to the nucleus of Gudden (Fig. 321) and red nucleus. The fibres entering the mammillary body from the fillet (and other sources) constitute its *peduncle*. (See also Endbrain).

On the right is seen the posterior part of the *nucleus lenticularis* of the corpus striatum.

### THE ENDBRAIN OR TELENCEPHALON.

The endbrain consists of *pallium* (dorsal expanded part), *corpus striatum*, and *rhinencephalon*. Two principal parts of the pallium may be distinguished; the olfactory pallium or rhinopallium (archipallium), including principally the cornu ammonis and gyrus dentatus; and the neopallium including the greater part of the cerebral hemispheres. The rhinencephalon<sup>1</sup> includes the olfactory nerves and bulb, the trigonum olfactorium, the tuberculum olfactorium or anterior perforated space, and the gyrus hippocampi, in part at least (pyriform lobe).

The olfactory nerve is composed of axones of cells in the olfactory mucous membrane which terminate in the olfactory bulb. They there form synapses with the dendrites of the mitral cells, the axones of which constitute the secondary tract, part of which decussates in the

<sup>&</sup>lt;sup>1</sup> The term rhinencephalon is often used to include also the olfactory pallium.

pars olfactoria of the anterior cerebral commissure. A secondary tract ("lateral root") proceeds, with tertiary tracts, to the cortex of the gyrus hippocamp; and thence to the cornu ammonis. Efferent axones of cornu ammonis cells are collected in the fimbria and descend by the

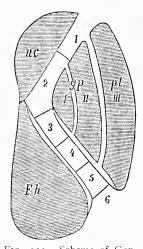


Fig. 322.—Scheme of General Arrangement of fibres in Internal Capsule. (von Bechterew.) I, II, III, The three parts of the lenticular nucleus; nc, nucleus caudatus; Fh, thalamus; gp, globus pallidus; pt, putamen; 1, fibres of anterior thalamic peduncle; 2, fibres of medial (frontal) pons system; 3, fibres of motor cranial nerves; 4, pyramidal fibres; 5, pyramidal fibres mingled with those of the afferent (sensory) path; 6, fibres of the lateral pons system. The various systems are not sharply marked off as indicated, but are more or less intermingled.

fornix to the mammillary body, the further caudal connections of which have been described (p. 477). Fibres of the fimbria also cross, forming the commissure of the fornix (olfactory pallial commissure). Secondary olfactory tracts also pass to the trigonum, whence tertiary neurones pass as the stria medullaris to the ganglion habenulæ (see p. 477 and Fig. 321). The principal commissure of the rhinencephalon is the anterior cerebral commissure.

The corpus striatum consists of the nucleus caudatus and nucleus lenticularis, the connections and significance of which are obscure. They receive collaterals from the descending pallial fibres which pass by them and also apparently send out fibres to join the latter. They also have connections with rhinenencephalon and thalamus.

The **pallium** consists of an extensive external convoluted sheet of gray matter (cortex pallii or cortex cerebri) and of white matter underlying the gray. In the white matter may be distinguished the corona radiata composed of the afferent and efferent pallial fibres connecting the pallium with other parts of the brain (projection fibres). The remaining fibres of the white matter are association fibres of the pallium and are either crossed

or commissural, connecting the two hemispheres (corpus callosum and fornix commissure), or are uncrossed. The term association fibres is often restricted to the latter.

The afferent connections of the neopallium (p. 469) and rhino-pallium (pp. 477, 478) have been summarized and also the efferent connections of the rhinopallium (p. 478).

The following are the principal descending or efferent connections

of the neopallium: (1) The pyramidal or pallio-spinal tract. This is composed of the axones of the giant cells (of Betz) of the arm, body, and leg precentral motor areas. They descend in the corona radiata, the posterior limb of the internal capsule, middle part of the pes, and thence through pons and medulla to the cord. Their decussation and further course has been described. (2) The descending tracts to the motor nuclei of the cranial nerves originate from precentral cells of the various areas controlling the muscles in question and pass down in the vicinity of the genu of the internal capsule. Their path is not so well known but they apparently do not pass down in the pes throughout their course (pp. 470, 467, etc.). (3) The pallio-pontile system to the pons (continuation to opposite cerebellar hemisphere). This originates in various parts of the cortex. The fibres from the occipital and temporal regions pass down in the extreme posterior part of the internal capsule and lateral part of the pes, those from the frontal region pass down in the anterior limb of the internal capsule and mesial part of the pes. (4) Pallio-tectal fibres to the midbrain roof. (5) Fibres to the substantia nigra and corpus subthalamicum. (6) Fibres to the red nucleus. (7) Pallio-thalamic fibres (see p. 469).

(8) Fibres, or collaterals, to the corpora striata. (Fig. 322.)

The crossed association fibres of the neopallium (corpus callosum) connect principally corresponding parts of the hemispheres. long uncrossed association fibres (furthest from the gray matter) form certain more or less well-defined bundles among which are the following: (1) The cingulum, a longitudinal bundle near the corpus callosum; also contains projection fibres and belongs to the olfactory part of the brain as well as to the neopallium. (2) The superior longitudinal fasciculus or fasciculus arcuatus; connects frontal with occipital and part of temporal lobes. (3) The inferior longitudinal bundle connecting temporal and occipital lobes. It may, however, be a projection bundle. (4) The uncinate fasciculus connecting frontal and temporal lobes. (5) The perpendicular fasciculus of Wernicke connecting inferior parietal and fusiform lobules. Projection fibres may form portions of these bundles.

Shorter association fibres nearer the gray matter connect adjoining convolutions (fibræ propriæ of Meynert) and in the gray matter itself are fibres which fall under this category.

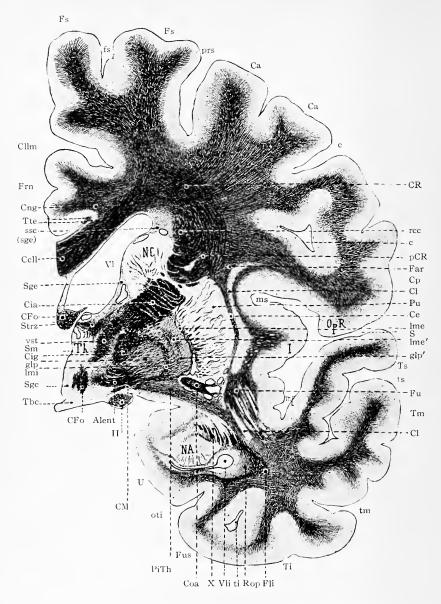


Fig. 323.—Transverse Section through the Cerebral Hemispheres, Corpora Striata and Thalamus. Weigert preparation. (Dejerine.) II, Tractus opticus; Alent, ansa lenticularis; c, sulcus centralis (Rolandicus); Ca, gyrus centralis anterior; Cell, corpus callosum; Ce, capsula externa; CFe, columna fornicis; Cia, crus anterior capsul. int.; Cig, genu capsul. int.; Cl, claustrum; ellm, sulcus callosomarginalis; Cng, cingulum; Coa, commissura anterior; Cp, gyrus centralis posterior (ascending parietal convolution); CR, corona radiata; Far, fasciculus arcuatus; Fli, fasciculus longitudinalis inferior; Frn, gyrus fornicatus; Fas, sulcus frontalis superior; Fs, gyrus frontalis superior; Figsciculus uncinatus; Fus, gyrus fusiformis; glp, globus pallidus (inner segment); glp', globus pallidus (outer segment); I, insula; Ime, lamina medullaris externa nuclei lenti-

### PRACTICAL STUDY.

## 13. Transverse Section through the Cerebral Hemispheres, Corpora Striata and Thalamus. (Fig. 323)

First distinguish in general (1) the *pallium*, its cortex and white matter, (2) the *corpus striatum* and its divisions, *i.e.*, the *caudate nucleus* and the *putamen* and *globus pallidus* (two subdivisions of the lenticular nucleus) and (3) the thalamus and other structures of the interbrain.

Afferent Roots, their Terminal Nuclei, Secondary Tracts, and Tertiary Neurones.—The optic tract here forms a part of the ventral surface of the brain. The geniculo-cortical portion of the optic path forming a part of the optic radiation may be seen. Other afferent pallial connections are hardly distinguishable among the fibres connecting thalamus and pallium.

Efferent Suprasegmental Neurones.—A great part of the pes has now entered the corona radiata. The part now about to enter the corona is the anterior limb of the internal capsule (Fig. 322). The ansa lenticularis is, according to some authorities, composed of fibres or collaterals from the pes to the lenticular nucleus. The fibres of the anterior peduncle of the thalamus are evident. They are considered by some as composed of cortico-thalamic fibres. The anterior pillars of the fornix (efferent rhinopallial) are shown cut through twice, the upper section shows its earlier course emerging from the fimbria, the lower section is near its termination in the mammillary body.

For other structures of thalamus, epithalamus, and hypothalamus see Fig. 323. The Pallium.—In the white matter distinguish as far as possible the corona radiata, the corpus callosum, and the long association bundles (inferior longitudinal fasciculus, fasciculus uncinatus, and fasciculus arcuatus) (see p. 479). Note the nucleus amygdaliformis, the anterior perforated space and the anterior commissure, belonging to the rhinencephalon.

Other details shown in figure 323 should be studied.

The Cerebral Cortex.—The following types of cells are found in the cerebral cortex: (1) Pyramidal cells. This is the prevailing type and is characterized by a long apical dendrite usually directed toward the surface of the brain. This dendrite gives off branches, and usually reaches the outer cortical layer, there to break up into a number of branches. From the cell body are also given off a number of basal

cularis; lmc', supplementary lamina of the outer segment of the globus pallidus: lmi, lamina medullaris interna nuclei lenticularis; mp and ms, sulcus circularis (Reili): NA, nucleus amygdaliformis; Nc, nucleus caudatus; OpR, operculum; oti, sulcus occipitotemporalis inferior; pCR, pes coronæ radiatæ; PiTh, pedunculus inferior thalami; prs, sulcus præcentralis; Pns, putamen; rcc, stratum reticulum coronæ radiatæ; Rop, radiatio optica; S, fissura Sylvii (posterior branch): Sgc, substantia grisea centralis; sM, sulcus Monroi; Sgc, substantia grisea subependymalis; ssc, stratum subcallosum; Strz, stratum zonale thalami; Tbc, tuber cinereum; Th, thalamus opticus; ti, sulcus temporalis inferior; Ti, gyrus temporalis inferior; Ts, gyrus temporalis medius; ts, sulcus temporalis superior; ts, sulcus temporalis superior; ts, sulcus temporalis superior; ts, sulcus temporalis superior; ts, tenia tecta; ts, uncus; ts, ventriculus lateralis; ts, ventriculus lateralis (cornu inferios): ts, pedunculus anterior thalami; ts, pedunculus putaminis; ts, Commissure of Meynert.

dendrites. By the Golgi and Ehrlich methods, gemmules can be demonstrated on the dendrites. The axone proceeds from the base of the cell (opposite to the apical dendrite) and usually passes into the white matter. It gives off several collaterals on its way to the white matter. (2) Stellate cells. These have dendrites passing in various directions. Many, especially the smaller (granules), may have short axones (Golgi's second type). (3) Polymorphous cells of a triangular or spindle shape are usually found in the deepest layers of the cortex and send their axones into the white matter. (4) Horizontal cells (of Cajal), found in the outer layer, with long horizontal dendrites and axones confined to the outer layer. (5) Inverted pyramidal cells (of Martinotti) with axones directed toward the surface. (Fig. 325.)

The largest cells of the cortex (giant cells of Betz) are very rich in chromophilic substance arranged similarly to that in the efferent root cells of cord and brain. The medium and small cells have fewer chromophilic bodies which are often in the shape of irregular masses, either near the periphery of the cell or around the nucleus. The neurofibrils vary in their arrangement according to the shape of the cell.

The neuroglia cells and fibres are in general similar to those in other parts of the nervous system.

The cells of the cortex are arranged in layers which have the same general character throughout, but in various regions exhibit variations such as suppression, diminution, enlargement, or subdivision of certain layers. The cell layers of the cortex are: (1) Molecular layer (zonal layer, plexiform layer of Cajal). This contains the horizontal cells, other cells with short axones, and also receives the axones of the Martinotti cells. Besides this, it contains the terminal branches of the apical dendrites of the pyramidal cells. (2) External granular laver, very often termed the layer of small pyramids. The dendrites of the cells of this layer mostly enter the first layer, their axones pass downward into the white matter. (3) Pyramidal layer, often called the layer of superficial medium and large pyramids. This is composed principally of typical pyramids sending dendritic branches into the first layer and axones into the white matter. The larger cells are in the deeper part (sublayer of large pyramids). This layer also contains many granule cells with short axones and cells of Martinotti. (4) Internal granular layer. Here the predominating elements are stellate cells, the larger usually sending their axones into the white matter. Among these are many short axone granules, the axones of which end in the

same layer or in more superficial layers. (5) Ganglionic layer or deep layer of large and medium sized pyramids. These send their axones into the white matter. Mingled with them are short axone and Martinotti cells. (6) Multiform layer or layer of polymorphous cells. These

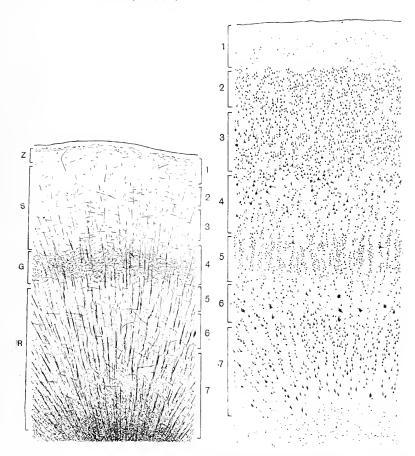


FIG. 324.—Vertical Sections of Calcarine Area of Adult Human Cortex. *Left*, Weigert preparation showing fibre arrangement. *Right*, Arrangement of cells. (Campbell.) *G*, Line of Gennari; *R*, radiary layer; *S*, supraradiary layer; *Z*, layer of superficial tangential fibres in molecular layer, 1, molecular layer; 2, external granular (small pyramid) layer; 3, pyramid layer; 4 (large granules) and 5 (small granules), internal granular layer; 6, ganglionic layer (containing solitary cells of Meynert); 7, multiform layer.

usually send their axones into the white matter. Mingled with them are short axone and Martinotti cells. (Figs. 324, 325 and 326.)

The cells of the cortex obviously fall into two classes: efferent projection cells and association cells. Which cells are projection cells is not definitely known, except in the case of the precentral motor cortex

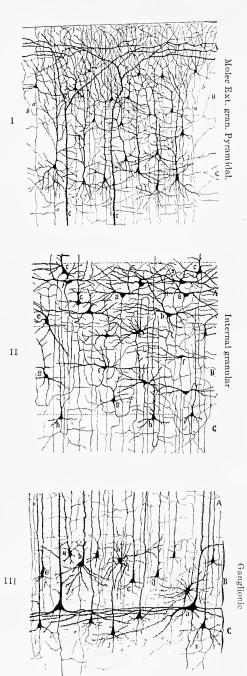


Fig. 325.

where it has been established that these cells are the cells of Betz, the axones of which form the pyramidal tract. An examination of this area shows that the association cells must enormously outnumber the efferent projection cells in the cortex. The association cells comprise the short axone cells and cells the

Fig. 325.—Vertical section of Calcarine Area of Cortex of an Infant 15-20 days old. (Cajal, combined from three, *I*, *II* and *III*, somewhat overlapping figures. The multiform layer is not included). Golgi's method,

I.—A, Molecular layer; B, external granular layer (of small pyramids); C, pyramidal layer (of medium pyramids); a, descending axones; b, ascending collaterals; c, apical dendrites of large pyramidal cells in ganglionic layer.

II.—A, Sublayer of large stellate cells; B, sublayer of small stellate cells; C, outer part of ganglionic layer; a, crescentic stellate cells; b, and f. horizontal, spindle-shaped stellate cells; c, medium-sized pyramidal cells; e, stellate cells with arched axones; g, triangular stellate cells with stout, arched collaterals; h, pyramidal cells with arched axones.

III .-- A, Part of internal granular layer; B, sublayer of small pyramidal cells with arched ascending axones; C, sublayer of large pyramids; a, large pyramidal cell; b, medium-sized pyramidal cell with long descending axone; c, small pyramidal cell with arched ascending axone; d, pyramidal cell with axone split into two arched ascending branches; e, pyramidal cells whose axone sends out various ascending branches; f,g,h, stellate cells with ascending axones which branch in B and in the sublayer of small stellate cells; i,j,k, pyramidal cells with arched ascending axones which send branches into the ganglionic layer.

fibres of which enter the white matter, but terminate in some other part of the cortex forming the association fibres of the white matter. (Compare p. 479.)

It is thus evident that every part of the cortex contains terminations of association fibres. The areas containing the terminations of afferent projection fibres are those which receive the thalamocortical continuations of the afferent pallial paths and the continuations of the olfactory paths. From observations made with the Golgi method it seems probable that the latter are represented by coarse fibres which may ramify throughout the greater part of the thickness of the cortex, but are confined mainly to the third and fourth layers. The principal areas of the cortex receiving the afferent projection fibres are the olfactory hippocampal area, the calcarine (visual) area (fibres from lateral geniculate body), the transverse temporal gyri of Heschl (auditory fibres from medial geniculate body), and the pre- and post-central areas (postcentral only, according to some authorities—area of general sensation from body and head—fibres from ventrolateral thalamic nuclei). (Fig. 327.)

The medullated fibres of the cortex consist of radially, obliquely, and tangentially running fibres. The radial fibres enter the cortex from the white matter in bundles known as the radiations of Meynert which extend a variable distance toward the periphery, diminishing until they end usually in the third layer. They consist mainly of the axones of the adjoining cells passing to the white matter. Their fibres are of varying caliber, the coarsest originating from the largest cells. The oblique fibres form a dense plexus of coarse and fine fibres between the radial fibres, the interradiary plexus. Toward the surface (in the second and third cell layers) they form a delicate plexus of fine fibres. This latter plexus lies principally superficial to the radiations of Meynert and is the supraradiary plexus. A denser aggregation of irregular fibres constitutes the line or stria of Baillarger located in the layer of superficial large pyramids. It is probable that this represents a layer especially rich in terminals of fibres from the white matter. Other striæ are also described. Besides representing the terminals of such fibres the oblique fibres in general are also composed of medullated collaterals of axones of pyramids and possibly arborizations of short axone cells. A few coarser fibres ascending to the molecular layer are ascending fibres from Martinotti cells. The deep tangential fibres, most marked on the sides of the convolutions and in the sulci, are considered short association fibres belonging to the

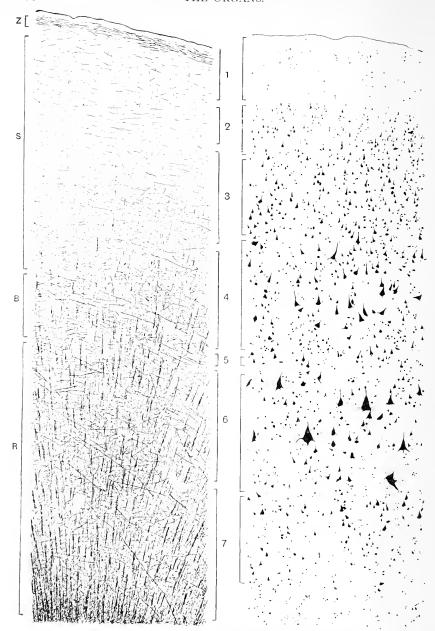
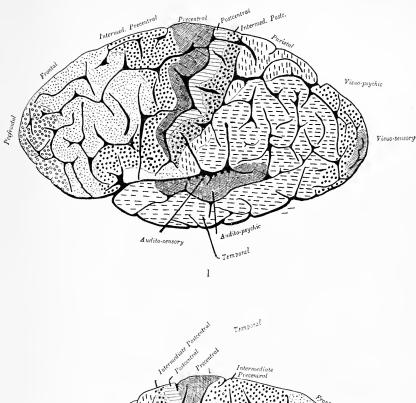
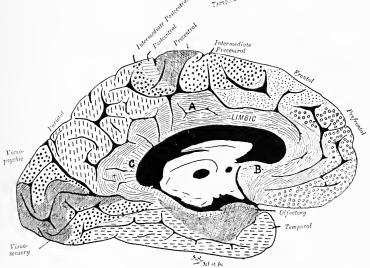


FIG. 326.—Vertical Sections of Precentral or Motor Area of Adult Human Cortex. Left, Weigert preparation showing fibre arrangement. Right, Arrangement of cells. (Campbell.) B, Position of line of Baillarger, its position obscured by surrounding wealth of fibres; R, radiary layer; S, supraradiary layer; Z, layer of superficial tangential fibres in molecular layer, dense and well defined; 1, molecular layer; 2, external granular layer (small pyramids), 3 (medium-sized) and 4 (large), pyramid layer; 5, internal granular layer, indistinct and with scattered granule or stellate cells; 6, ganglionic layer (large deep pyramids); 7, multiform layer.





Π

Fig. 327.—Diagram (orthogonal) showing Cortical Areas as determined by the Arrangement and Distribution of Fibres and Cells (A. W. Campbell). Large portions of important areas are concealed within fissures, e.g. the calcarine or visual (visuo-scn-sory, within the calcarine fissure) precentral (motor) and postecutral (within the fissure of Rolando) and especially the acoustic (audito-sensory) which is almost completely hidden within the Sylvian fissure. A, B and C, parts of the limbic lobe.

fibræ propriæ of Meynert. In the molecular layer are the *superficial* tangential fibres consisting of the axones of the horizontal cells and the terminals of the axones of Martinotti cells. (Figs. 324 and 326.)

The cortex is divided into various areas by various investigators, the areas being distinguished (a) by the time of medullation (myelogenetic method of Flechsig), (b) by the number and arrangement of the medullated fibres (myeloarchitecture), especially the number, thickness, and distinctness of the striæ, such as that of Baillarger, formed by them and (c) by the number and arrangement of the cells (cytoarchitecture). Many such areas have been thus distinguished by different investigators with results agreeing in many respects but differing in others. The areas most clearly defined and concerning which there is perhaps the most general agreement are the various sensory (afferent projection) areas already enumerated (p. 485) and the motor (efferent projection) precentral area (Fig. 327). These areas myelinate first (at or soon after birth), next areas adjacent to them, and last areas occupying a considerable portion of the human pallium but much less extensive in other mammals. There is much difference of opinion as to the extent to which these last myelinating areas are supplied with projection fibres. According to some authorities the areas myelinating last have no projection fibres and are consequently entirely composed of association cells and fibres. Perhaps the two best-marked of the various areas are the motor and visual areas the structure of which is shown in figures 324, 325 and 326. The motor precentral cortex is characterized by the presence of the giant cells of Betz, by an almost complete absence of an internal granular layer and by a great wealth of fibres. The calcarine or visual area is characterized by a strongly marked line of Gennari (=Baillarger) and by a double or triple internal granular layer containing large granules in place, apparently, of the superficial large pyramids. The line of Gennari is probably partly composed of the terminals of the optic path.

### TECHNIC.

<sup>(1)</sup> The general structure of the cerebellum is well brought out by staining sections of formalin-Müller's fluid-fixed material with hæmatoxylin-picro-acid-fuchsin (technic 3, p. 19), and mounting in balsam.

<sup>(2)</sup> The arrangement of the cell layers of both cerebellum and cerebrum, as well as certain details of internal structure of the cells, can be studied in sections of alcohol- or formalin-fixed material stained by the method of Nissl (technic, p. 35).

- (3) The distribution of the medullated nerve fibres of either the cerebellar or cerebral cortex is best demonstrated by fixing material in Müller's fluid (technic 4, p. 6) or in formalin-Müller's fluid, and staining rather thick sections by the Weigert or Weigert-Pal method (technic, p. 29).
- (4) The external morphology of the cerebellar and cerebral neurones and the relations of cell and fibre can be thoroughly understood only by means of sections stained by one of the Golgi methods (technic, pp. 32 and 33). Especially in the case of the cerebellum, sections should be made both at right angles, and longitudinal to the long axis of the convolution. Golgi preparations from embryonic material and from the brains of lower animals furnish instructive pictures.
- (5) The silver method of Cajal should be used, especially with alcohol fixation (technic p. 34, No. 2), both for the neurofibrils and for the external morphology of the neurones. It is especially successful with the cerebellum.
  - (6) Neuroglia stains should also be used.

### The Pituitary Body.

The pituitary body or *hypophysis cerebri* consists of two lobes which are totally different both in structure and in origin.

THE ANTERIOR LOBE.—This is the larger, and is glandular in character. It is of ectodermic origin, developing as a diverticulum from the primitive oral cavity. Its mode of development is that of a compound tubular gland, the single primary diverticulum undergoing repeated division to form the terminal tubules. The original diverticulum ultimately atrophies and disappears, leaving the gland entirely unconnected with the surface. The gland is enclosed in a connective-tissue capsule, from which trabeculæ pass into the organ forming its framework. The gland cells are arranged in slightly convoluted tubules and rest upon a basement membrane. Between the tubules is a vascular connective tissue. Some of the gland cells are small cuboidal cells with nuclei at their bases and a finely granular basophile protoplasm (chief cells). Others, somewhat less numerous than the preceding, are larger polygonal cells with centrally placed nuclei and protoplasm containing coarse acidophile (eosinophile) granules (chromophile cells). While presenting different appearances and usually described as two kinds of cells, it is probable that chromophile cells and chief cells represent merely different functional conditions of the same cell. Some alveoli in the posterior portion of the lobe frequently contain a colloid substance similar to that found in the thyreoid.

As in all ductless glands, the blood supply is rich and the relations of capillaries to gland cells are extremely intimate, dense networks of capillaries surrounding the alveoli on all sides.

THE POSTERIOR LOBE.—This, like the anterior, is surrounded by a connective-tissue capsule which sends trabeculæ into its substance. In the human adult the lobe consists mainly of neuroglia with a few scattered cells, which probably represent rudimentary ganglion cells. In the human embryo, and in many adult lower animals, the nervous elements are much more prominent and more definitely arranged. Thus Berkley describes the posterior lobe of the pituitary body of the dog as consisting of three distinct zones: (1) An outer zone of three or four layers of cells resembling ependymal cells, connective-tissue septa from the capsule separating the cells into irregular groups; (2) A middle zone of glandular epithelium, some of the cells of which are arranged as rather indefinite alveoli which may contain colloid. is termed the pars intermedia. The epithelial cells are derived from the oral invagination. (3) An inner layer of nerve cells and neuroglia cells. These react to the Golgi stain, the nerve cells having axones and dendrites. Most of the axones appeared to pass in the direction of the infundibulum, but could not be traced into the latter. The posterior lobe is of ectodermic origin, developing as a diverticulum from the floor of the third ventricle. The remains of the diverticulum constitute the infundibulum.

### The Pineal Body.

The pineal body originates as a fold of the wall of the primary brain vesicle. It lies upon the dorsal surface of the inter- and mid-brain, being connected with the former. The pineal body is apparently of the nature of a rudimentary sense organ, being sometimes referred to as the *median* or *pineal eye*. In man it is surrounded by a firm connective-tissue capsule, which is a continuation of the pia mater. This sends trabeculæ into the organ, which anastomose and divide it into many small chambers. The latter contain tubules or alveoli lined with cuboidal epithelium. This may be simple or stratified, and frequently almost completely fills the tubules. Within the tubules are often found calcareous deposits known as "brain sand."

### TECHNIC.

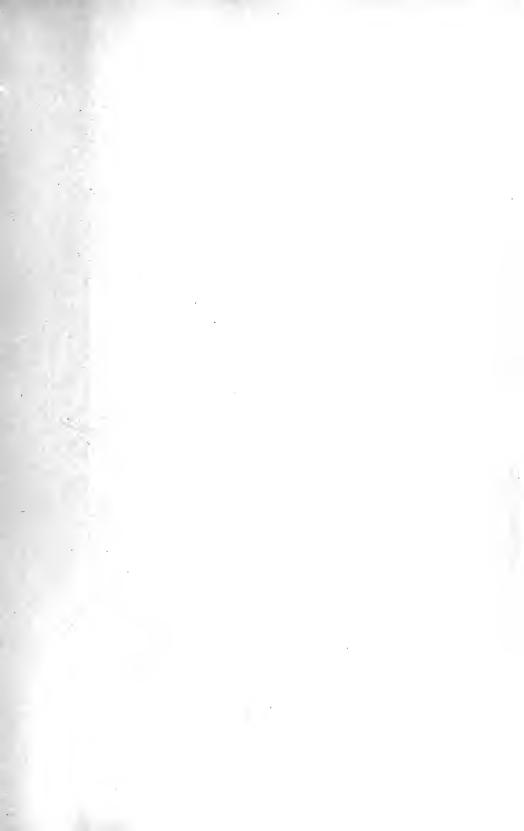
The general structure of the pituitary body and of the pineal body can be studied by fixing material in formalin-Müller's fluid (technic 5, p. 7) and staining sections with hæmatoxylin-eosin (technic 1, p. 18).

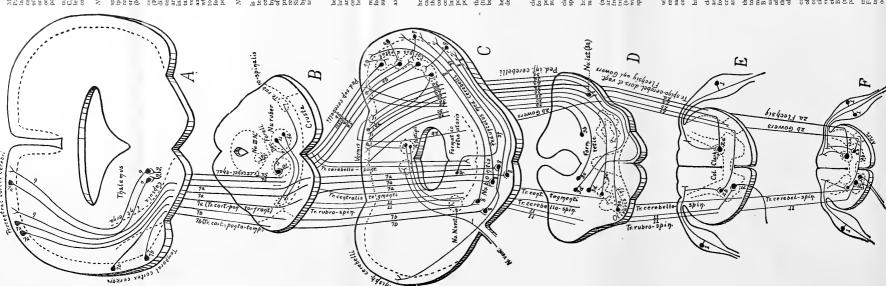
## Table of Cranial and Spinal Nerves.

				4		
Nerve	Cells of origin	Distribution of peripheral processes	Cent. processes (root fibres and central tracts)	Terminal nuclei	Axones of terminal nuclei (secondary tracts) and their distribution	Tertiary tracts
Olfactorius, Olfactory, cpi lial cells,     Opticus Ganglion cells retina     III. Oculomotor- Nucleus nerve ius in midbrain,     IV, Trochlearis, Nucleus nerve in midbrain.	I. Olfactorius. Olfactory cpithelial cells.  II. Opticus Ganglion cells of retina  II. Oculomotor- Nucleus nerve III ius  ius. In midbrain.  V. Trochlearis. Nucleus nerve IV in midbrain.	L. Olfactorius. Olfactory epithelial cells.      L. Opticus Ganglion cells of retinaretima retina in midbrain. In palpebras sup., and radix brevis gang. Ciliaris.      V. TriconhearisNucleus nerve IV Mus. obliquus superius.		clls in bulbus olfactorius.  Corpus quadrigeminum 'anterius. Corpus geniculatum ex. Corpus geniculatum ex. Corpus geniculatum ex. Corpus Thalami	Fila olfactoria. Cells in bulbus olfactorius. Tractus olfactorius, to various parts of rhinen- To rhinopallium.  Corpus quadrigeminum Tractus tect-bulb. et spin., fasc. long, med. to anterius.  Corpus geniculatum ex. Optic radiations to occipital cortex cerebri.  Pulvinar thalami Optic radiations to occipital cortex cerebri. (?)	To rhinopallium.
(a) afferent Ganglion Ganglion Ganglion Ganglion Besonce in mucleus.?  (b) efferent Motor nucleus. VI. Abducens Nucleus VI in VII. Facialis.  (a) efferent Nucleus VI in dulla.	Ganglion Gasseri (and mesencepha- lic nucleus. ?)  Motor nucleus V  Nucleus VI in me- dulla.  Nucleus VI in in	seci Rami ophthal, max. ha- and mandib to skin of heed and face, epi- helium of mouth and nose, teeth, meninges. V Museles of jaw, etc. (masseferieus, tem- portalis, prerygodeus, pal, tens, tympani, mylohyoideus). me- Muse, rectus lateralis, in Muse, of face tympani, in Muse, of face tympani,	Tractus spina. S lis V.	(a) affection Ganglion Gasseri Rami ophthal, max. Tractus spina-Sensory nucleus V and nucleus and mandib. to skin lis V.  (and mesencepha- and mandib. to skin lis V.  (substant gelat, Rolandi)  (helium of mouth and nouth and nose, tecter, meninges.  (b) effection	and nu. To motor nuclei (reflex).  spinalis Uncossed tract in dorsal part formatio reticularis Thal. rad. to cent. Corlex cerebri.  Crossed tract via lemniscus to thalamus. Thalamic radia-To cerebellum?  To cerebellum?	Thal, rad, to cent, cortex cerebri, Thalamic radiations to central cortex cerebri.
(b) afferent VIII, Acusticus.			Fase, solitarius, l	funa, digast., sylohy.  Ant. part of tongue Fasc. solitarius. Nucleus fasciculi solitarii. (tasto), palate.	Not precisely known.	
(a) vestibularis.	(a) vestibularis. Gang, of Scatha		Tractus vestib. I spinalis.	Ampullæ semicirc, ca. Tractus vestib, Nucl. tract. vestib, spin- nals, utriculus, sac. spinalis, acilis, culus, nufculus, nucleus medialis ("prin- cipal") Nucleus lateralis (Deit- crs), Nucleus superior (von Bechterew's).	Nucl. tract. vestib. spin-   Crossed asc. in post, long, fase, to midibrain and mids. adis.   Crossed asc. in post, long, fase, to midibrain and midsens medialis ("prin- crossed and uncrossed desc. in post, long, fase, to vent. col. cord and motor spinal nerves (reflex).   Uncrossed to ventro-lateral cols, cord and motor spinal nerves (reflex).   Uncrossed to ventro-lateral cols, cord and motor spinal nerves spinal nerves (reflex).   Uncrossed to midibrain and nuclei nerves VI.   IV, and III (reflex) (from Deiters').   Cerebellum Fastigio-bulbaris to Deiters', etc. (reflex).	
			_			

# Table of Cranial and Spinal Nerves. -Continued.

Tertiary tracts		cortex cerebri.			Thalamic rad. Thalamic radia- tions to central cortex cerebri.
si (secondary tribution					dex). Lits. alis.
Axones of terminal nuclei (secondary tracts) and their distribution	Nucl. accessorius	Not precisely known.	Not precisely known.		Posterior root Motor spinal nuclei (reflex).  Posterior root Tautomeric and hetero-Motor nuclei spinal nerves (reflex).  Collaterals.  Posterior root Column of Clarke
Terminal nuclei	Nucl. accessorius Nucl. oliv. sup. (reflex) Nucl. corporis trapezoidei. Tuberculum acusticum	Nucleus fasc. solitarii.	membranes Fasc. solitarius, Nucl. fasciculi solitarii cosophagus, heart, and scera uscles, heart, ia sympath.)		Posterior root Motor spinal nuclei (reflex). collaterals. collaterals. Posterior root meric cells of cord. Posterior root Tautomeric and heterocollaterals. Posterior root Tautomeric and heterocollaterals. Posterior root Meric cells of cord. Posterior root, Nucl. columns Goll and posterior root. Burdach.
Cent. processes (root fibres and central tracts)		Fasc. solitarius. 1	Fasc. solitarius. I		Posterior root collaterals.
Distribution of Peripheral processes	Organ of Corti	Gang, jugulare sup. Post. part of tongue Fasc, solitarius, Nucleus fasc. solitarii and gang. petro- (faste), muc. memb. sum. sum. op pharynx, etc. Motor nucleus—Muscles of pharynx, ant. continuation (Stylopharyngeus).	A 12 25 75	ells, Musc. sternocleido- 7th mastoideus and 8. trapezus. me- Muscles of tongue.	Vol. str. muscles. Sympath, gang. Receptors of body
Cells of origin	(b) cochlearis Gang, spiralis(X. Glossophar-	Gang, jugulare sup. land gang, petrosum.  Motor nucleus—ant. continuation nucl. ambig.	(a) afferent Gang, jugulare and Mucous membr gang, plexiform, pharynx, csoph or nodosum, inngs, heart, other viscera.  (b) efferent (a) nucl, dorsalis Smooth muscles, heart, other viscera, ale cincreæ) in glands(wa symp medulla.  (b) nucl, ventralis Muscles of larynx, (ambiguus) in medulla.  NI Accessorius.	(a) medullary = part of X b.  portion. (b) spinal por-Anterior horn cells, M u s c. sternocle from the part of the strong cerv. segments.  XII. Hypoglossus Nucl. XII in me-Muscles of tongue, pinales.	(a) efferent (som.) Anterior horn cells. Vol. str. muscles. (b) afferent Gang. spinales Receptors of body to afferent Gang. spinales
Nerve	(b) cochlearis IX. Glossophar-	-se	(a) afferent (b) efferent	(a) medullary = part of X b. portion. (b) spinal por- Anterior horn tion.  XII. Hypoglossus Nucl. XII in Spinales.	(a) efferent (som.) (b) afferent





spinal neurone—spinal grapiton cells; per spinal neurone—spinal grapiton cells; per receptora; contral processes ending in muscle-tendon receptora; contral processes or their colds erals ending: (a) in the column of Clark (b) around other column cells of the cord. Neurone No. 2—20, Clarke's colum No. r.—Peripheral e—spinal ganglion ce see ending in (muscle-teral processes or their

cell, stirrer or of total spinorarchebia.

(Healest, first or of total spinorarchebia.

(Healest, Sow of these awared interfer of these awared interfer of these awared to a mount cells whose awared (a following automore of the words of the spinorarchebia automore can be believed or awared spinorarchebia track of the sweat spinorarchebia track of the sweat spinorarchebia track or or awared or of the lateral words awared (a) pass we differ some of the sweat of the lateral we differ some of the spinorarchebia track or or of the sweat o

Cerebellum

The nost clearly established contraction is that of the versibular curee whose first remainst in the nucleus fastigit or in the esteblate cortex. The connections indicated by 3b, 3c, 3c, 3c and 3f, might serve as parts of creatial more connections, but it is more probable that these fibres are corteblate estimates with bodies in the cerebellum Similar fibres to the corteblum as companies of the contraction of the parts of the contraction of the parts of the corteblum are outplanting in the unclei gradies and cumstants.

From Cerabellum to Cerabral Cortex.

Narmen No. 4 (m.3).—Chis of the cerebeliar cortex, their assores passing to the
itarial or dentate nucleas (and mucle algobosus
and embelliomis, not indicated) of the
cerebellum (4 a from wermis, and 4 b from
hemisphere).

themsphero; No. 5.—Cells of the dentate Neuron No. 5.—Cells of the dentate formis), their acones (and muele globosus and embolicomis), their acones (5. 0) passing via the superior penducte to thalamuse of Neurone No. 6.—Cells of thalamus, their axones passing to the cerebral cortex.

From Cerebral Contex to Cereballum.

Naturam Vo. 1,—19.—16 cells 6 frional cerehal contex, their acouse passing vie internal
expassile travous the internal malled parts of
the crusts to the pointle nuclei (tracus cortico-poullis frontalis). 7. A. Cells in temporal
cerebral cortex, their axouse passing vie the
internal capacita and their axouse passing vie the
pointle model (tracus cortico-poullis tempontils). Neurone No. 8.—Cells of pontile nuclei.

Name No. 8.—Cells of ponile nacid, their axones passing via the middle pedunde (transverse ponile fibres) to opposite cerebellar femishere.

Namen No. 9.—Cells in the carebellar henisphere, their axones passing to the dentate nucleus.

From Cerebellum to Periphery,
Normon Vo. 10.—Cells in dentate nucleus (and muclei goloosus and emboliforms), Instra accome passive get the superror
peduncie to opposite red mucleus (also to
nucleus N. III and to reductant formation).
Normone No. 11.—Cells in the red nucleus, their accome passing with the red nugen, and it accome passing with the red nupedunt their accome passing with the red nupedunt their accome passing with the red nupedunt their accome passing with the red nupedunt to the red number of the red

Journal 10 to American Serious prior spinal nerve to mark shorter pathway from the modificant nuclei (n. fastigil) to the medulis (vestibalis nuclei) and thence to the cord-also possibly directly from carebellum to cord (carebello-spinal trach—is given under Carebellar Relates Arrs (see below). It is idoutrul whether faits part say is involved in the crebro-cerebello-spinal spinoper in the crebro-cerebello.

Carelalur Rights Atos.

Gravialur Rights Atos.

From partiphery to crebellum and return without involving the cerebralum. In these reflexes the paths to the cerebellum are the same as in the preceding periphero-cerebellocerebral pathway.

From the cerebellum there are two (perhaps more) paths: ion peahucle (p) to the cerebellum there is the periphero-cerebral are of appearable to peak third merebral to peak third and theme by throe-spinal tract to ord.

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### CHAPTER XII.

### THE ORGANS OF SPECIAL SENSE.

### The Organ of Vision.

THE eyeball and optic nerve constitute the organ of vision. To be described in connection with them are the eyelid and the lacrymal apparatus.

The Eyeball or Bulbus Oculi.—This is almost spherical, although slightly flattened antero-posteriorly. It consists of a wall enclosing a cavity filled with fluid.

The wall of the eyeball consists of three coats: (a) An external fibrous coat—the *sclera* and *cornea*; (b) a middle vascular—the *chorioid*; and (c) an internal nervous—the *retina* (Fig. 328).

The Sclera (Figs. 328 and 329).—This consists of dense fibrous tissue with some elastic fibres. The fibres run both meridionally and equatorially, the tendons of the straight muscles of the eyeball being continuous with the meridional fibres, those of the oblique muscles with the equatorial fibres. The few cells of the sclera lie n distinct, very irregular cell spaces, and frequently contain pigment granules. Pigmented cells in considerable numbers are regularly present near the corneal junction, at the entrance of the optic nerve, and on the inner surface of the sclera. Where the optic nerve pierces the sclera, the continuity of the latter is broken by the entering nerve fibres, forming the *lamina cribosa* (Fig. 337). The pigmented layer of the sclera next the chorioid is known as the *lamina fusca*, and is lined internally by a single layer of flat non-pigmented endothelium. Anteriorly a loose connective tissue attaches the sclera to the scleral conjunctiva.

THE CORNEA (Figs. 330 and 333).—This is the anterior continuation of the sclera so modified as readily to allow the light to pass through it. It is about 1 mm. thick and consists of five layers, which from before backward are as follows (Fig. 330):

- (1) Anterior epithelium.
- (2) Anterior elastic membrane or membrane of Bowman.
- (3) Substantia propria corneæ.

- (4) Posterior elastic membrane or membrane of Descemet.
- (5) Posterior endothelium or endothelium of Descemet.
- (1) The anterior epithelium (Fig. 330), 1) is of the stratified squamous type and consists of from four to eight layers of cells. The deepest cells are columnar and rest upon the anterior elastic membrane. The middle cells are polygonal and are connected by short intercellular bridges. The surface cells are flat. Along the margin

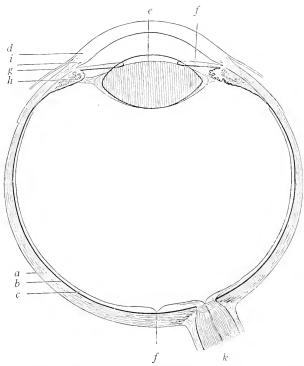


Fig. 328.—Diagram of Eyeball showing Coats. (Merkel-Henle.) a, Sclera; b, chorioid; c, retina; d, cornea; e, lens; f, iris; g, conjunctiva; h, ciliary body; i, sclero-corneal junction and canal of Schlemm; f, fovea centralis; k, optic nerve.

of the cornea the epithelium is continuous with that of the conjunctiva (Fig. 333).

(2) The anterior elastic membrane (Fig. 330, 2) is a highly developed basement membrane, its anterior surface being pitted to receive the bases of the deepest epithelial cells. It is apparently homogeneous, and while called an elastic membrane, does not conform chemically to either fibrous or elastic tissue. By means of special technic, a fibrillar structure has been demonstrated.

(3) The substantia propria (Fig. 330, 3) constitutes the main bulk of the cornea. It consists of connective tissue the fibrils of which are doubly refracting and are cemented together to form bundles and lamellæ. In the human cornea the lamellæ are about sixty in number. The lamellæ are parallel to one another and to the surface of the cornea, but the fibres of adjacent lamellæ cross one another at an angle of about twelve degrees. The lamellæ are united by cement substance. Fibres running obliquely through the lamellæ from posterior to anterior elastic membranes hold the lamellæ firmly together. They are known as perforating or arcuate fibres.

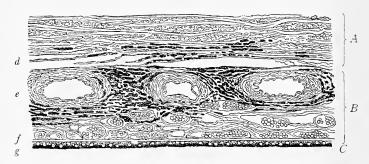


Fig. 329.—Vertical Section through Sclera, Chorioid, and Pigment Layer of Retina. (Merkel-Henle.) A, Sclera; B, chorioid; C, pigment layer of retina; d, lamina suprachorioidea; e, Haller's layer of straight vessels; f, choriocapillaris; g, vitreous membrane.

Between the lamellæ are irregular flat cell spaces which communicate with one another and with the lymph spaces at the margin of the cornea by means of canaliculi. Seen in sections vertical to the surface of the cornea, these spaces appear fusiform. In the spaces are the connective-tissue cells of the cornea or *corneal corpuscles*. These are flat cells corresponding in shape to the spaces and sending out processes into the canaliculi (Figs. 331 and 332).

- (4) The posterior elastic membrane or membrane of Descemet (Fig. 330, 4) resembles the anterior, but is much thinner. Like the anterior, it does not give the chemical reaction of elastic tissue.
- (5) The posterior endothelium or endothelium of Descenet (Fig. 330, 5) consists of a single layer of flat hexagonal cells, the nuclei of which frequently project slightly above the surface.

The cornea contains no blood-vessels.

THE CHORIOID.—This is made up of four layers which from without inward are as follows (Fig. 329):

- (1) The lamina suprachorioidea.
- (2) The layer of straight vessels—Haller's layer.
- (3) The capillary layer—choriocapillaris.
- (4) The vitreous membrane—lamina citrea—membrane of Bruch.
- (1) The lamina snprachorioidea (Fig. 329, d) is intimately connected with the lamina fusca of the sclera and consists of loosely arranged bundles of fibrous and elastic tissue among which are scat-

tered pigmented and non-pigmented connective-tissue cells. Numerous lymph spaces are found between the bundles of connective tissue and between the lamina suprachorioidea and lamina fusca. The latter are known as the *perichorioidal lymph spaces* (Fig. 333).

(2) The layer of straight vessels (Fig. 329, e) consists of fibro-elastic tissue containing numerous pigmented and non-pigmented cells, supporting the large blood-vessels of the layer. The latter can be seen with the naked eye, and, running parallel straight courses, give to the layer a striated appearance. The arteries lie to the inner side. The veins which are larger than the arteries converge toward four points—venæ vorticosæ—one in each quadrant of the cyeball.

A narrow boundary zone, rich in elastic fibres and free from pigment,

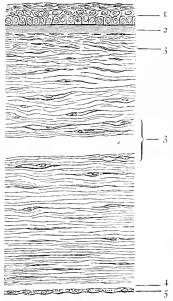


Fig. 330.—Vertical Section of Cornea. (Merkel-Henle.) 1, Anterior epithelium; 2, anterior elastic membrane; 3, substantia propria corneæ; 4, posterior elastic membrane; 5, posterior endothelium.

limits this layer internally. It is much more highly developed in some of the lower animals than in man. Formed of connective-tissue bundles in ruminants and horses, it is known as the *tapetum fibrosum*, while in the carnivora its structure—several layers of flat cells—gives it the name of the *tapetum cellulosum*.

(3) The *choriocapillaris* (Fig. 329, f) consists of connective tissue supporting a dense network of capillaries, which is most dense in the region of the macula lutea. This layer is usually described as free from pigment, although it not infrequently contains some pigmented cells.

(4) The vitreous membrane (Fig. 329, g) is a clear, apparently structureless membrane about two microns thick. Its outer surface is grooved by the capillaries of the choriocapillaris, while its inner surface is pitted by the retinal epithelium.

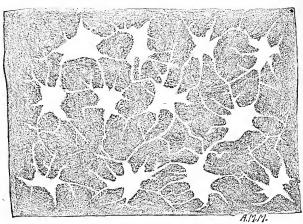


Fig. 331.—Section of Human Cornea cut Tangential to Surface — × 350 (technic 9, p. 81) — showing corneal cell spaces (lacunæ) and anastomosing canaliculi.

THE CILIARY BODY.—This is the anterior extension of the chorioid and consists of the ciliary processes and the ciliary muscle (Fig. 333). It extends from the *ora serrata* (a wavy edge which marks the anterior

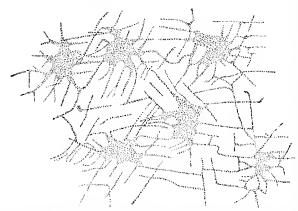


Fig. 332.—Section of Human Cornea cut Tangential to Surface—×350 (technic 8, p. 81)—showing corneal cells and their anastomosing processes.

limit of the nervous elements of the retina—see Retina) to the margin of the iris (see below).

The ciliary processes (Fig. 333), from seventy to eighty in number,

are meridionally-running folds of the chorioid from which are given off numerous irregular secondary folds. The processes begin low at the ora serrata, gradually increase in height to about 1 mm., and end abruptly at the margin of the iris. The ciliary processes consist of connective tissue containing many pigmented cells and supporting numerous blood-vessels. Invaginations lined with clear columnar epithelium have been described as ciliary glands. The ciliary folds

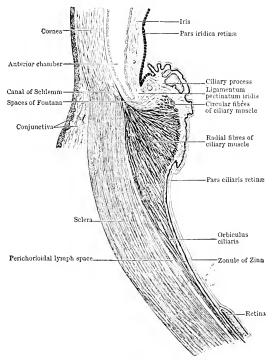


Fig. 333.—Vertical Section through Human Sclero-corneal Junction. (Cunningham.)

are covered by the vitreous membrane, and internal to the latter is a continuation forward of non-nervous elements of the retina—pars ciliaris retinæ (Fig. 333). This consists of two layers of columnar epithelial cells, the outer layer being pigmented, the inner non-pigmented.

The *ciliary muscle* (Fig. 333) is a band of smooth muscle which encircles the iris. It lies in the outer anterior part of the ciliary body, and on cross section has a generally triangular shape. It is divisible into three groups of muscle cells: (a) An inner circular group near the base of the iris—circular muscle of Müller; (b) an outer meridional

group lying next to the sclera and known as the tensor chorioideæ, and (c) a middle radial group. The meridional and radial groups both take origin in the posterior elastic lamina of the cornea, the former passing backward along the margin of the sclera to its insertion in the ciliary body near the ora serrata, the latter radiating fan-like to a broad insertion in the ciliary body and processes.

The ciliary body is closely attached to the sclero-corneal junction by the *ligamentum pectinatum* (Fig. 333), a continuation of the posterior elastic lamina of the cornea. Within the ligament are spaces (*spaces* 



Fig. 334.—Vertical Section through Iris. (Merkel-Henle.) a, Anterior endothelium; b, stroma or substantia propria; c, vitreous membrane; d, pigment layer; v, blood-vessel.

of Fontana) lined with endothelium. These are apparently lymph spaces, and communicate with each other, with similar spaces around the canal of Schlemm, and with the anterior chamber. The canal of Schlemm (Fig. 333) is a venous canal which encircles the cornea, lying in the sclera close to the corneal margin. Instead of a single canal there may be several canals.

THE IRIS (Fig. 334).—This represents a further continuation forward of the chorioid. Its base is attached to the ciliary body and ligamentum pectinatum. From this point it extends forward as a diaphragm in front of the lens, its centre being perforated to form the pupillary opening. It is deeply pig-

mented, and to its pigment the color of the eye is due. Four layers may be distinguished, which from before backward are as follows:

- (1) The anterior endothelium.
- (2) The stroma.
- (3) The vitreous membrane.
- (4) The pigmented epithelium.
- (1) The anterior endothelium is a single layer of pigmented cells continuous with the posterior endothelium of the cornea (Fig. 334, a).
- (2) The *stroma* is divisible into two layers: an anterior reticular layer, containing many cells, some of which are pigmented, and a vascular layer, the vessels of which are peculiar in that their walls con-

tain almost no muscle, but have thick connective-tissue sheaths. In the posterior part of the stroma are bundles of smooth muscle. Those nearest the pupillary margin encircle the pupil forming its sphincter muscle, while external are scattered radiating bundles forming the dilator muscle.

- (3) The *vitreous membrane* is continuous with, and has the same structure as the membrane of Bruch.
- (4) The *pigmented epithelium* (Fig. 334, d) consists of several layers of cells and is continuous with the pars ciliaris retinæ. Except in albinos, both layers are pigmented.

The Retina.—The retina is the nervous tunic of the eye. It lines the entire eyeball, ending only at the pupillary margin of the iris. Its nervous elements, however, extend only to the *ora serrata*, which marks the outer limit of the ciliary body (Fig. 333). The nervous part of the retina is known as the *pars optica retina*, the non-nervous extension over the ciliary processes as the *pars ciliaris retina*, its further continuation over the iris as the *pars iridica retina*. Modifications of the optic portion of the retina are found in the region of the macula lutea and of the optic nerve entrance.

The Pars Optica Retine.—This is the only part of the retina directly concerned in the reception of impulses, and may be regarded as the extremely complex sensory end-organ of the optic nerve. It is divisible into ten layers, which from without inward are as follows (Fig. 335):

- (1) Layer of pigmented epithelium.
- (2) Layer of rods and cones.
- (3) Outer limiting membrane.
- (4) Outer nuclear layer.
- (5) Outer molecular layer.
- (6) Inner nuclear layer.
- (7) Inner molecular layer.
- (8) Layer of nerve cells.
- (9) Layer of nerve fibres.
- (10) Inner limiting membrane.

Layer of neuro-epithelium.

Ganglionic layer.

The layer of pigmented epithelium (Fig. 335, B, 1) consists of a single layer of regular hexagonal cells (Fig. 25, p. 69). The nuclei lie in the outer part of the cell, while from the inner side thread-like projections extend down between the rods and cones of the layer next internal. The pigment has the form of rod-shaped granules. Its

distribution seems to depend upon the amount of light being admitted to the retina. When little or no light is being admitted, the pigment is found in the body of the cell, the processes being wholly or almost free from pigment; when the retina is exposed to a bright light, some of the pigment granules pass down into the processes so that the pigment becomes more evenly distributed throughout the cell.

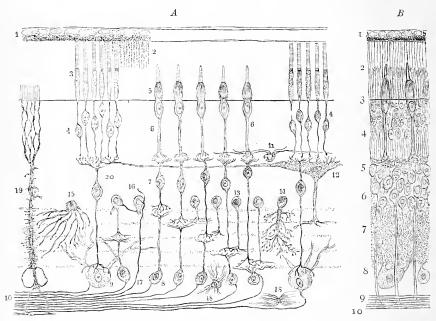


Fig. 335.—A, Scheme of retina as shown by the Golgi method. B, Vertical section of retina to show layers as demonstrated by the hæmatoxylin-eosin stain. (Merkel-Henle.) B.—I, Layer of pigmented epithelium; 2, layer of rods and cones; 3, outer limiting layer; 4, outer nuclear layer; 5, outer molecular layer; 6, inner nuclear layer; 7, inner molecular layer; 8, layer of nerve cells; 9, layer of nerve fibres; 10, inner limiting layer. A.—I, Pigment layer; 2, processes of pigmented epithelial cells extending down between rods and cones; 3, rods; 4, rod-cell nuclei and rod fibres; 5, cones; 6, cone fibres; 7, bipolar cells of inner nuclear layer; 8, ganglion cells of nerve-cell layer; 9, larger ganglion cells of nerve-cell layer; 10, fibres of optic nerve forming layer of nerve fibres; 11 and 12, types of horizontal cells; 13, 14, 15, and 16, types of cells the bodies of which lie in the inner nuclear layer; 17, efferent optic-nerve fibre ending around cell of inner nuclear layer; 18, neuroglia cells; 19, Müller's fibre; 20, rod-bipolar cell of inner nuclear layer.

The layer of rods and cones and the outer nuclear layer (Fig. 335, B, 2, 4) are best considered as subdivisions of a single layer, the neuro-epithelial layer. This consists essentially of two forms of neuro-epithelial elements, rod visual cells and cone visual cells. These, with supporting connective tissue, constitute the layer of rods and cones and the outer nuclear layer, the separation into sub-layers being due

to the sharp demarcation between the nucleated and non-nucleated parts of the cells, and the separation of the two parts by the perforated *outer limiting membrane*.

The rod visual cell (Fig. 335, A, 4) consists of rod, rod-fibre, and nucleus. The rod (Fig. 335, A, 3) is a cylinder from 30 to  $40\mu$  in length and about  $2\mu$  in diameter. It is divisible into an outer clear portion, which contains the so-called "visual purple" and an inner granular portion. At the outer end of the latter is a fibrillated ellipsoidal body, much more distinct in some of the lower animals, the ellipsoid of Krause. At its inner end the rod tapers down to a fine fibre, the rod fibre, which passes through a perforation in the outer limiting membrane into the outer nuclear layer, where it expands and contains the nucleus of the rod visual cell. These nuclei are situated at various levels in the fibre and constitute the most conspicuous element of the outer nuclear layer (Fig. 335, B, 4).

The cone visual cell (Fig. 335, A, 5, 6) consists of cone, cone-fibre, and nucleus. The cone (Fig. 335, A, 5) is shorter and broader than the rod, and like the latter is divisible into two parts. The outer part is short, clear, and tapering, the inner part broad and granular, and like the rod contains a fibrillated ellipsoid body. The cone fibre (Fig. 335, A, 6) is much broader than the rod fibre, passes completely through the outer nuclear layer and ends in an expansion at the margin of the outer molecular layer. The nucleus of the cone cell usually lies just beneath the outer limiting membrane.

The remaining layers of the retina must be considered in relation on the one hand to the neuro-epithelium, on the other to the optic nerve. The inner nuclear layer (Fig. 335, B, 6) and the layer of nerve cells (Fig. 335, B, 8) are composed largely of nerve-cell bodies, while the two molecular layers (Fig. 335, B, 5, 7) are formed mainly of the ramifications of the processes of these cells. In the inner nuclear laver are two kinds of nerve elements, rod bipolar cells and cone bipolar cells. The bodies of these cells with their large nuclei form the bulk of this layer. From the rod bipolars (Fig. 335, A, 20) processes (dendrites) pass outward to ramify in the outer molecular layer around the terminations of the rod fibres. From the cone bipolars (Fig. 335, A, 7) similar processes (dendrites) extend into the outer molecular layer where they ramify around the terminations of the cone cells. Two other forms of nerve cells occur in the inner nuclear layer. One is known as the horizontal cell (Fig. 335, A, 12). Its processes ramify almost wholly in the outer molecular laver. The other lies along the

inner margin of the inner nuclear layer and sends its dendrites into the inner molecular layer (Fig. 335, A, 13, 14, 15, and 16). Many of these latter cells appear to have no axone and are consequently known as amacrine cells.

The outer molecular layer is thus seen to be formed mainly of terminations of the rod and cone visual cells, of the dendrites of the rod and cone bipolars, and of the processes of the horizonal cells.

From the cone bipolar a process (axone) extends inward to ramify in the inner molecular layer, while from the rod bipolar a process (axone) passes inward through the inner molecular layer to terminate around the cells of the nerve-cell layer.

The *layer of nerve cells* (Fig. 335, B, 8) consists for the most part of large ganglion cells whose dendrites ramify in the inner molecular layer, and whose axones pass into the layer of nerve fibres and thence into the optic nerve. Some small ganglion cells are also found in this layer, especially in the region of the macula lutea (see page 505).

The inner molecular layer is thus seen to be composed mainly of the processes (axones) of the rod and cone bipolars and of the dendrites of the ganglion cells of the nerve-cell layer.

The layer of nerve fibres (Fig. 335, B, 9) consists mainly of the axones of the just-described ganglion cells, although a few centrifugal axones of brain cells (Fig. 335, A, 17) are probably intermingled.

The outer and inner limiting layers or membranes (Fig. 335, B, 3, 10) are parts of the sustentacular apparatus of the retina, being connected with the cells or fibres of Müller (Fig. 335, A, 19 and Fig. 336). The latter form the most conspicuous elements of the supportive tissue of the retina. They are like the nerve elements proper, of ectodermic origin and are elongated cells which extend through all the retinal layers, excepting the layer of rods and cones and the pigment layer. The inner ends of the cells, which are conical and fibrillated, unite to form the inner limiting membrane (Fig. 336, 10). Through the inner molecular layer the cell takes the form of a narrow stalk with numerous fringe-like side fibrils (Fig 336, 7). This widens in the inner nuclear layer, where cup-like depressions in the sides of the Müller's cell are caused by the pressure of the surrounding nerve cells (Fig. 336, b). This wide portion of the cell in the inner nuclear layer contains the nucleus (Fig. 336, a). In the outer molecular layer the cell again becomes narrow (Fig. 336, 5) and in the outer nuclear layer broadens out into a sponge-like reticulum (Fig. 336, 4), which supports the rod and cone bipolars. At the inner margin of the layer of rods and

cones the protoplasm of the Müller's cells spreads out and unites to form the so-called outer limiting membrane (Fig. 336, 3), from which delicate fibrils (*fibre baskets*) pass outward between the rods and cones. In addition to the Müller's cells, which are neuroglia elements, spider cells also occur in the retina (Fig. 335, A, 18).

The retina of the macula lutea presents certain peculiarities. Its name is derived from the yellow pigment which is distributed diffusely through the inner layers, extending as far out as the outer molecular layer. The ganglion-cell layer and the inner nuclear layer are thicker than in other parts of the retina. In the layer of rods and cones there is a gradual reduction in the number of rods, while the number of cones is correspondingly increased.

In the centre of the macula is a depression, the *fovea centralis*. As the retina approaches this area it becomes greatly thinned, little remaining but the layer of cone cells and the somewhat thickened layer of pigmented epithelium.

At the ora serrata the nervous elements of the retina cease. The non-nervous re tinal extension over the ciliary body (pars ciliaris retinæ) and over the iris (pars iridica retinæ) have been described in connection with the ciliary body and iris.

The Optic Nerve.—The optic nerve (Fig. 337, d) is enclosed by two connective-tissue sheaths, both of which are extensions of the brain membranes. The outer dural sheath (Fig. 337, a) is continuous with the

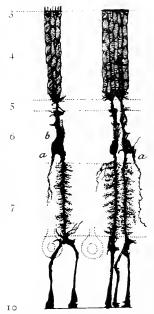


Fig. 336.—Two Müller's Fibres from Retina of Ox showing Relation to Layers of Retina. (Ramón y Cajal.) 3, Outer limiting layer; 4, outer nuclear layer; 5, outer molecular layer; 6, inner nuclear layer; 7, inner molecular layer; 8, layer of nerve cells; 9, layer of nerve fibres; 10, inner limiting layer; a, nucleus; b, cup-like depression caused by pressure from surrounding cells.

dura mater of the brain posteriorly, while anteriorly it blends with the sclera. The inner *pial sheath* (Fig. 337, b) is an extension of the pia mater and is separated from the outer sheath by the subdural space (Fig. 337, c). The pial sheath is divisible into two sub-layers: an outer fibrous layer (the so-called *araclmoid*), and an inner vascular layer. These two layers are separated by a narrow space, the *subaraclmoid space*. The optic nerve fibres, in passing through the sclera and cho-

rioid, separate the connective-tissue bundles so that they form a lattice-work, the already mentioned  $lamina\ cribrosa\ (Fig.\ 337,\ h)$ . The optic nerve fibres are medullated, but have no neurilemma. As they pass

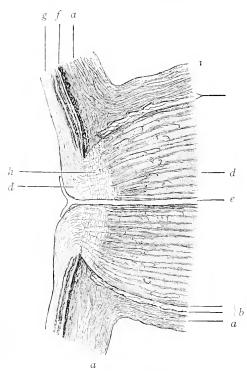


Fig. 337.—Section through Entrance of Optic Nerve into Eyeball. (Merkel-Henle.) a, Dural sheath; b, pial sheath, inner and outer layers; c, space between inner and outer layers of pia mater; d, optic nerve; e, central artery of retina: a', sclera; f, chorioid; g, retina; h, lamina cribrosa.

through the lamina cribrosa the medullary sheaths are lost, the fibres reaching the retina as naked axones.

RELATIONS OF OPTIC NERVE TO RETINA AND BRAIN.

The rod and cone visual cells are the neuro-epithelial beginnings of the visual tract (Fig. 335, A, 3, 4, 5, and 6). By their expanded bases in the outer molecular layer, the rod and cone cells communicate with the neurone system No. I. of the optic tract. This comprises (a) rod neurones, (b) cone neurones, (c) horizontal neurones.

NEURONE SYSTEM No. I.—(a) Rod neurones. The cell bodies of these neurones (Fig. 335, A, 20) lie in the inner nuclear layer. Their

dendrites enter the outer molecular layer where they form networks around the expanded bases of the rod cells. Their axones pass through the inner molecular layer and end in arborizations around the bodies and dendrites of cells of the nerve-cell layer (neurone system No. II.). (b) Cone neurones (Fig. 335, A, 7). These have their cell bodies in the inner nuclear layer. Their dendrites pass to the outer molecular layer where they form networks around the expanded bases of the cone cells. Their axones pass only into the inner molecular layer where they end in arborizations around the dendrites of neurones whose cell bodies are in the layer of nerve cells (neurone system No. II.). (c) Horizontal neurones (Fig. 335, A, 11 and 12. These serve as associa-

tion neurones between the visual cells and may be divided into *rod* association neurones and cone association neurones. The cone association neurones are the smaller and more superficial, and both dendrites and axones end in the outer molecular layer around the terminal expan-

sions of the cone visual cells (Fig. 335, A, 11). The rod association neurones are larger, more deeply seated, and behave in a similar manner toward the rod visual cells (Fig. 335, A, 12). Some of these cells send processes to the inner molecular layer.

NEURONE SYSTEM No. II.— This has been already partly described in connection with the axone terminations of neurone system No. I. The cell bodies of the second neurone system (Fig. 335, A, 8, 9) are in the layer of nerve cells and are, as above noted, associated either directly or by means of their dendrites with the axones of the first neurone system. Their axones pass into the layer of nerve fibres and ultimately become fibres of the optic nerve (Fig. 335, A, 10).

The optic nerves (Fig. 338, No) unite at the base of the brain to form the *optic decussation* or *chiasma* (Fig. 338, CM). Here the

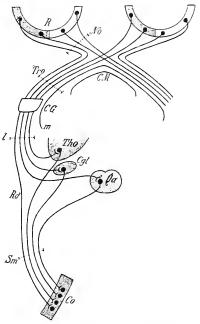


FIG. 338.—Diagram showing Main Relations of Optic Tract. (Testut.) R. Retina; No, optic nerve: CM, optic decussation or chiasma: Tro, optic tract; Tho, thalamus: Cgl, lateral geniculate body; Qa, anterior corpus quadrigeminum; Rd, fibre of optic tract passing directly to cortex; Sm, third neurone system of optic tract (excepting Rd) connecting thalamus, lateral geniculate body, and anterior corpus quadrigeminum with the cortex, Co.

axones from the mesial part of the retina cross to the optic tract of the opposite side, while those of the lateral part of the retina remain in the optic tract of the same side. The axones of the optic tract (Fig. 338, Tro) terminate in the thalamus, in the lateral geniculate body, and in the anterior corpus quadrigeminum (Fig. 338).

NEURONE System No. III.—The neurones of this system have their cell bodies in the thalamus, lateral geniculate body, and anterior corpus quadrigeminum (Fig. 338). The axones of the two former terminate in the cortical visual centers in the occipital lobe (Fig. 338.

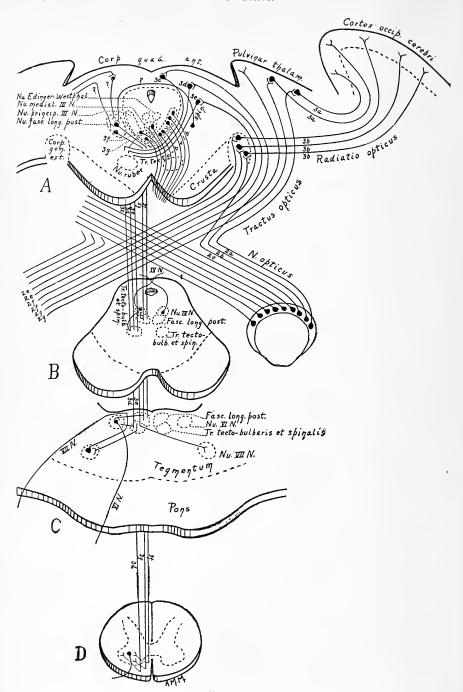


Fig. 339.

### EXPLANATION OF FIG. 339.

Fig. 339.—Diagram of the Optic (II) Nerve and some of its Principal Connections. 4, Level of II and III nerves; B, level of IV nerve; C, level of VI and VII nerves; D, spinal cord. The rods and cones (sensory cells) and the bipolar cells (=Neurone No. 1) of the retina are not indicated.

Neurone No. 2.—2 a, Axones of ganglion cells in temporal part of retina pass to pulvinar of thalamus of same side; 2b, axones of ganglion cells in retina pass to anterior corpus quadrigeminum of same side; 2c, axones of ganglion cells in retina pass to external geniculate body (Corp. gen. ext.) of same side; 2c, axones of ganglion cells in nasal side of retina cross in optic chiasma and pass to external geniculate body of opposite side; 2f, axones of ganglion cells in nasal side of retina cross in optic chiasma and pass to anterior corpus quadrigeminum of opposite side; 2g, axones of ganglion cells in nasal side of retina cross in

optic chiasma and pass to pulvinar of thalamus of opposite side.

Neurone No. 3.—3 a, Axones of cells in pulvinar to cortex of occipital lobe of cerebrum (this connection is disputed); 3 b, axones of cells in external geniculate body to cortex of occipital lobe of cerebrum; 3 a and 3 b constitute the primary optic radiation; 3 c, 3 d and 3 e, axones of cells in middle layer of tectum (roof) of anterior corpus quadrigeminum decussate ventral to posterior longitudinal fasciculus (dorsal tegmental decussation or decussation of Meynert) and form the tractus tecto-bulbaris et spinalis (Tr. tecto-bulb. et spin.) to bulb (medulla) and anterior column of cord, innervating by collaterals and terminals, directly or indirectly, chiefly the nuclei of III, IV, VI, and VII cranial nerves and motor nuclei of spinal nerves. 3 f and 3 g (possibly another neurone intercalated between these and optic terminals), axones of cells in nucleus of posterior longitudinal fasciculus (Nu. fasc. long. post.) (Nucleus of Darkschewitsch) form part of posterior longitudinal fasciculus and descend on same side to anterior column of cord next to anterior median fissure, innervating nuclei of III, IV, and VI cranial nerves and motor nuclei of spinal nerves.

Neurone No. 4.—Axones of cells in above-mentioned motor nuclei. Axones from cells in median nucleus of III nerve (Nu. med. III N.), and possibly in Edinger-Westphal nucleus, probably innervate the intrinsic muscles of eyeball (ciliary and pupillary reflex path).

It is evident from the diagram that the cerebral pathway of the optic nerve is via the external geniculate body (and pulvinar of thalamus), and the reflex pathway is via the anterior colliculus (anterior corpus quadrigeminum).

Co). The axones of the latter form descending reflex paths (see Anterior Corpora Quadrigemina, p. 467).

The Lens.—The lens is composed of lens fibres which are laid down in layers (Fig. 340, a). The lens fibre is a long hexagonal, flattened prism with serrated edges. Most of the lens fibres are nucleated, the nucleus lying at about the centre of the fibre near the axis of the lens. The most central of the lens fibres are usually non-nucleated. The fibres extend meridionally from before backward

b c a

through the entire thickness of the lens. They are united by a small amount of cement substance. The lens is surrounded by the lens capsule (Fig. 340, b), a clear homogeneous membrane which is about 12 $\mu$  thick



Fig. 340.—From Longitudinal Section through Margin of Crystalline Lens, showing longitudinal sections of lens fibres and transition from epithelium of capsule into lens fibres. (Merkel-Henle.) a, Lens fibres; b, capsule; c, epithelium.

Fig. 341.—From Cross Section of Crystalline Lens, showing transverse sections of lens fibres and surface epithelium. (Merkel-Henle.) a, Lens fibres; b, epithelium.

over the anterior surface of the lens, about half as thick over the posterior surface. Between the capsule and the anterior and lateral surfaces of the lens is a single layer of cuboidal epithelial cells (Fig. 340, c), the lens epithelium. Attached to the capsule of the lens anteriorly and posteriorly are membrane-like structures which constitute the suspensory ligament of the lens. These pass outward and unite to form a delicate membrane, the zonula ciliaris or zonule of Zinn (Fig. 333). This bridges over the inequalities of the ciliary processes and,

continuing as the hyaloid membrane, forms a lining for the vitreous cavity of the eye. The triangular space between the two layers of the suspensory ligament and the lens is known as the *canal of Petit*.

The *vitreous body* is a semifluid substance containing fibres which run in all directions and a small number of connective-tissue cells and leucocytes. Traversing the vitreous in an antero-posterior direction is the so-called *hyaloid* or *Cloquet's canal*, the remains of the embryonic hyaloid artery (page 516).

Blood-vessels.—The blood-vessels of the eyeball are divisible into two groups, one group being branches of the central artery of the retina, the other being branches of the ciliary artery.

The central artery of the retina enters the eyeball through the centre of the optic nerve. Within the eyeball it divides into two branches, a superior and an inferior. These pass anteriorly in the nerve-fibre layer, giving off branches, which in turn give rise to capillaries which supply the retina, passing outward as far as the neuro-epithelial layer and anteriorly as far as the ora serrata. The smaller branches of the retinal arteries do not anastomose. In the embryo a third vessel exists, the hyaloid artery. This is a branch of the central retinal artery and traverses the vitreous to the posterior surface of the lens, supplying these structures. The hyaloid canal, or canal of Cloquet, of the adult vitreous, represents the remains of the degenerate hyaloid artery (page 516). The veins of the retina accompany the arteries.

The ciliary arteries are divisible into long ciliary arteries, short ciliary arteries, and anterior ciliary arteries. The long ciliary arteries are two in number and pass one on each side between the chorioid and sclera to the ciliary body, where each divides into two branches, which diverge and run along the ciliary margin of the iris. Here the anastomosis of the two long ciliary arteries forms the greater arterial circle of the iris. This gives rise to small branches which pass inward supplying the surrounding tissues and unite near the margin of the pupil to form the lesser arterial circle of the iris. The branches of the short ciliary arteries pierce the sclera near the optic nerve entrance, supply the posterior part of the sclera, and terminate in the choriocapillaris of the chorioid. The anterior ciliary arteries enter the sclera near the corneal margin and communicate with the choriocapillaris and with the greater arterial circle of the iris. The anterior ciliary arteries also supply the ciliary and recti muscles and partly supply the sclera and conjunctiva. Small veins accompany the ciliary arteries; the larger veins of this area are peculiar, however, in that

they do not accompany the arteries, but as venæ vorticosæ converge toward four centres, one in each quadrant of the eyeball. At the sclero-corneal junction is a venous channel, the canal of Schlemm, which completely encircles the cornea (Fig. 333).

Lymphatics.—The eyeball has no distinct lymph-vessel system. The lymph, however, follows certain definite directions which have been designated by Schwalbe "lymph paths." He divides them into anterior lymph paths and posterior lymph paths. The anterior lymph paths comprise (a) the anterior chamber which communicates by means of a narrow cleft between iris and lens with the posterior chamber; (b) the posterior chamber; (c) the lymph canaliculi of the sclera and cornea and the canal of Petit. The posterior lymph paths include (a) the hyaloid canal (see above); (b) the subdural and intra-pial spaces, including the capsule of Tenon; (c) the perichorioidal space, and (d) the perivascular and pericellular lymph spaces of the retina.

**Nerves.**—The nerves which supply the eyeball pass through the sclera with the optic nerve and around the eyeball in the suprachorioid layer. From these nerves, branches are given off as follows:

- $\left(\tau\right)$  To the chorioid, where they are intermingled with ganglion cells.
- (2) To the ciliary body, where they are mingled with ganglion cells to form the *ciliary plexus*. The latter gives off branches to the ciliary body itself, to the iris, and to the cornea. Those to the cornea first form a plexus in the sclera—the plexus annularis—which encircles the cornea. From this, branches pierce the substantia propria of the cornea, where they form four corneal plexuses, one in the posterior part of the substantia propria, a second just beneath the anterior elastic membrane, a third sub-epithelial, and a fourth intra-epithelial. The fibres of the last named are extremely delicate and terminate freely between the epithelial cells. Krause describes end-bulbs as occurring in the substantia propria near the margin of the sclera, while according to Dogiel some of the fibres are connected with end-plates.

### THE LACRYMAL APPARATUS.

The lacrymal apparatus of each eye consists of the gland, its excretory ducts, the lacrymal canal, the lacrymal sac, and the nasal duct.

The *lacrymal gland* is a compound tubular gland consisting of two main lobes. Its structure corresponds in general to that of a

serous gland. The excretory ducts are lined with a two-layered columnar epithelium which becomes simple columnar in the smaller ducts. The alveoli are lined with irregularly cuboidal serous cells, which rest upon a basement membrane beneath which is a richly elastic interstitial tissue.

The *lacrymal canals* have a stratified squamous epithelial lining. This rests upon a basement membrane beneath which is the stroma containing many elastic fibres. External to the connective tissue are some longitudinal muscle fibres.

The *lacrymal sac* is lined with a two-layered stratified or pseudostratified columnar epithelium resting upon a basement membrane. The stroma contains much diffuse lymphatic tissue.

The nasal duct has walls similar in structure to those of the lacrymal sac. In the case of both sac and duct the walls abut against periosteum, a dense vascular plexus being interposed.

The blood-vessels, lymphatics, and nerves of the lacrymal gland have a distribution similar to those of other serous glands.

### THE EYELID.

The eyelid consists of an outer skin layer, an inner conjunctival layer, and a middle connective-tissue layer.

The epidermis is thin and the papillæ of the derma are low. Small sebaceous glands, sweat glands, and fine hairs are present.

The *conjunctiva* (Fig. 342, d) is a mucous membrane consisting of a lining epithelium and a stroma. The epithelium is stratified columnar consisting of two or three layers of cells. Among these cells are cells resembling goblet cells. Although not always upon the surface, they are believed to be mucous cells, probably analogous to the so-called Leydig's cells found in the larvæ of amphibians and fishes. Diffuse lymphoid tissue is regularly present in the stroma, while lymph nodules are of rare occurrence. Small glands, similar to the lacrymal glands in structure, are usually present (Fig. 342, k).

At the margin of the eyelid where skin joins mucous membrane are several rows of large hairs, the eyelashes (Fig. 342, h). Connected with their follicles are the usual sebaceous glands (Fig. 342, g) and the glands of Mall, the latter probably representing modified sweat glands.

The middle layer contains the tarsus (Fig. 342, e) and the muscular structure of the eyelid (Fig. 342, b). The tarsus is a plate of dense fibrous tissue which lies just beneath the conjunctiva and ex-

tends about two-thirds the height of the lid. It contains the tarsal or *Meibomian glands* (Fig. 342, e). These are from thirty to forty in number, each consisting of a long duct which opens externally on

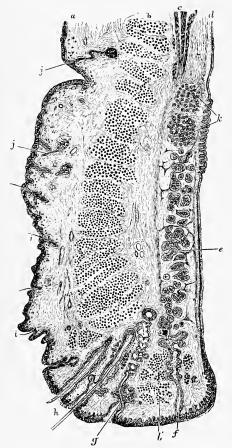


Fig. 342.—Vertical Section through Upper Eyelid. (Waldeyer.) a, Skin; b, orbicularis muscle; b', ciliary bundle of muscle; e, involuntary muscle of eyelid; d, conjunctiva; e, tarsus containing Meibomian glands; f, duct of Meibomian gland; g, sebaceous gland with duct lying near eyelashes; h, eyelashes; i, small hairs in outer skin; j, sweat glands; k, posterior tarsal glands.

duct which opens externally on the margin of the lid behind the lashes (Fig. 342, f), and internally into a number of branched tubules. The duct is lined with stratified squamous epithelium. The tubules resemble those of the sebaceous glands. Between the tarsus and the skin are the muscular structures of the eyelid in which both smooth and striated muscle are found.

Blood-vessels.—Two main arteries pass to the eyelid, one at each angle and unite to form an arch, the tarsal arch, along the margin of the lid. A second arch, the external tarsal arch, is formed along the upper margin of the tarsus. From these arches are given off capillary networks which supply the structures of the lid.

Lymphatics.—These form two anastomosing plexuses, one anterior, the other posterior to the tarsus.

Nerves.—The nerves form plexuses in the substance of the lid. From these, terminal fibrils pass to the various structures of the lid. Many of the fibres end freely in fine net-

works around the tarsal glands, upon the blood-vessels, and in the epithelium of the conjunctiva. Other fibres terminate in end-bulbs which are especially numerous at the margin of the lid.

### DEVELOPMENT OF THE EYE.

The eyes begin their development very early in embryonic life. As *optic depressions* they are visible even before the closure of the med-

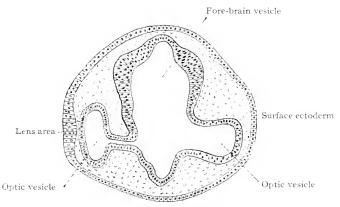


Fig. 343.—Section through head of chick of two days' incubation. (Duval.) The formation of the optic vesicle and stalk appears to be somewhat more advanced on the left than on the right.

ullary groove. As a result of the closure of this groove, the optic depressions are transformed into the *optic vesicles*. The connection between vesicle and brain now becomes narrowed so that the two are

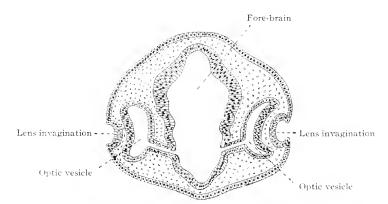


Fig. 344.—Section through head of chick of three days' incubation. (Duval.)

connected only by the thin *optic stalk*. The surface of the optic vesicle becomes firmly adherent to the epidermis and as a result of proliferation of ectodermic cells at this point is pushed inward (invaginated).

forming the *optic cup*. The invagination of the optic vesicle extends also to the stalk, the sulcus in the latter being known as the *chorioid fissure*. The latter serves for the introduction of mesenchyme, and

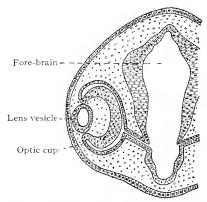


Fig. 345.—Showing somewhat later stage in development of optic cup and lens than is shown in Fig. 344. (Duval.)

the development of the hyaloid retinal artery. Three distinct parts may now be distinguished in the developing eye, which at this stage is known as the *secondary optic vesicle*: (a) The proliferating epidermis

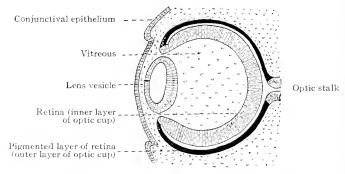


Fig. 346.—Diagram of developing lens and optic cup. (Duval.) The cells of the inner wall of the lens vesicle have begun to elongate to form lens fibers. The epithelium over the lens is the anlage of the corneal epithelium. The mosodermal tissue between the latter and the anterior wall of the lens vesicle is the anlage of the substancia propria corneae.

which is to form the lens; (b) the more superficial of the invaginated layers which is to become the retina; and (c) the surrounding mesodermic tissue from which the outer coats of the eye are to develop.

#### TECHNIC.

- (1) For the study of the general structures of the eveball the eye of some large animal, such as an ox, is most suitable. Fix the eve for about a week in ten-percent, formalin. Then wash in water and bisect the eve in such a manner that the knife passes through the optic-nerve entrance and the centre of the cornea. The half eye should now be placed in a dish of water and the structures shown in Fig. 328 identified with the naked eve or dissecting lens. On removing the vitreous and retina, the pigmented epithelium of the latter usually remains attached to the chorioid from which it may be scraped and examined in water or mounted in glycerin. In removing the lens note the lens capsule and the suspensory ligament. The lens may be picked to pieces with the forceps, and a small piece, after further teasing with needles, examined in water or mounted in glycerin or eosin-glycerin. The retinal surface of the chorioid shows the iridescent membrane of Bruch. By placing a piece of the chorioid, membrane-of-Bruch-side down, over the tip of the finger and gently scraping with a knife in the direction of the larger vessels, the latter may be distinctly seen. By now staining the piece lightly with hæmatoxylin and strongly with eosin, clearing in oil or origanum and mounting in balsam, the choriocapillaris and the layer of straight vessels become distinctly visible with the low-power lens. In removing the chorioid note the close attachment of the latter to the sclera, this being due to the intimate association of the fibres of the lamina suprachorioidea and of the lamina fusca. If the brown shreds attached to the inner side of the sclera be examined, the pigmented connective-tissue cells of the sclera can be seen.
- (2) For the study of the finer structure of the coats of the eye, a human eye if it is possible to obtain one, if not, an eye from one of the lower animals, should be fixed in formalin-Müller's fluid (technic 5, p. 7) and hardened in alcohol. (A few drops of strong formalin injected by means of a hypodermic needle directly into the vitreous often improves the fixation.) The eye should next be divided into quadrants by first carrying the knife through the middle of the cornea and of the optic-nerve entrance and then dividing each half into an anterior and a posterior half. Block in celloidin, cut the following sections, and stain with hæmatoxy-lin-eosin (technic 1, p. 18).
- (a) Section through the sclero-corneal junction, including the ora serrata, ciliary body, iris, and lens. Before attempting to cut this section almost all of the lens should be picked out of the block, leaving only a thin anterior and lateral rim attached to the capsule and suspensory ligament. The block should then be so clamped to the microtome that the lens is the last part of the block to be cut. The above precautions are necessary on account of the density of the lens, making it difficult to cut.
- (b) Section through the postero-lateral portion of the eyeball to show structure of sclera, chorioid, and retina. This section should be as thin as possible and perpendicular to the surface.
- (c) Section through the entrance of the optic nerve. Hæmatoxylin-picro-acid-fuchsin also makes a good stain for this section. It is instructive in cutting the eye to cut a small segment from the optic nerve and to block it with the optic-nerve entrance material in such a manner that it is cut transversely. In this way

both longitudinal and transverse sections of the optic nerve appear in the same section.

- (d) For the study of the neurone relations of the retina material must be treated by one of the Golgi methods (page 32).
- (4) The connective-tissue cells and cell spaces of the cornea may be demonstrated by means of technics 8 and 9, page 81.
- (5) The different parts of the lacrymal apparatus may be studied by fixing material in formalin-Müller's fluid and staining sections in hæmatoxylin-eosin.
- (6) The Eyelid. An upper eyelid, human if possible, should be carefully pinned out on cork, skin side down, and fixed in formalin-Müller's fluid. Vertical sections should be stained with hæmatoxylin-eosin or with hæmatoxylin-picro-acid-fuchsin.

# The Organ of Hearing.

The organ of hearing comprises the external ear, the middle ear, and the internal ear.

## THE EXTERNAL EAR.

The external ear consists of the pinna or auricle, the external auditory canal, and the outer surface of the tympanic membrane.

The *pinna* consists of a framework of elastic cartilage embedded in connective tissue and covered by skin. The latter is thin and contains hairs, sebaceous glands, and sweat glands.

The external auditory canal consists of an outer cartilaginous portion and an inner bony portion. Both are lined with skin continuous with that of the surface of the pinna. In the cartilaginous portion of the canal the skin is thick and the papillæ are small. Hair, sebaceous glands, and large coiled glands (ceruminous glands) are present. The last named resemble the glands of Mall (page 513) and are probably modified sweat glands. Their cells contain numerous fat droplets and pigment granules. They have long narrow ducts lined with a two-layered epithelium. In children these ducts open into the hair follicles; in the adult they open on the surface near the hair follicles. The secretion of these glands plus desquamated epithelium constitutes the ear wax. In the bony portion of the canal the skin is thin, free from glands and hair, and firmly adherent to the periosteum.

The tympanic membrane (ear drum) separates the external ear from the middle ear. It consists of three layers: a middle layer or substantia propria, an outer layer continuous with the skin of the external ear, and an inner layer continuous with the mucous membrane of the middle ear.

The substantia propria consists of closely woven connective-tissue fibres, the outer fibres having a radial direction from the head of the malleus, the inner fibres having a concentric arrangement and being best developed near the periphery.

The outer layer of the tympanic membrane is skin, consisting of epidermis and of a thin non-papillated corium, excepting over the manubrium of the malleus, where the skin is thicker and papillated.

The inner layer is mucous membrane and consists of a stroma of fibro-elastic tissue covered with a single layer of low epithelial cells.

Blood-vessels.—Blood is supplied to the tympanic membrane by two sets of vessels, an external set derived from the vessels of the external auditory meatus and an internal set from the vessels of the middle ear. These give rise to capillary networks in the skin and mucous membrane, respectively, and anastomose by means of perforating branches at the periphery of the membrane. From the capillaries the blood passes into two sets of small veins, one extending around the periphery of the membrane, the other following the handle of the malleus.

**Lymphatics.**—These follow in general the course of the blood-vessels. They are most numerous in the outer layer.

**Nerves.**—The larger nerves run in the substantia propria. From these, branches pass to the skin and mucous membrane, beneath the surfaces of which they form plexuses of fine fibres.

#### THE MIDDLE EAR.

The middle ear or tympanum is a small chamber separated from the external ear by the tympanic membrane and communicating with the pharynx by means of the Eustachian tube. Its walls are formed by the surrounding bony structures covered by periosteum. It is lined with mucous membrane and contains the car ossicles and their ligamentous and muscular attachments. The epithelium is of the simple low cuboidal type. In places it may be ciliated and not infrequently assumes a pseudostratified character with two layers of nuclei. Beneath the epithelium is a thin stroma which contains some diffuse lymphoid tissue and blends with the dense underlying periosteum. Small tubular glands are usually present, especially near the opening of the Eustachian tube.

The *fenestra rotunda* is covered by the secondary tympanic membrane. This consists of a central lamina of connective tissue covered

on its tympanic side by part of the mucous membrane of that chamber, on the opposite side by a single layer of endothelium.

The *ossicles* are composed of bone tissue arranged in the usual systems of lamellæ. The *stapes* alone contains a marrow cavity. Over their articular surfaces the ossicles are covered by hyaline cartilage.

The Eustachian Tube.—This is a partly bony, partly cartilaginous canal lined with mucous membrane. The epithelium of the latter is of the stratified columnar ciliated variety consisting of two layers of cells. In the bony portion of the tube the stroma is small in amount and intimately connected with the periosteum. In the cartilaginous portion the stroma is thicker and contains, especially near the pharyngeal opening, lymphoid tissue and simple tubular mucous glands.

## THE INTERNAL EAR.

The internal ear consists of a complex series of connected bony walled chambers and passages containing a similar-shaped series of membranous sacs and tubules. These are known, respectively, as the osseous labyrinth and the membranous labyrinth. Between the two is a

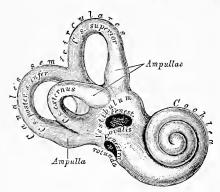


Fig. 347.—The Bony Labyrinth.  $\times$ 3. (Heitzmann.)

lymph space, which contains the so-called *perilymph*, while within the membranous labyrinth is a similar fluid, the *endolymph*.

The bony labyrinth consists of a central chamber, the *vestibule*, from which are given off the three *semicircular canals* and the *cochlea*. The vestibule is separated from the middle ear by a plate of bone in which are two openings, the *fenestra ovalis* and the *fenestra rotunda*. Just

after leaving the vestibule each canal presents a dilatation, the ampulla. As each canal has a return opening into the vestibule and as the anterior and posterior canals have a common return opening (the canalis communis), there are five openings from the vestibule into the semicircular canals (Fig. 347). The bony labyrinth is lined with periosteum, covered by a single layer of endothelial cells.

The Vestibule and the Semicircular Canals.—In the vestibule the membranous labyrinth is subdivided into two chambers, the sac-

cule and the utricle, which are connected by the utriculo-saccular duct. From the latter is given off the endolymphatic duct which communicates, through the aqueduct of the vestibule, with a subdural lymph space, the endolymphatic sac. The saccule opens by means of the ductus reuniens into the cochlea, while the utricle opens into the ampullæ of the semicircular canals. The saccule and utricle only partly fill the vestibule, the remaining space, crossed by fibrous bands and lined with endothelium, constituting the perilymphatic space.

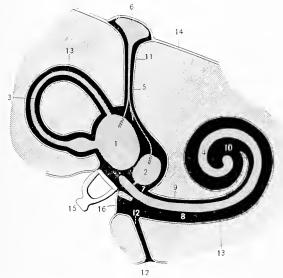


Fig. 348.—Diagram of the Perilymphatic and Endolymphatic Spaces of the Inner Ear. (Testut.) Endolymphatic spaces in gray; perilymphatic spaces in black. 1, Utricle; 2, saccule; 3, semicircular canals; 4, cochlear canal; 5, endolymphatic duct; b, subdural endolymphatic sac; 7, canalis reuniens; 8, scala tympani; 9, scala vestibuli; 10, their union at the helicotrema; 11, aqueduct of the vestibule; 12, aqueduct of the cochlea; 13, periosteum; 14, dura mater; 15, stapes in fenestra ovalis; 16, fenestra rotunda and secondary tympanic membrane.

SACCULE AND UTRICLE.—The walls of the saccule and of the utricle consist of fine fibro-elastic tissue supporting a thin basement membrane. upon which rests a single layer of low epithelial cells. In the wall of each chamber is an area of special nerve distribution, the *macula acustica*. Here the epithelium changes to high columnar and consists of two kinds of cells, sustentacular and neuro-epithelial. The *sustentacular cells* are long, irregular, nucleated cylinders, narrow in the middle, widened at each end, the outer end being frequently split and resting upon the basement membrane. The *neuro-epithelial cells* or "hair cells" are short cylinders which extend only about halfway through

the epithelium. The basal end of the cell is the larger and contains the oval nucleus. The surface of the cell is provided with a cuticular margin from which project several long hair-like processes, the *auditory hairs*. Small crystals of calcium carbonate are found on the surfaces of the hair cells. These are known as *otoliths* and are embedded in a soft substance, the *otolithic membrane*. The hair cells are the neuro-epithelial end-organs of the vestibular division of the auditory nerve and are, therefore, closely associated with the nerve fibres. The latter

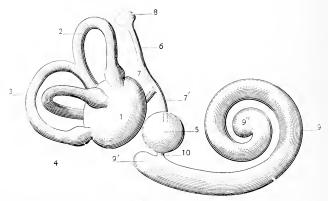


Fig. 349.—Diagram of the Right Membranous Labyrinth. (Testut.) 1, Utricle; 2 superior semicircular canal; 3, posterior semicircular canal; 4, external semicircular canal; 5, saccule; 6, endolymphatic duct; 7 and 7', canals connecting utricle and saccule respectively with the endolymphatic duct; 8, endolymphatic sac; 9, cochlear duct; 9', its vestibular cul-de-sac; 4'', its terminal cul-de-sac; 10, canalis reuniens.

on piercing the basement membrane lose their medullary sheaths and split up into several small branches, which form a horizontal plexus between the basement membrane and the bases of the hair cells. From this plexus are given off fibrils which end freely between the hair cells.

Semicircular Canals.—The walls of the semicircular canals are similar in structure to the walls of the saccule and utricle; they also bear a similar relation to the walls of the bony canal. Along the concavity of each canal the epithelium is somewhat higher, forming the *raphé*. In each ampulla is a *crista acustica*, the structure of which is similar to that of the maculæ of the saccule and utricle. With the adjoining high columnar cells, this forms the so-called *semilunar fold*. As in the case of the maculæ the hair cells have otoliths upon their surfaces, the otolithic membrane here forming a sort of dome over the hair cells known as the *cupula*.

The Cochlea.—The bony cochlea consists of a conical axis, the modiolus, around which winds a spiral bony canal. This canal in

man makes about two and one-half turns, ending at the rounded tip of the cochlea or *cupola*. Projecting from the modiolus partly across the bony canal of the cochlea is a plate of bone, the *bony spiral lamina* (Fig. 351, x). This follows the spiral turns of the cochlea, ending at the cupola in a hook-shaped process, the *hamulus*. Along the outer side of the canal, opposite the bony spiral lamina, is a projection of thickened periosteum, the *spiral ligament* (Fig. 351, h). A connective-tissue membrane, the *membranous spiral lamina* (Fig. 351, s), crosses

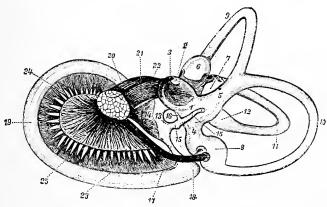


Fig. 350.—The Membranous Labyrinth from the Right Internal Ear of a Human Embryo at the Fifth Month; seen from the Medial Side. (After Retzius, from Barker.) 1–5, Útricle; 2, utricular recess; 3, macula acustica of utricle; 4, posterior sinus; 5, superior sinus; 6, 7, 8, superior, lateral, and posterior ampullæ; 9, 10, 11, superior, posterior, and lateral semicircular canals; 12, widened mouth of lateral semicircular canal opening into the utricle; 13, saccule; 14, macula acustica of the saccule; 15, endolymphatic duct: 16, utriculo-saccular duct; 17, ductus reuniens; 18, vestibular cul-de-sac of cochlear duct: 10, cochlear duct; 20, facial nerve; 21–24, auditory nerve; 21, its vestibular branch; 22, saccular branch; 23, branch to inferior ampulla; 24, cochlear branch; 25, distribution of cochlear branch within the bony spiral lamina.

the space intervening between the spiral ligament and the bony spiral lamina, thus completely dividing the bony canal of the cochlea into two parts, an upper, scala vestibuli (Fig. 351, l) and a lower, scala tympani (Fig. 351, k). These are perilymphatic spaces, the scala vestibuli communicating with the perilymph space of the vestibule, the scala tympani communicating with the perivascular lymph spaces of the veins of the cochlear duct. The scala vestibuli and the scala tympani communicate with each other in the cupola by means of a minute canal, the helicotrema.

THE COCHLEAR DUCT (Membranous Cochlea or Scala Media).—This is a narrow, membranous tube lying near the middle of the bony cochlear canal and following its spiral turns from the vestibule,

where it is connected with the saccule through the canalis reuniens, to its blind ending in the cupola. It is triangular in shape on transverse section, thus allowing a division of its walls into upper, outer, and lower (Fig. 351, Dc).

The upper or vestibular wall is formed by the thin membrane of Reissner (Fig. 351, b) which separates the cochlear duct from the

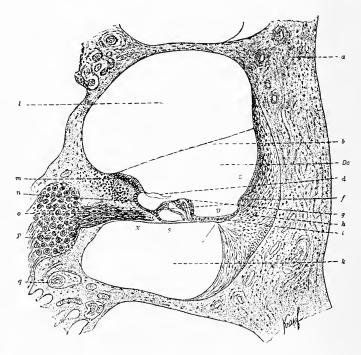


Fig. 351.—Section through a Single Turn of the Cochlea of a Guinea-pig. (Böhm and von Davidoff.) a, Bone of cochlea; l, scala vestibuli; Dc, scala media or cochlear duct; k, scala tympani; b, membrane of Reissner; d, membrana tectoria or membrane of Corti; f, spiral prominence; g, organ of Corti; h, spiral ligament; h, basilar membrane (outer portion—zona pectinata—covered by cells of Claudius); h, spiral vascularis; h, external spiral sulcus; h, crista basilaris; h, membranous spiral lamina; h, bony spiral lamina; h, spiral limbus; h, internal spiral sulcus; h, medullated peripheral processes (dendrites) of cells of spiral ganglion passing to the organ of Corti; h, spiral ganglion; h, blood-vessel.

scala vestibuli. The membrane consists of a thin central lamina of connective tissue covered on its vestibular side by the vestibular endothelium, on its cochlear side by the epithelium of the cochlea.

The outer wall of the cochlear duct is formed by the spiral ligament, which is a thickening of the periosteum. The outer part of the spiral ligament consists of dense fibrous tissue, its projecting part of more loosely arranged tissue. From it, two folds project

slightly into the duct. One, the crista basilaris (Fig. 351, r), serves for the attachment of the membranous spiral lamina; the other, the spiral prominence (Fig. 351, f), contains several small veins. Between the two projections is a depression, the external spiral sulcus (Fig. 351, v). That part of the spiral ligament between the spiral prominence and the attachment of Reissner's membrane is known as the stria vascularis (Fig. 351, z). It is lined with granular cuboidal epithelial cells, which, owing to the absence of a basement membrane, are not sharply separated from the underlying connective tissue. For this reason the capillaries extend somewhat between the epithelial cells, giving the unusual appearance of a vascular epithelium.

The lower or tympanic wall of the cochlear duct has an extremely complex structure. Its base is formed by the already mentioned bony and membranous division-wall between the scala media and the scala tympani (bony spiral lamina and membranous spiral lamina).

The bony spiral lamina has been described (page 523).

The membranous spiral lamina consists of a substantia propria or basilar membrane, its tympanic covering, and its cochlear covering.

The basilar membrane (Fig. 351) is a connective-tissue membrane composed of fine straight fibres which extend from the bony spiral lamina to the spiral ligament. Among the fibres are a few connective-tissue cells. On either side of the fibre layer is a thin, apparently structureless membrane.

The *tympanic covering* of the basilar membrane consists of a thin layer of connective tissue—an extension of the periosteum of the spiral lamina—covered over by a single layer of flat endothelial cells.

The cochlear covering of the basilar membrane is epithelial. Owing to the marked difference in the character of the epithelium, the basilar membrane is divided into an outer portion, the zona pectinata (Fig. 351, i) and an inner portion, the zona tecta (Fig. 351, s). The epithelium of the former is of the ordinary columnar type; that of the latter is the highly differentiated neuro-epithelium of Corti's organ.

The Organ of Corti.—The spiral organ or the organ of Corti (Fig. 351, g, and Fig. 352) is a neuro-epithelial structure running the entire length of the cochlear canal with the exception of a short distance at either end. It rests upon the membranous portion of the spiral lamina, and consists of a complex arrangement of four different kinds of epithelial cells. These are known as: (1) pillar cells, (2) hair cells, (3) Deiter's cells, and (4) Hensen's cells (Fig. 352).

(1) The pillar cells are divided into outer pillar cells and inner

pillar cells. They are sustentacular in character. Each cell consists of a broad curved protoplasmic base which contains the nucleus, and of a long-drawn-out shaft or pillar which probably represents a highly specialized cuticular formation. The end of the pillar away from the base is known as the *head*. The head of the outer pillar presents a convexity on its inner side, which fits into a corresponding concavity on the head of the inner pillar, the heads of opposite pillars thus "articulating" with each other. From their articulation the pillars diverge,

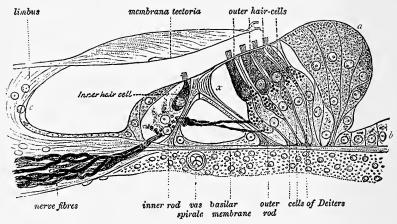


Fig. 352.—Semidiagrammatic Representation of the Organ of Corti and Adjacent Structures (Merkel-Henle.) a, Cells of Hensen; b, cells of Claudius; c, internal spiral sulcus; x, Nuel's space. The nerve fibres (dendrites of cells of the spinal ganglion) are seen passing to Corti's organ through openings (foramina nervosa) in the bony spiral lamina. The black dots represent longitudinally-running branches, one bundle lying to the inner side of the inner pillar, a second just to the outer side of the inner pillar within Corti's tunnel, the third beneath the outer hair cells.

so that their bases which rest upon the basilar membrane are widely separated. There are thus formed by the pillars a series of arches known as *Corti's arches*, enclosing a triangular canal, *Corti's tunnel*. This canal is filled with a gelatinous substance and crossed by delicate nerve fibrils. As the outer pillar cells are the larger, they are fewer in number, the estimated number in the human cochlea being forty-five hundred of the outer cells and about six thousand of the inner cells.

(2) The hair cells or auditory cells lie on either side of the arches of Corti, and are thus divided into inner hair cells and outer hair cells. Both inner and outer hair cells are short, cylindrical elements which do not extend to the basilar membrane. Each cell ends below in a point, while from its free surface are given off a number of fine stiff hairs

The inner hair cells lie in a single layer against the inner side of the inner pillar cells, one hair cell resting upon about every two pillars.

The outer hair cells lie in three or four layers to the outer side of the outer pillar cells, being separated from one another by sustentacular cells, the cells of Deiter, so that no two hair cells come in contact.

- (3) Deiter's Cells (Fig. 352).—These like the pillar cells are sustentacular. Their bases rest upon the basilar membrane, where they form a continuous layer. Toward the surface they become separated from one another by the hair cells. The long slender portions of the Deiter's cells, which pass in between the hair cells, are known as phalangeal processes. Between the innermost of the outer hair cells and the outer pillar is a space known as Nuel's space (Fig. 352, x).
- (4) Hensen's Cells (Fig. 352, a).—These are sustentacular cells, which form about eight rows to the outer side of the outermost Deiter's cells. These cells form the outer crest of Corti's organ and consequently have a somewhat radial disposition, their free surfaces being broad, their basal ends narrow. They decrease in height from within outward, and at the end of Corti's organ become continuous with the cells of Claudius (Fig. 352, b), the name given to the cochlear epithelium covering the basal membrane to the outer side of Corti's organ.

The phalangeal processes of the Deiter's cells are cemented together and to the superficial parts of the outer pillars in such a manner as to form a sort of cuticular membrane, the *lamina reticularis*, through which the heads of the outer hair cells project. This membrane also extends out as a cuticula over the cells of Hensen and of Claudius.

The Membrana Tectoria.—This is a peculiar membranous structure attached to a projection of the bony spiral lamina known as the *spiral limbus* (Fig. 352), the concavity beneath its attachment being the *internal spiral sulcus* Fig. 352, c). The membrane is non-nucleated and shows fine radial striations. It bridges over the internal spiral sulcus and ends in a thin margin, which rests upon Corti's organ just at the outer limit of the outer hair cells.

**Blood-vessels.**—The arteries consist of two small branches of the auditory—one to the bony labyrinth, the other to the membranous labyrinth. The latter divides into two branches—a vestibular and a cochlear. The vestibular artery accompanies the branches of the auditory nerve to the utricle, saccule, and semicircular canals. It supplies these parts, giving rise to a capillary network, which is coarse meshed except in the cristæ and maculæ, where the meshes are fine. The

cochlear artery also starts out in company with the auditory nerve, but accompanies it only to the first turn of the cochlea. Here it enters the modiolus where it gives off several much coiled branches, the glomerular arteries of the cochlea. Branches from these pierce the vestibular part of the osseous spiral lamina and supply the various structures of the cochlear duct. The veins accompany the arteries, but reach the axis of the modiolus through foramina in the tympanic part of the bony spiral lamina.

Lymphatics.—The scala media contains endolymph and is in communication with the subdural lymph spaces by means of the endolymphatic duct, the endolymphatic sac, and minute lymph channels connecting the latter with the subdural spaces. The perilymph spaces—scala tympani and scala vestibuli—are connected with the pial lymph spaces by means of the perilymphatic duct. Lymph spaces also surround the vessels and nerves. These empty into the pial lymphatics.

**Nerves.**—The vestibular branch of the auditory nerve divides into branches which supply the saccule, utricle, and semicircular canals, where they end in the maculæ and cristæ as described on page 521. The ganglion of the vestibular branch is situated in the internal auditory meatus. The cochlear branch of the auditory nerve enters the axis of the modiolus, where it divides into a number of branches which pass up through its central axis. From these, numerous fibres radiate to the bony spiral laminæ, in the bases of which they enter the spiral ganglia (Fig. 351, p).

The cells of the spiral ganglia are peculiar, in that while of the same general type as the spinal ganglion cell they maintain their embryonic bipolar condition (see page 376) throughout life. Their axones follow the already described course through the modiolus and thence through the internal auditory meatus to their terminal nuclei in the medulla (see page 441). Their dendrites become medullated like the dendrites of the spinal ganglion cells and pass outward in bundles in the bony spiral laminæ (Fig. 351, 0, and Fig. 352). From these are given off branches which enter the tympanic portion of the lamina, where they lose their medullary sheaths and pass through the foramina nervosa (minute canals in the tympanic part of the spiral lamina) to their terminations in the organ of Corti. In the latter the fibres run in three bundles parallel to Corti's tunnel. One bundle lies just inside the inner pillar beneath the inner row of hair cells (Fig. 352). A second bundle runs in the tunnel to the outer side of the inner pillar

(Fig. 352). The third bundle crosses the tunnel (tunnel-fibres) and turns at right angles to run between the cells of Deiter beneath the outer hair cells (Fig. 352). From all of these bundles of fibres are given off delicate terminals which end on the hair cells.

#### Development of the Ear.

The essential auditory part of the organ of hearing, the membranous labyrinth, is of ectodermic origin. This first appears as a thickening followed by an invagination of the surface ectoderm in the region of the posterior cerebral vesicle. This is known as the auditory pit. By closure of the lips of this pit and growth of the surrounding mesodermic tissue is formed the otic vesicle or otocyst, which is completely separated from the surface ectoderm. Diverticula soon appear passing off from the otic vesicle. These are three in number and correspond respectively to the future endolymphatic duct, the cochlear duct and the membranous semicircular canals. Within the saccule, utricle, and ampullæ special differentiations of the lining epithelium give rise to the maculæ and cristæ acusticæ. Of the cochlear duct the upper and lateral walls become thinned to form Reissner's membrane and the epithelium of the outer wall, while the lower wall becomes the basilar membrane, its epithelium undergoing an elaborate specialization to form the organ of Corti.

Of the cochlea, only the membranous cochlear duct develops from the otic vesicle; the scala vestibuli, scala tympani, and bony cochlea developing from the surrounding mesoderm. The mesodermic connective tissue at first completely fills in the space between the cochlear duct and the bony canal. Absorption of this tissue takes place, resulting in formation of the scala tympani and scala vestibuli.

During the differentiation of the above parts a constriction appears in the body of the primitive otic vesicle. This results in the incomplete septum which divides the utricle from the saccule.

The middle ear is formed from the upper segment of the pharyngeal groove, the lower segment giving rise to the Eustachian tube.

The external ear is developed from the ectoderm of the first branchial cleft and adjacent branchial arches. The tympanic membrane is formed from the mesoderm of the first branchial arch, its outer covering being of ectodermic, its inner of entodermic origin.

#### TECHNIC.

(1) For the study of the general structure of the pinna and walls of the external auditory meatus, material may be fixed in formalin-Müller's fluid (technic 5,

- p. 7) and sections stained with hæmatoxylin-eosin (technic 1, p. 18). In sections of the wall of the cartilaginous meatus the ceruminous glands may be studied, material from children and from new-born infants furnishing the best demonstrations of these glands.
- (2) For the study of the inner ear the guinea-pig is most satisfactory on account of the ease with which the parts may be removed. Remove the cochlea of a guinea-pig with as much as possible of the vestibule and semicircular canals and fix in Flemming's fluid (technic 7, p. 7). A small opening should be made in the first turn of the cochlea in order to allow the fixative to enter the canal. After forty-eight hours the cochlea is removed from the fixative and hardened in graded alcohols (page 8). The bone is next decalcified, either by one of the methods mentioned on page 9 or in saturated alcoholic solution of picric acid. If one of the aqueous decalcifying fluids is used, care must be taken to carry the material through graded alcohols. Embed in celloidin or paraffin, cut sections through the long axis of the modiolus, through the utricle and saccule, and through the semicircular canals. Stain with hæmatoxylin-eosin and mount in balsam.
- (3) The neurone relations of the cristæ, macuke, and cochlear duct can be demonstrated only by means of the Golgi method. The ear of a new-born mouse or guinea-pig furnishes good material. The cochlea together with some of the base of the skull should be removed and treated by the Golgi rapid method (page 32). Sections should be thick and must of course be cut through undecalcified bone. Good results are difficult to obtain.

## The Organ of Smell.

The olfactory organ consists of the olfactory portion of the nasal mucosa. In this connection it is, however, convenient to describe briefly the *olfactory bulb* and the *olfactory tract*.

The Olfactory Mucosa.—This has been described (page 264). The peculiar olfactory cells there described are not neuro-epithelium but are analogs of the spinal ganglion cell, being the only example in man of the peripherally placed ganglion cell found in certain lower animals. Each cell sends to the surface a short dendrite which ends in several short, stiff, hair-like processes. From its opposite end each cell gives off a longer centrally directed process (axone), which as a fibre of one of the olfactory nerves passes through the cribriform plate of the ethmoid (Fig. 353, ethm) to its terminal nucleus in the olfactory bulb (Fig. 353).

The Olfactory Bulb.—This is a somewhat rudimentary structure analogous to the much more prominent olfactory brain lobe of some of the lower animals. It consists of both gray matter and white matter arranged in six fairly distinct layers. These from below upward are as follows: (a) The layer of olfactory fibres; (b) the layer of glomeruli; (c) the molecular layer; (d) the layer of mitral cells; (e) the granule

layer; (f) the layer of longitudinal fibre bundles. Through the centre of the last-named layer runs a band of neuroglia which represents the obliterated lumen of the embryonal lobe. The relations of these layers to the olfactory neurone system are as follows:

The layer of olfactory fibres (Fig. 353, a) consists of a dense plexiform arrangement of the axones of the above-described olfactory cells.

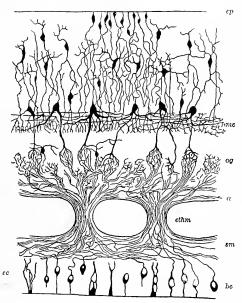


Fig. 353.—Diagram of Structure of Olfactory Mucosa and Olfactory Bulb. (Ramón y Cajal.) bc, Bipolar cells of olfactory mucosa; sm, submucosa; ethm, cribriform plate of ethmoid; a, layer of olfactory fibres; og, olfactory glomeruli; me, mitral cells; ep, epithelium of olfactory ventricle.

From this layer the axones pass into the layer of olfactory glomeruli where their terminal ramifications mingle with the dendritic terminals of cells lying in the more dorsal layers, to form distinctly outlined spheroidal or oval nerve-fibre nests, the *olfactory glomeruli* (Fig. 353, 0g). The latter mark the ending of neurone system No. I. of the olfactory conduction path.

The molecular layer contains both small nerve cells and large nerve cells. These send their dendrites into the olfactory glomeruli. The smaller cells belong to Golgi Type II. (see page 117) and appear to be association neurones between adjacent glomeruli. The axones of the larger cells, the so-called brush cells, become fibres of the *olfacory tract*.

Of the mitral cells (Fig. 353, me), the main dendrites end in the olfactory glomeruli, while their axones, like those of the brush cells, become fibres of the *olfactory tract*.

In addition to the fibres which pass through it (axones of mitral and of brush cells), the granular layer contains numerous nerve cells. Many of these are small and apparently have no axones (amacrine cells.) Their longer dendrites pass toward the periphery, their shorter dendrites toward the olfactory tract. Larger multipolar cells, whose axones end in the molecular layer, also occur in the granular layer.

The layer of longitudinal fibre bundles consists mainly of the centrally directed axones of the mitral and brush cells. These fibres run in distinct bundles separated by neuroglia. Leaving the bulb they form the olfactory tract by means of which they pass to their cerebral terminations.

The brush cells and mitral cells with their processes thus constitute neurone system No. II. of the olfactory conduction path.

#### TECHNIC.

- (1) Carefully remove the olfactory portion of the nasal mucosa (if human material is not available, material from a rabbit is quite satisfactory). This may be recognized by its distinctly brown color. Fix in Flemming's fluid (technic 7, p. 7), or in Zenker's (technic 9, p. 8). Stain thin vertical sections with hæmatoxylin-eosin (technic 1, p. 18) and mount in balsam.
- (2) For the study of the nerve relations of the olfactory cells material should be treated by the rapid Golgi method (page 32).

# The Organ of Taste.

The organ of taste consists of the so-called taste buds of the lingual mucosa. These have been mentioned in connection with the papillæ of the tongue (page 199) and under sensory end-organs (Fig. 268).

The taste buds are found in the side walls of the circumvallate papillæ (page 199), of some few of the fungiform papillæ, in the mucosa of the posterior surface of the epiglottis, and especially in folds (foliate papillæ) which occur along the postero-lateral margin of the tongue.

The taste bud (Fig. 354) is an ovoid epithelial structure embedded in the epithelium and connected with the surface by means of a minute canal, the gustatory canal (Fig. 354, a), the outer and inner ends of which are known, respectively, as the outer and inner taste pores.

Each taste bud consists of two kinds of cells, neuro-epithelial cells

or gustatory cells and sustentacular cells (Fig. 354). The gustatory cells are long, delicate, spindle-shaped cells which occupy the centre

of the taste bud, each ending externally in a cilium-like process, which usually projects through the inner pore. The inner end of the cell tapers down to a fine process, which may be single or branched. The sustentacular cells are long, slender cells which form a shell several cells thick around the gustatory cells. Sensory terminals of the glossopharyngeal nerves (Fig. 354, b) end within the taste buds in a network of varicose fibres—intrageminal fibres. Other sensory terminals of the same nerve end freely in the epithelium between the taste buds. These are finer and smoother than the intrageminal

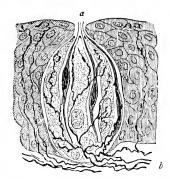


Fig. 354.—Taste-bud from Side Wall of Circumvallate Papilla. (Merk l-Henle.) a, Taste-pore; b, nerve fibres, some of which enter the taste-bud—intrageminal fibres; while others end freely in the surrounding epithelium—intergeminal fibres.

fibres and are known as intergeminal fibres (Fig. 354).

#### TECHNIC.

- (1) The general structure of the taste buds is shown in the sections of tongue (technic, p. 200).
- (2) For the study of the nerve terminals the method of Golgi should be used (page 32).

# General References for Further Study.

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