A TEXTBOOK OF
HISTOLOGY

By

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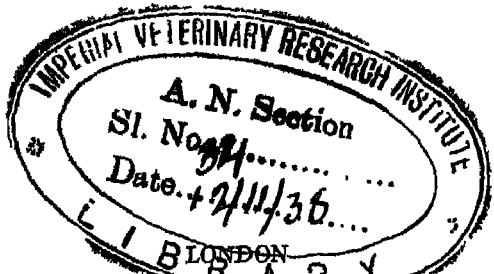

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PREFACE

The purpose of this text is something more than a precocious preparation for premedical students. The author has had a long and satisfactory association as professor of zoology at the University of Georgia. Subsequent experience as professor of microscopic anatomy in the Medical School has led him to question the balance in training secured by the old sequence of general biology, comparative anatomy, embryology and genetics. This preface is written as an appeal to biologists to admit histology into the college curriculum on the same footing as the last three sister sciences.

These subdivisions of advanced biology are generally introduced to extend the principles somewhat dogmatically developed in the first year course. It is self-evident that the "cell theory" may be more rationally expounded in histology than in comparative anatomy. "Evolution" may be made to take on a newer and less pedantic form under the microscope than under the scalpel. Embryology and genetics are both "unfinished business" except in terms of histology. Neither can have the practical significance nor the range of correlation of histology. The physiologist must be somewhat of a histologist and the biochemist must interpret his material in terms of cell behavior. Popular medical education, based on its hygiene of balanced diets, alkalies, vitamins, is so much quibble without a sound knowledge of cellular make-up.

For the student of the social sciences, ignorance of the organization of the nervous system and the rôle of the endocrines precludes the development of a complete and rational system of psychology, and its appenda, education, criminology, social adjustment.

Lastly, for those who have a special aptitude for the techni-

cal, the methods of histology offer a special fascination. The preparation of sections, the methods of study and methods of representation appeal to the mechanic, the artist and the scientist alike. The problems are still so numerous that there is no limit to the method of experimentation and practical results are assured. Furthermore, public health laboratories and local hospitals offer an opportunity to many young women who "want to make their own way and who hate teaching." Training should be supplemented by courses in bacteriology and clinical laboratory methods.

Now a word or two with respect to this particular text. Written on assignment, the organization is definitely planned to give the separate sub-divisions a balance. Short chapters allow easy, definite text assignments that may be correlated with a reasonable amount of laboratory work. With twelve exceptions the text-figures are original free-hand or camera lucida drawings made from preparations in the collection of the Department of Microscopic Anatomy, University of Georgia Medical School. Students with average ability may readily be taught to duplicate the preparations and studies on laboratory animals if human material is not available.

As to orginality, no modern text may lay claim to any great degree. Henle organized the science in 1841 and his figures and statements are a heritage prized by all modern authors. In raising the section on marrow to the significant position of a chapter heading, we hope to have made a distinct contribution.

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Chapter I

INTRODUCTION

Histology (G. *histos*, tissue; *logos*, treatise) is that branch of science which deals with the finer visible structure of the body. As an organized science it had its origin in the detailed dissections of Bichat (1801) on the mucous, serous and fibrous membranes. Today it has come to mean the microscopical anatomy of the various organs, although many of its concepts date back beyond the period of the effective use of the compound microscope. In the seventeenth century, Malpighi had already described the layers of the skin, the corpuscles of the kidney and spleen; Havers had discovered the canals in bone; Peyer had found the massive lymph nodes of the intestine and Glisson had studied the capsule of the liver. In 1745, Lieberkühn described the villi and the glands of the small intestine, and in 1753, Zinn had published a complete atlas on the finer structure of the eye.

Histology, however, did not take its place as a separate branch of anatomy until after the elaboration of the cell theory in 1839. Henle wrote the first real text in 1841. Histology is barely one hundred years old.

The cell theory, stated in simple terms, is that every plant and every animal is composed of cells or cell products. The simpler animals and simpler plants are composed of single cells. A single cell may thus carry out all of the processes which, taken in their totality, constitute that mysterious and complex phenomenon which we call life. Cells, then, are functional as well as structural units.

The jelly-like (colloidal) material of which cells are composed is called protoplasm (G. *protos*, first; *plasma*, thing formed). It is colorless, highly refractile, and viscous.

Chemically it is composed of water, some salts, and three major types of carbon compounds—proteins, carbohydrates and fats.

In the typical cell, two separate and discrete parts are regularly recognizable—the cytoplasm and the nucleus (L. diminutive of *nux*, a nut). Both parts are essential for continued maintenance of life in the cell, although the specific rôle of each part can only be guessed at (Fig. 1).

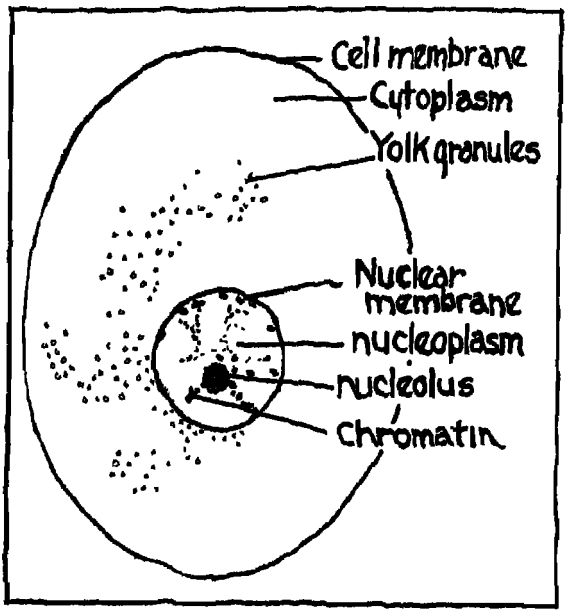


FIG. 1. Drawing of a large single cell, the egg or ovum. The ovum contains a large central nucleus which bears a discrete deeply staining nucleolus and numerous small granules of chromatin. The nuclear membrane is sharply defined. The cytoplasm is filled with fine granules confined to the central portion more than to the periphery. A discrete cell membrane is present.

The living nucleus is generally spherical, is a bit more refractive than the cytoplasm, and is generally centrally placed. Few structures are recognizable in it unless the cell has been "fixed." In cells, specially treated and stained, a great many complex structures can be identified in the nucleus. Chief among these are the nuclear membrane, the chromatin

and the nucleolus. The nuclear membrane is very thin, and flexible. It is constantly present except for the short period during which the cell is in the process of division. It serves to retain the more fluid content of the nucleus, probably regulates the interchange of materials between nucleus and cytoplasm and at the same time serves as a supportive framework for the reticulum or network of fibers that pervade the nucleus.

The chromatin (G. *chroma*, color) consists of an elaborate series of fine or coarse granules, evenly or irregularly dispersed throughout the nucleus, supposedly on a system of fine fibrils, the linin network. Chromatin is of great significance. The laws of heredity, established by the science of genetics, have been correlated with the distribution of chromatin, and the current opinion prevails that chromatin controls the development of the specific character of the cell.

Many cells, particularly young cells, show one or more very large specific granules that differ by certain methods of staining from the chromatin. These are the nucleoli (L. dim. of nucleus).

In addition to this system of granules and fibrils, a nuclear sap or ground substance fills in the interstices or prevailing spaces. This is generally pale staining or is completely removed by many techniques of preparation. The relative amount of ground substance to chromatin is of considerable interest. In old senescent cells a pycnotic nucleus is produced by a condensation of chromatin to the extent that no ground substance shows. Young cells generally show a vesicular or "swollen" nucleus in which the ground substance is greatly increased. This character is sometimes made use of in the identification of certain cell types.

The nucleus, like the cytoplasm, is colloidal in nature and hence plastic. In cells that are laterally compressed, it too may be compressed and become rod-shaped instead of spherical. Its position is not always permanently fixed in the cell. It may be pushed from a central to a basal position or it may

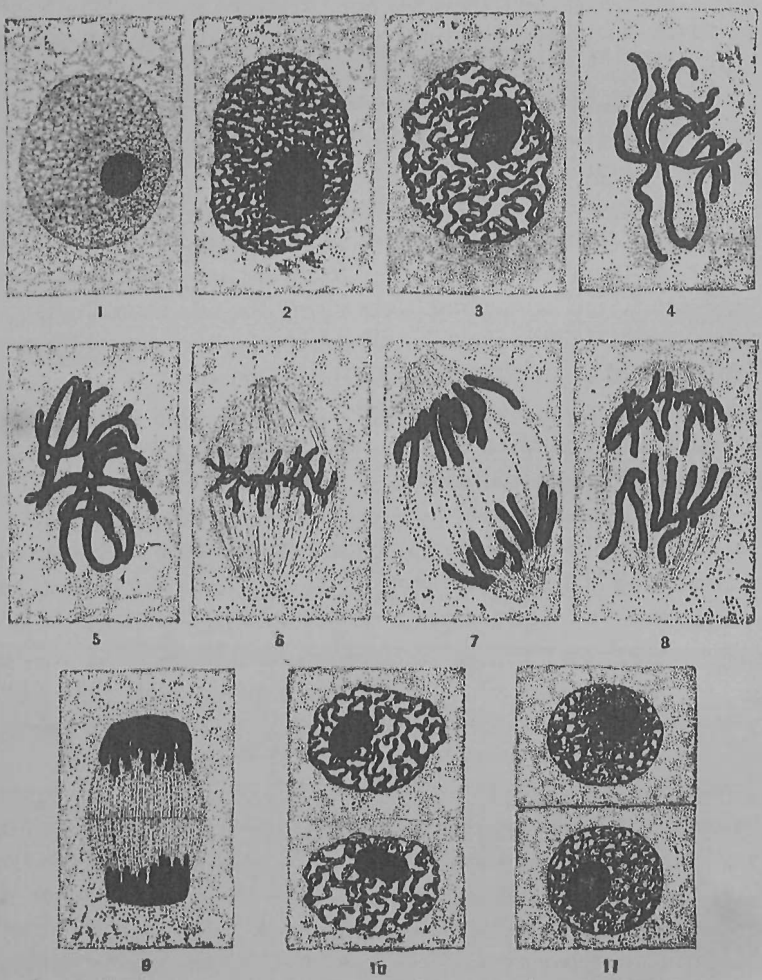


FIG. 2. Series of drawings representing the stages of mitosis or cell division seen in the growing root tip of the onion: *1*, vegetative nucleus; *2*, fine spireme; *3*, coarse or open spireme; *4*, *5*, segmentation of the spireme into chromosomes; *6*, arrangements of the chromosomes in the equatorial plate of the spindle (metaphase); *7*, *8*, migration of the daughter chromosomes to the spindle poles (anaphase); *9*, telophase,—showing the formation of the cell plate; *10*, late telophase, with reconstruction of the chromatin masses into vegetative nuclei; *11*, daughter cells. (After Bailey.)

migrate to a peripheral position. We sometimes premise or postulate the functional state of a cell by the position of the nucleus.

The special changes through which the nucleus goes at the time the cell divides is called mitosis. The process is represented in Figure 2.

The cytoplasm constitutes the cell body and is subject to a great deal more variation than is the nucleus. Permanent variation from the "spheroid" form occurs as a result of "differentiation" according to the law of the "division of labor" among cells. Thus the form of a nerve cell is very different from that of a muscle (Figs. 14, 94). Temporary variation in form occurs according to the physiological state of cells. A young goblet cell has a very marked difference in form from an old one just ready to discharge its mucus (Fig. 49).

While the ideal "spheroid" form of a cell might be expected on the basis of the colloidal nature of the cell, this form is rarely realized in a tissue, owing (1) to differentiation within the cell and (2) to the external forces modifying it because of its plasticity.

Among the substances easily recognized within the cytoplasm are (1) vacuoles filled with gases, oils, fluids; (2) granules of stored substances such as yolk, glycogen (animal starch), pigments; (3) granules of elaborated substances such as secretory granules, pro-enzymes or particles which become the digestive ferments when extruded; (4) granules permanently retained in the cell such as those of various leucocytes or white blood corpuscles; (5) granules representing digestive debris of materials eaten such as blood pigment in cells of the spleen; (6) fibrils in muscle cells.

In many cells, such as the white blood corpuscles, two zones of cytoplasm may be made out: a clear outer exoplasm and an inner granular endoplasm.

The cell "wall" itself is a variable. Sometimes it is rigid due to the presence of cellulose or chitin; sometimes it is a true

separable membrane and sometimes it is nothing more than a "surface condensation." The membrane is of extreme importance since it is semi-permeable and by osmosis regulates the intake and output of the cell. Its action is considered to be "selective," by which it may confer specific functions on particular cells.

Many other "cell-organs" have been described, following the use of particular techniques on particular cells. Cilia, flagella, mitochondria, centrosomes, astral rays will be discussed in those sections of the text where they have a particular significance.

In concluding this chapter, it should be indicated that while the cell is defined as the unit of structure and function, and retains to a certain degree its primitive autonomous capacities of irritability, metabolism, growth and reproduction, there is also present in the composite body a certain organizing principle that makes the "individual" the real unit. A man is something more than an aggregate of four quadrillion cells.

Chapter II

GENERAL CONCEPTS

With the exception of the one-celled animals and one-celled plants, all organisms, including man, are cellular composites. Each individual is made up of a set of special organs, designed to carry out special functions effectively. Thus the lungs are thin-walled sacs in which oxygen and carbon-dioxide exchange may be made by simple diffusion between the blood stream and the air. The liver stores sugar and secretes bile and possibly performs seven or more other important acts.

Each organ in turn is made up of a series of tissues. We recognize, for convenience in description, four types of tissue—epithelia, muscle, connective tissue and nerve. The stomach, as an organ, contains all four of these types compounded in such a fashion as to become an autonomous organ of whose presence we are little aware.

Tissues in their turn are composed of cells or cell products, generally of one more or less uniform type.

The science of embryology teaches us that all of these cells in tissue and organ had their beginning in a single cell, the fertilized egg. By the continuous process of growth, cell multiplication and cell differentiation, the fertilized egg rapidly becomes a complex organism. The detailed description we will leave for a future chapter. For the present it is enough to say that at one stage, the growing egg is a hollow ball made up of three layers of cells. These three layers are the germ layers (Fig. 3). The outer is the ectoderm (G. *ektos,* outside; *derma,* skin); the middle is the mesoderm (G. *mes,* middle) and the inner is the endoderm (G. *endon,* inside). These three layers are important in establishing interrelations between certain cell

groups, and are convenient in various attempts to analyze changes in form and function that occasionally occur.

In a general way, the various tissues of the body may be referred to the three layers. The following table is meant only as an introduction to the problem. A complete classification is only possible after a thorough study of embryology.

Endoderm

1. Epithelial lining of the alimentary tract from the back of the mouth to the anal canal.
2. All associated glands such as thyroid, thymus, parathyroid, liver, pancreas, gastric glands, crypts of Lieberkühn, etc.
3. Epithelial lining of the larynx, trachea, bronchi and lungs.
4. Practically all of the lining epithelium of the urinary bladder.

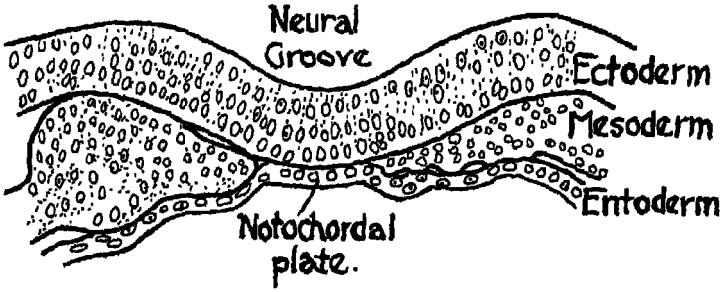


FIG. 3. The three primary germ layers—ectoderm, mesoderm, endoderm, as seen in a transection of a human embryo, 1.4 mm. The neural groove and the notochordal plate are also represented.

Mesoderm

1. Muscle—striate, cardiac and smooth (except for those of iris).
2. All connective tissue such as tendons, fascia, ligaments.
3. Bone and cartilage, and associated bursae.
4. Serous membranes, such as peritoneum, pleura, mesentery, omentum.
5. Muscular and fibrous coats of the digestive and respiratory organs. Muscular and fibrous coats of the bladder.
6. Entire kidney, ureter, spleen, vagina, uterus, tubes.
7. Germinal epithelium and supportive tissue of ovary or testis.
8. Entire blood vascular system including heart, arteries, veins, capillaries, marrow, blood corpuscles, lymphatics.
9. All supportive tissue such as capsules, septa, reticulum in various organs (except the brain and cord and a certain sheath of nerves).

Ectoderm

1. Epithelium of the skin and its appendages such as hair, nails, sweat glands, mammary glands, cornea, conjunctiva.
2. Epithelial lining of the orifices of the body such as the mouth, anus, external auditory meatus, nostrils, male urethra.
3. Entire cerebrospinal and sympathetic nervous system including brain, cord, ganglia and nerves, with their nerve cells and supportive neuroglial framework.
4. Special organs derived as outgrowths from the nervous system such as the retina, epithelium of the iris, posterior lobe of the pituitary gland, the pineal gland, medulla of the adrenal gland.
5. Special organs derived from primitive ectoderm such as anterior lobe of pituitary, lens, sensory epithelium of inner ear.

It is evident from a comparison of the single cell or ovum, with the cells of the three germ layers and those of a mature organ such as a nerve cell or muscle cell (Figs. 1, 3, 94) that a marked change has come about in the forms of these cells. This process is called differentiation. Histologists are at a loss to explain why such a change has taken place, but embryologists and philosophers assume an evolutionary process or "perfecting principle" for both the individual and for the race.

Histologists use the term "cytomorphosis" in referring to this process. Many cells, such as nerve cells, differentiate relatively early in life and persist throughout the life of the individual. Other cells, such as the blood corpuscles, continue to be produced by the parent tissues and may live only for a short functional period. Red blood corpuscles are thought to "wear out" in about forty days. White blood corpuscles may live only a few days. Skin cells are constantly being formed in the basal layer of the skin, migrate to a more superficial position and gradually become scale-like and "scale" off. This general process of youth, maturity, old age and death, is present to varying degrees in all cells, and the sum total of the process is reflected in similar "ages" in the life of man.

The one generally accepted law of cytomorphosis that is of importance is that "differentiation is not reversible." An "old" cell cannot become "young" again, nor can it change its

form and function to that of some other type. Time and training have left their imprint on its character.

A necessary corollary to this law is immediately suggested to account for "repair" in the body when it has suffered some accidental injury or become diseased. A reserve of young undifferentiated cells is generally assumed to explain the observed facts of healing. In some tissues these are demonstrable; in others they are assumed. We know nothing as to how they are held in "reserve" to meet this premised "need" of the body. Practically they become of prime importance in the theories that attempt to account for tumors and "cancer," for here we think that there may have been a "release" from controlling factors and that "local revolutions" develop in the "growth harmony" of the body.

Chapter III

EPITHELIA

Epithelia are cellular membranes which cover the internal and external surfaces of the body and line all of the cavities. In these membranes the cells retain a continuous approximation or juxtaposition, separated only by the intercellular cement substance. The term is derived from the Greek (*epi*, upon; *thele*, nipple), and was originally applied to the membrane which would separate on boiling from the underlying papillae of the skin (Ruysch, 1703).

Epithelia may be classified into two major groups—simple and stratified. Simple epithelia are only one cell layer deep; stratified are composed of many layers (Fig. 4).

A single cell in a simple epithelium presents three borders—(1) a basal border, (2) a lateral border, (3) a free border. The basal border is in contact with a basement membrane, a fine fibrillar structure represented in section by a single line, and considered to have three possible origins. It may be a secretion from the epithelial cell; it may be produced by the underlying connective tissue; or it may be a combined secretion from both.

The lateral borders of adjacent epithelial cells are in immediate apposition, and are held together by "cement substance." In some simple columnar epithelia, this substance may be especially thickened near the free surfaces of the cells to form the so-called "terminal bars." Some epithelia present the appearance of protoplasmic continuity between adjacent cells in the so-called "intercellular bridges."

The free border of the epithelial cell is the one subject to the greatest amount of variation. It may present merely a surface condensation; then again it may be covered by a secretory

membrane, the cuticle; or yet it may possess locomotor processes such as cilia. Since this surface is the one from which secretions are made, various sized blebs of mucous may be adherent, or depressions may temporarily exist representing the space once occupied by the material extruded (Fig. 4).

Simple epithelia may be further classified according to the forms assumed by the cells, due in part at least to the pressure

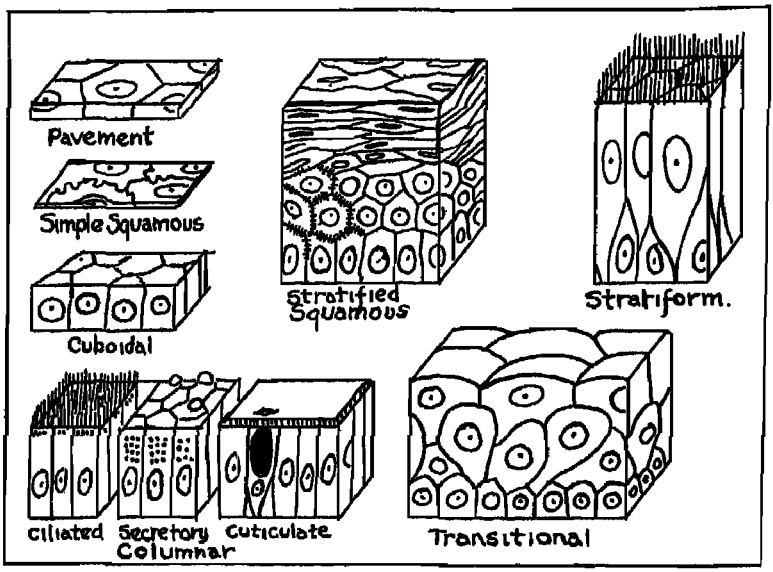


FIG. 4. Diagram of the various types of epithelia

relations existing in the membrane. Columnar cells have a long polar axis due in part to lateral compression. In cuboidal cells the two axes are practically equal. In pavement epithelium the polar axis is greatly reduced and in squamous epithelium the cells are flattened to the thinness of scales. Columnar and cuboidal epithelia constitute the bulk of the secretory surfaces of the body, and will be studied specifically when the separate organs are considered. Pavement epithelium is of a rather limited distribution being found in one

layer of Bowman's capsule in the kidney, in the pigmented layer of the retina, capsule cells of the spinal ganglia and the follicle cells of the primary ova (Fig. 4).

Simple squamous epithelium has a very wide distribution. Three subdivisions in this class have been recognized. (1) Endothelium lines the heart, arteries, veins, and sinuses of the brain, and forms the entire wall of the blood and lymph capillaries (Fig. 5). (2) Mesothelium is the simple squamous epi-

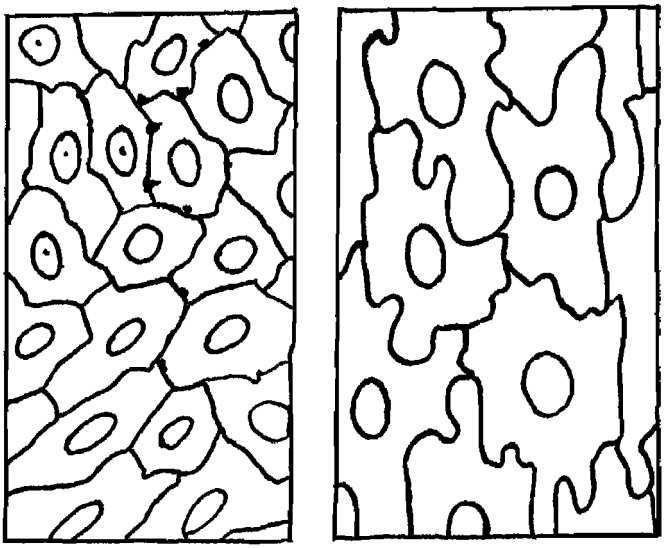


FIG. 5. Simple squamous epithelium. *A*, surface view of the mesothelial cells covering the mesenteries. *B*, surface view of the endothelial cells lining the veins. Similar cells line the arteries, capillaries and lymphatics.

thelium that lines the serous cavities of the body such as the pericardial, pleural and peritoneal (Fig. 5). (3) Mesenchymal epithelium is the simple squamous epithelium that lines the perilymph spaces of the internal ear (Fig. 89)—synovial membranes, bursae and tendon sheathes (according to some authorities).

In addition to columnar, cuboidal, pavement and squamous epithelia, a fifth type is sometimes recognized. This is the

pyramidal form (Fig. 55), a modified columnar, adapted to the construction of alveoli or swollen blind terminations which constitute the secretory portions of many glands. The base of the pyramidal cell rests on a basement membrane while the apex is turned toward the lumen of the duct.

Stratified epithelia are so-called because the cells occur in layers or strata. The cells vary in depth from two to thirty or more, and those of the various layers may be markedly different in form. The classification of the stratified epithelia is based on the character of the outermost layer; i.e., stratified squamous (Fig. 4), stratified columnar (Fig. 65). The deeper layers are the younger and are composed of "replacement cells" against the "wear and tear" of the outermost layer.

A thick stratified squamous epithelium clothes the entire body. Only on the cornea and the conjunctiva of the eyes, and on the ear drum, is it reduced to a few cell layers. This same epithelium is reflected inward over the mucocutaneous junctions such as the mouth and the vestibule of the nose. It continues through the pharynx and esophagus to the cardia of the stomach. At the posterior end of the body it is extended inward in the anal canal to the white line of Hilton and into the vaginal vault as far as the external os of the uterus (Figs. 45, 51, 71.).

The one outstanding character of the stratified squamous epithelium is the process of cornification which occurs in the outer layers. This occurs both on a dry surface like the skin or on a moist surface such as the mucous membranes. Attempts have been made to explain it on the basis of malnutrition of the cells in the outermost layers since in general "no capillaries are present within epithelia" and nutritive materials must diffuse from the underlying layers.

The outermost cells are flat and scale like,—may be vacuolated. They generally stain very poorly and show little structure. The nuclei are pycnotic or absent. The stratum germinativum or germinal layer is composed of an intermediate

zone of polyhedral cells and a single layer of basal cells. The latter are cylindrical in shape and rest on a basement membrane. The polyhedral cells show conspicuous intercellular bridges. When these cells are "dissociated" or torn apart, they have the appearance of "sand-spurs" and hence the name "prickle-cell" is frequently applied to them (Fig. 22). While both of these layers are collectively called the germinal layer, and both are active in repairing the skin in case of a wound, their behavior as far as tumor production is concerned is very different. Tumors from the basal cell layer are generally "benign;" those from the prickle cell layer are "malignant."

Stratified columnar epithelium consists of one or two rows of basal polyhedral, fusiform or pyramidal cells bearing a superficial layer of short columnar cells. This type of epithelium is rare, although frequently the so-called pseudo-stratified columnar epithelium is mistaken for it. The point of distinction between the two is that in the latter, every cell, in both the basal and the superficial zone, has a process which anchors it to the basement membrane. These processes are not always clearly distinguishable in ordinary preparations and hence the confusion in classification. Psuedo-stratified columnar may be plain as in the duct of the parotid and male urethra, or it may be ciliated as in the greater part of the respiratory passages and male sexual system.

Still another distinct type of epithelium exists as a "transition" between the stratified squamous and the stratified columnar. It is found in the urinary passages from the pelvis of the kidney, through the ureters and bladder to the first portion of the urethra. When the organs are distended, the superficial cells are stretched into a squamous shape; when the organ is contracted, the cells assume a more spherical form. The large superficial cells possess wings or flange-like processes that fit into the spaces between the deeper cells and anchor them in place. This cell type is important in differential diagnosis of diseases of the urinary tract by microscopic examination of the urine.

In conclusion, we may tabulate the epithelial forms as follows:

Simple	Columnar Cuboidal Pyramidal Pavement Squamous	Pseudo-stratified	Columnar
		Stratified	Columnar Squamous
		Transitional	

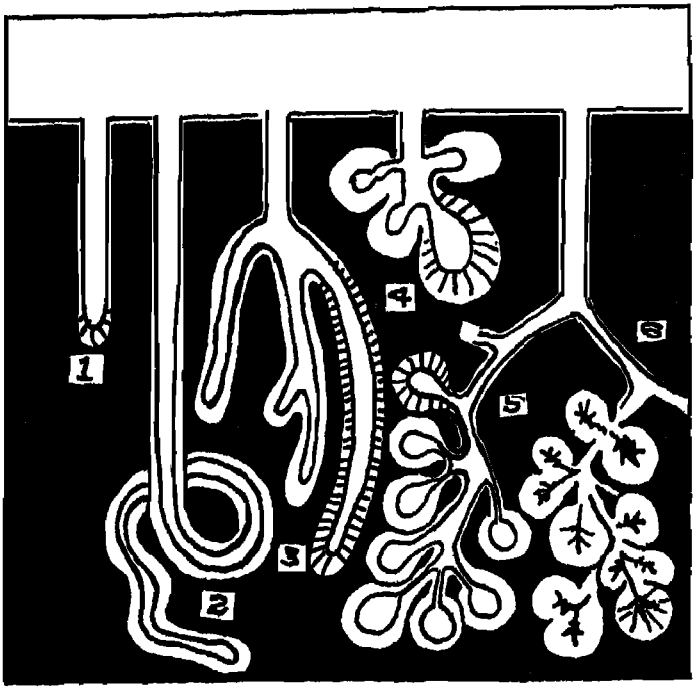


FIG. 6. Figure of the various types of glands. *1*, simple tubular; *2*, simple coiled tubular; *3*, branched tubular; *4*, branched alveolar; *5*, compound tubulo-alveolar; *6*, compound tubulo-acinar.

Since the parenchyma of all of the true glands is epithelial in origin we may briefly classify them here on form as simple, branched or compound; and tubular or alveolar according to the nature of the secretory end pieces (Fig. 6). All of the ductless glands (endocrine glands), with the exception of the thyroid, show a "corded" arrangement of their cells (Figs. 55, 79, 80, 81, 82, 83, 84).

Chapter IV

FIBROUS CONNECTIVE TISSUES

Connective tissues differ from epithelia in the enormous development of the intercellular substance. The cells are few in number and widely scattered on an interlacing system of fibers. Because of these fibers the connective tissues subserve a variety of functions. As subcutaneous tissue they permit a certain elasticity to the skin; as submucous tissues they permit changes in size of organs. They bind certain structures firmly together by tendon, ligament, fascia, aponeuroses. They form the flexible "skeleton" of the heart. They lend support to the most delicate cellular structures as capsules, septa and interstitial fibers. They serve as storehouses for reserve food such as fat. They hold fluids within their interstices. In case of injury, they actively repair cuts, breaks, tears. They encapsule and localize many foci of infection. Their cells clear away dead (necrotic) debris and are concerned in the production of the various immune bodies that combat the invasions of destructive micro-organisms. They form the hard supportive tissues of the body such as bone and cartilage, and certain dental tissues.

They have only one characteristic in common—they are all derived from mesenchyme.

The term mesenchyme was introduced by Hertwig in 1883 to refer to those cells which left the mesoderm as wandering cells and established themselves as cell aggregates or "condensations" in various locations. Adult connective tissue cells retain this type of behavior. They rarely lie in juxtaposition but are generally widely scattered throughout the tissue on a series of interlacing "fibers" (Fig. 7).

The nature and arrangement of these fibers give the tissues

their respective names. Three types of fibers have been isolated by various techniques: (1) white fibers; (2) yellow fibers; (3) reticular fibers. The white fibers (Fig. 7) are glistening, poorly refractile, non-elastic. They are very fine and are arranged in bundles of varying size. They are soluble in acetic acid and yield gelatin on boiling, hence the name "collagen" fibers. Yellow fibers are coarse, highly refractile,

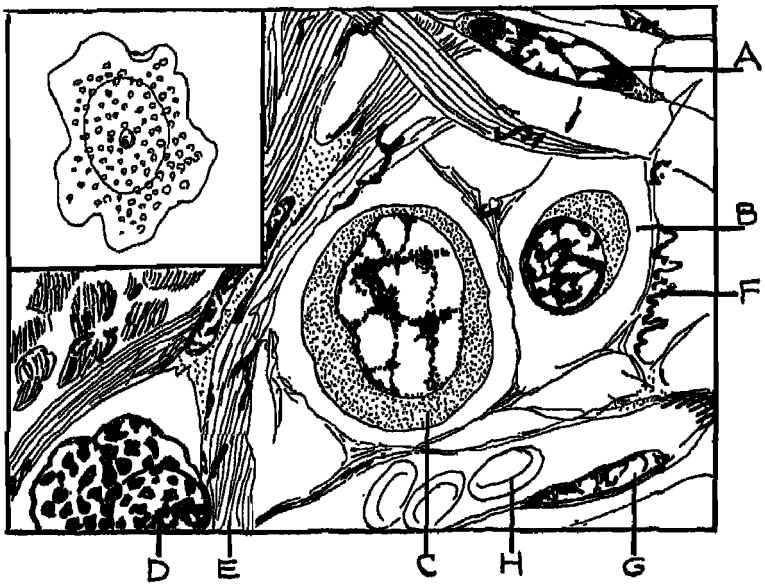
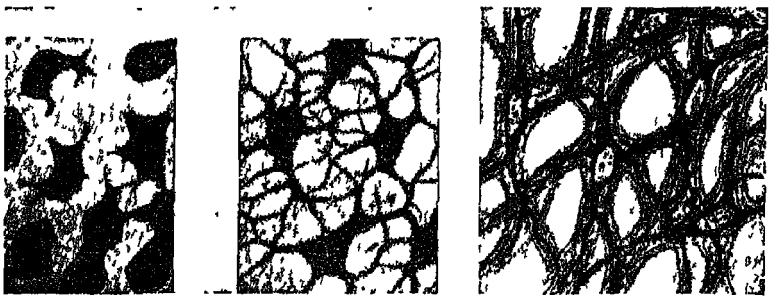


FIG. 7. Areolar connective tissue from the human scalp. *A*, fibroblast; *B*, plasma cell; *C*, histiocyte (clasmatocyte); *D*, same cell loaded with pigment (chromatophore); *E*, bundle of collagenous (white) fibers; *F*, single elastic fibers; *G*, endothelial cell lining a capillary; *H*, erythrocyte or red blood cell within the capillary.

elastic and non-soluble in acetic acid. They branch and fuse freely into elastic networks and as such form the "rebound" tissue in both the lung and in the aorta (Fig. 31). They do not yield gelatin on boiling but are made up of elastin. Reticular fibers are very delicate and produce a gelatin-like substance on boiling, reticulin. Reticular fibers may be stained specifically by colloidal silver; elastic fibers stain specifically with orcein

(Fig. 31); white fibers stain blue with aniline blue (Fig. 16) and may be identified from smooth muscle by picro-carmine.

Connective tissue cells are classified as either "fixed" or "free." The fixed cells are primarily concerned with the deposition of the intercellular substance; the free cells are "wanderers" in and out of specific localities. The fixed cells are the stellate fibroblasts or their modified forms such as tendon cell, spindle cell, chondrocyte, osteoblast, fat cell. Three principal types of "free" cell exist: (1) the histiocyte, (2) the plasma cell, (3) the mast cell (Fig. 7).



A B C

FIG. 8. Diagram of the evolution of connective tissue. *A*, mesenchyme, primordial connective tissue; *B*, reticular or mucoid connective tissue; *C*, young fibrous connective tissue. (After Cajal.)

Mast cells are very large flattened cells, generally distributed along the course of blood vessels. They are characterized by the presence of many large neutrophilic granules and a single rounded vesicular nucleus. Their function is unknown.

The plasma cell is a small cell, slightly larger than a blood lymphocyte. Its nucleus is coarsely granular with chromatin disposed in a "cart-wheel" fashion. This cell is generally considered to be a "tissue" lymphocyte. Some pathologists include the so-called "round-cell" in this class.

The histiocyte is a large cell showing a variety of shapes from ovoid to stellate. The cytoplasm may be finely granular or vacuolated. The nucleus is smaller and deeper staining than that of the fibroblast. Positive identification is made by so-

called vital staining methods, where trypan blue, or india ink is injected under the skin in the living animal. The histiocytes are phagocytic and take up the colloidal particles. Many names have been applied to them according to opinions of various investigators—clasmatocytes, rhagiocrin cells, adventitial cells; fixed macrophages; endotheliocytes. Together with a system of phagocytic cells that line the sinusoids of the body they constitute the so-called reticulo-endothelial system, a "police" system of the body, designed to keep down bacterial invasions.

The fibroblasts are so-called because it has been held that the fibers are differentiated from their cytoplasm (Fig. 8). The cells are fusiform or stellate. The nucleus is generally oval in outline and greatly flattened. The cytoplasm is generally very pale and rarely finely granular. It is generally held that fibroblasts are highly differentiated cells that do not give rise to other types, an opinion in which all investigators do not concur.

The origin of fibers has not been definitely settled. Some investigations indicate their formation from "amorphous ground substance" or plasma by a process of "clotting" somewhat after the fashion of fibrin formation in drawn blood. This is spoken of as the exogenous theory as opposed to the endogenous theory cited above.

A classification of the connective tissues is not as simple as that of epithelia, but the following table has some value for convenience in future description. It is purely morphologic, with no attempt to show genetic relationship. Many subvarieties exist under the major types listed below.

Table of Classification of Connective Tissues

1. Mesenchymatous	5. Dense white fibrous
2. Reticular	6. Dense yellow fibrous
3. Areolar	7. Chondroid (cartilage)
4. Adipose	8. Osteoid (bone)

Connective tissues have but one feature in common—they are all derived from mesenchyme. In this embryonic form, the

cells are stellate or spindleshaped and their processes lie in juxtaposition to form a fine network with the intervening spaces filled with "tissue juice" or "amorphous ground substance." According to older opinions, the processes fuse and the cytoplasm becomes continuous from cell to cell to form a syncytium.

Reticular connective tissue resembles mesenchyme but is characterized by the presence of delicate fibrils (Fig. 8, *B*). It constitutes the framework of the lymph nodes and spleen and the interstitial support for the liver cords and the kidney tubules. Developmentally, the fibrils precede the coarser white fibers and are generally supposed to be related to them (Fig. 8, *B*, *C*). The tissue is more cellular than that of the higher types.

Adenoid tissue is a particular kind of reticular tissue comprising the stroma which supports the digestive epithelium (Fig. 49). It is heavily invaded by lymphocytes and other white blood corpuscles, thus forming a diffuse lymphoidal tissue.

Areolar tissue is widespread. It is composed of both collagenous and elastic fibers bound together in wide meshed interlacing network. Fibroblasts and histiocytes predominate as cell types, with varying numbers of plasma cells, mast cells and migrants from the blood stream (Fig. 7). The tissue serves as a bed for the passage of blood vessels, lymphatics and nerves. It is extremely active in "inflammation."

Dense areolar (plexiform) differs from the preceding in the preponderance of large coarse white fiber bundles, as seen in the derma of the skin (Fig. 39).

Membranous connective tissue is of the areolar type in which the fiber bundles are distributed in such a fashion as to form simple membranes, as capsules, sheaths (Fig. 20), or aponeuroses. In the cornea, the sheets occur as a series of plates or laminae. In these membranes the white fibers predominate, but in the fenestrated membranes, yellow fibers interlace in such a fashion as to produce a network perforated by minute openings or fenestrae. In the larger blood vessels,

as the aorta, the membrane is made up of twenty to fifty lamellae (Fig. 31). The interstices are occupied by a mucoid connective tissue, smooth muscle, blood vessels and nerves.

Adipose tissue is a loose connective tissue in which the fat cells have replaced most of the other elements. The fat cells are usually arranged in lobules bounded by areolar tissue, and

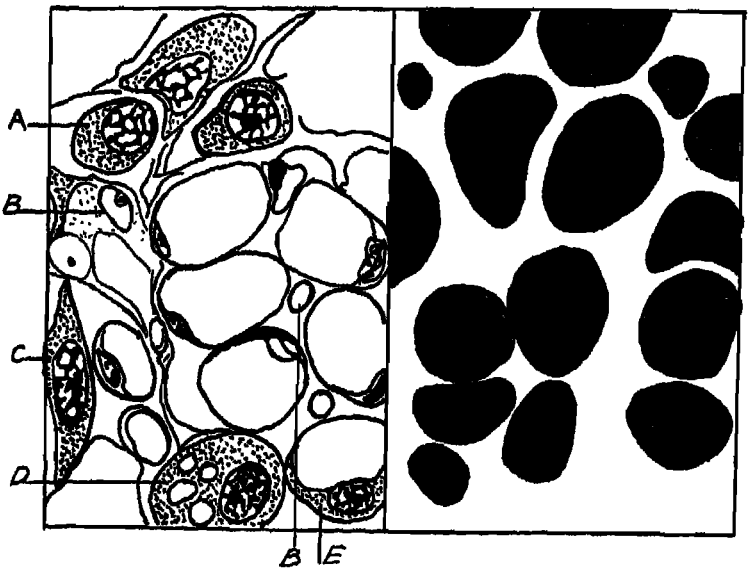


FIG. 9. Developing fat from the subcutaneous tissue of the sole of the foot of a new-born child. *A*, steatoblast; *B*, capillaries; *c*, fibroblast; *d*, Steatoblast in which small fatty vacuoles are present; *E*, the "signet-ring" fat cell in which the fusion of fatty vacuoles is complete and the cytoplasm is reduced to a thin membrane. At the right is a preparation of fat blackened with osmic acid.

a dense capillary plexus. The steatoblast or fat cells are recruited from the primitive fibroblasts. They are characterized by the accumulation of small droplets of neutral fat within the cytoplasm (Fig. 9). The separate droplets coalesce and form one large fluid sphere bounded only by a thin cytoplasmic membrane. As a result the nucleus is pressed to one side, giving the cell the so-called "signet-ring" form. In ordinary

techniques, where alcohol and xylol are used as solvents, the fat is dissolved from the cell and only the membrane and nucleus are seen in the section (Fig. 39). Fats may be stained specifically—blackened by osmic acid; orange with Sudan III and red with Scharlach R.

The dense white fibrous and the dense yellow fibrous connective tissues may be grouped together as the fasciculated connective tissues. The fiber bundles all course in a single direction, forming the tough ligaments and tendons. The cells are few in number and since they occupy the angular spaces between the fiber bundles, they become "winged" due to lateral pressures. In the tendon, they are generally arranged in small groups in linear order. In ligaments the arrangement of fiber and cell is less regular.

The chondroid and osteoid connective tissues will be considered in the next chapter under the heading of impregnated connective tissues.

Chapter V

IMPREGNATED CONNECTIVE TISSUES

The impregnated connective tissues are rare except in the vertebrates. The fibrous nature of the ground substance of cartilage and bone is obscured by an organic matrix, but it may be demonstrated by proper techniques. Cartilage is the more primitive, since it occurs at an earlier age in the embryo and persists as the permanent skeleton in the lower vertebrate forms such as the shark.

CARTILAGE

Cartilage (gristle) is a solid, translucent substance—generally formed into flexible plates that cut readily with the knife. With the exception of the articular and the epiphyseal cartilages, the plates are invested by a thick, tough, fibrous, adherent, vascular membrane, the perichondrium. The plate is not penetrated by nerves and but rarely by blood vessels (Fig. 10). Hyaline cartilage is composed of cells, the chondrocytes, embedded in a ground substance or matrix. It forms the articular cartilage of the joints, the costal cartilages, cartilage of the nose, larynx, trachea and bronchi. The intervertebral disks and the symphysis pubis are made of a special variety of hyaline cartilage invaded by white fibrous connective tissue. The external ear and the epiglottis contain cartilages permeated by bundles of coarse elastic fibers.

Cartilage cells (Fig. 10) lie in smooth-walled cavities, the lacunae (L. dim. of *lacus*, a hollow), which in life they completely fill. Near the surface of the plate the cells are flattened ellipsoids, single, and not markedly different from the "swollen" fibroblasts of the perichondrium. In the deeper zones, they form nests of two, four, or more spherical or ovoid cells, with

flattened adjacent surfaces that give the impression of all having been derived by the division of a single superficial cell.

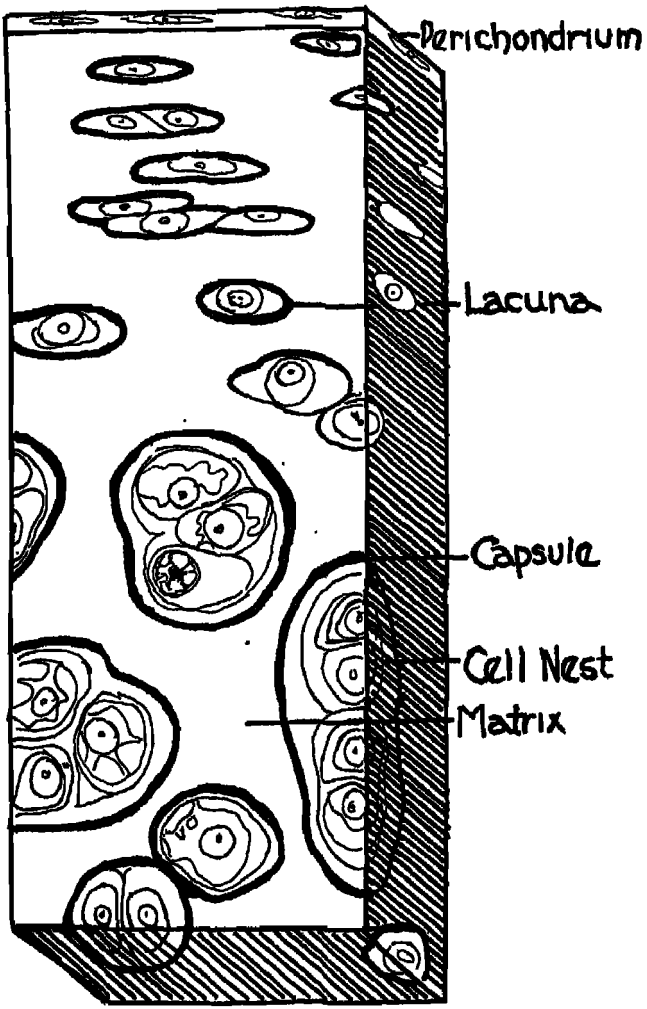


FIG. 10. Stereogram presenting the microscopic characteristics of hyaline cartilage.

The cytoplasm of the cells may show fat vacuoles or glycogen granules. The nuclei are large, spherical and pale staining. A single nucleolus is generally present.

The matrix is homogeneous, non-granular. Chemically it is composed of a chondromucin, chondroitin-sulphuric acid and an albuminoid. The staining reaction in young cartilage is basophilic. It is most marked in the capsule surrounding each cell. In the interterritorial zones between the nests, the reaction may be eosinophilic like that of the collagen fibers of the perichondrium. No system of discrete canals penetrate the matrix. Nutrition is carried on by diffusion and is considered poor.

Growth of cartilage presents an interesting problem. The bulk of the growth is at the surface under the perichondrium. Periodic internal or interstitial growth is considered to take place by general softening, active cell division and deposition of new matrix. This seems to occur at the epiphyseal line in spite of a tremendous weight bearing. A third type of growth has been postulated, i.e., cataclysmic, by which the interterritorial matrix is increased by destruction of the cell nests.

Calcification occurs in the deeper zones in old cartilage, but it is never transformed into bone. Fractured cartilages are repaired by a metaplasia, or cartilaginous transformation of the fibrous scar tissue, formed at the break.

BONE

Bone is a live, dense connective tissue. It is composed of a firm, elastic, gelatinous ground substance known as ossein (30 to 40 per cent), impregnated with calcareous salts (60 to 70 per cent). Its specific gravity is 1.961. Its ash is composed of 85 per cent calcium phosphate; 10 per cent calcium carbonate; and small amounts of calcium fluoride, magnesium phosphate and sodium chloride.

Bone is hard, but it cuts readily with the hack-saw. It has three times the elasticity of white pine and twice its ultimate strength. It is white and smooth, but presents a whole series of minute rugositics and pits for attachment of its covering sheath, the periosteum. Minute pores penetrate the cortical

layer for the passage of the periosteal blood vessels, while near the center of the shaft of the long bone is the foramen for the nutrient artery.

The shapes and sizes of individual bones conform to a hereditary pattern determined in part by the stresses and strains to which the bones are subjected. Wolff's law of bony architecture (1892) may be summarized as a minimum of

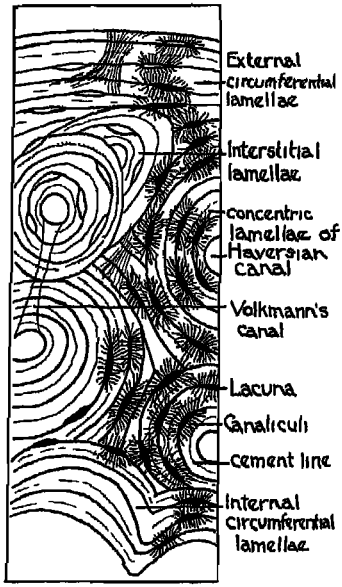


FIG. 11. Portion of a transverse polished section of the human carpal bone, showing the arrangement of the various sets of lamellae, the Haversian canals and the lacunae.

material disposed to give a maximum of strength; a mechanical principal used by bridge builders (Fig. 12).

Two varieties of bone are ordinarily recognized; compact and spongy. The flat bones show two outer tables of compact bone, separated by a middle layer of spongy bone, the diploë. Long bones show an outer cylinder of compact bone; spongy bone in the extremities, and a central medullary cavity filled with "yellow" marrow. Spongy bone is made up of a series of

fused spines or spicules forming trabeculae (L. dim of *trabs*, a beam). The interstices are occupied by "red" marrow. Compact bone, in the mammals, is made up of a series of minute cylinders, whose long axes parallel the long axis of the bone.

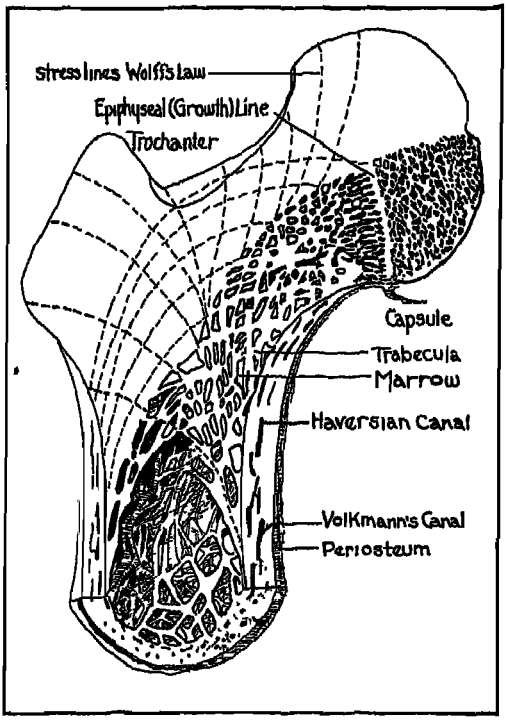


FIG. 12. Stereogram of the head of the human femur showing the spongy and compact bone, the marrow cavity, the epiphyseal line. To the left the lines of stress are indicated illustrating Wolff's law, that the trabeculae are laid down in conformity to the principle of greatest strength with a minimum of material.

In polished sections these can just be seen by the naked eye (Fig. 12).

In cross sections of bone, ground to microscopic thinness, a definite structural pattern is seen (Fig. 11). Hollow cylinders, 0.02 to 0.3 mm. in diameter, are made up of a series of cylindrical plates, the concentric lamellae, two to twenty in number.

Between the plates are small cavities, the lacunae. Extending from the lacunae are numerous intercommunicating and branching canaliculi. In life the lacunae are occupied by the bone cells, osteocytes. Their fine processes ramify the canaliculi. The central canals of the cylinders (Haversian Canals, —named for their discoverer, Clopton Havers, 1650–1702) are occupied by fibrous connective tissue, blood vessels, lymphatics and nerves. These are continuous at the inner wall of the bone, with the loose fibrous tissue that lines the medullary cavity, the endosteum. Those near the outer wall communicate with the same layers in the periosteum. Within the thickness of the shaft, free lateral and end to end communication is made between the separate Haversian canals by the so-called Canals of Volkmann.. The osteogenic layer (bone producing) of the endosteum is thus in direct continuity with the same layer in the periosteum, and in young bone, both actively lay down bone.

In the angles between the cylinders, similar plates, the interstitial lamellae, course in interrupted arcs. They represent portions of former Haversian systems, partially replaced by growth reorganization. Near the outer surface of the shaft, the plates conform to the curvature of the bone. These are called the outer circumferential lamellae. The inner circumferential lamellae form the immediate wall of the medullary cavity.

Each lamella presents two zones, a granular and a non-granular. These are due to a difference in the deposition of the calcareous matter on the two sets of fibers that make up the organic matrix. Cement lines are occasionally seen, coursing the plates.

The periosteum is a tough fibrous membrane of two layers: an outer, loose vascular adventitial layer and a firm compact fibro-elastic cambium. Some of the fibers of the cambium (fibers of Sharpey) are incorporated into the substance of the outer circumferential lamellae and anchor the periosteum firmly

to the bone. Occasionally Sharpey's fibers, incompletely calcified, may be seen in the interstitial lamellae—evidence of abandoned lines of former attachment.

In the periosteum of the new-born, a row of deepstaining, epithelioid cells are seen on the immediate surface of the growing bone. These are the osteoblasts. Similar cells can be found on any growing bone spicule, for instance in the endosteum. It is generally conceded that these cells are "bone formers," as their name implies (G. *osteon*, bone; *blastos*, germ).

Large, isolate, multinucleate cell masses are also found in this same position. These are the osteoclasts or "bone destroyers." It is thought that they control the resorption of bone in the "modelling" process of bone growth. They may rest in small depressions, Howship's lacunae.

Chapter VI

BONE GROWTH. JOINTS

Long bones grow in diameter by subperiosteal accretion. The medullary cavity increases in diameter by resorption of the inner lamellae with subsequent remodelling of the inner Haversian systems. This fact has been shown by the experimental staining of growing bones by feeding the dye "Dutch Madder." Growth in length of long bones occurs at the so-called "metaphysis," the zone next to the epiphyseal cartilage which separates the articular head from the shaft.

The histogenesis of bone presents many interesting problems. Two types of formation occur—(1) in membranes, (2) by cartilage replacement. While the latter method is considered the more primitive, the first method is the simpler. It consists of four steps—(1) a gelatinous edema or swelling of the fibers and ground substance of the connective tissue; (2) increased fibril formation; (3) formation of a homogeneous basophilic "osseoid" tissue; (4) calcification. The fibroblasts of the region become swollen and epithelioid in character. They arrange themselves in rows about the calcifying spicules. Those that are "trapped" and surrounded by fibrils become mature bone cells or osteocytes. Spicules fuse to form trabeculae enclosing primary marrow spaces. These are gradually modelled into the Haversian systems previously described. The whole organization follows closely the conformation of a plexiform blood supply.

Endochondrial bone formation is the common method of skeletal origin, since a cast of the long bones is first laid down in a solid hyaline cartilage. Four successive steps are recognized in the replacement of cartilage—(1) a spontaneous softening

of the middle of the cartilaginous shaft; (2) the perichondrium becomes osteogenic and a cylindrical collar of trabeculate bone is formed about the center of the shaft; (3) subperiosteal buds composed of primitive osteoblasts, fibroblasts and capillary

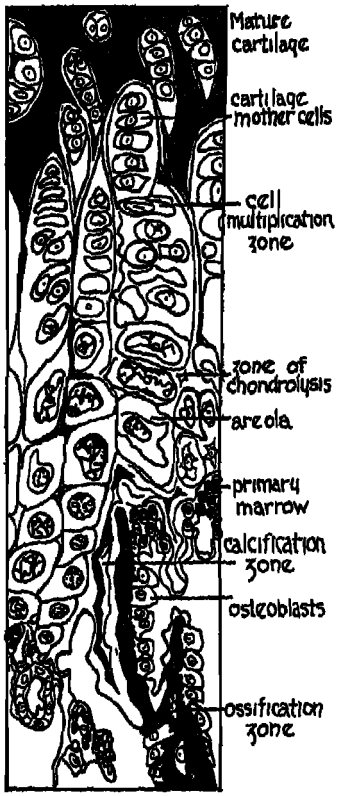


FIG. 13. Camera lucida drawing through the epiphyseal line to show the five zones of activity concerned with the extension of a long bone.

loops, invade the softened cartilage and digest out a primary medullary cavity; (4) these buds extend further into the cartilaginous plugs at the two ends of the bony cylinder and establish the primary epiphyseal line.

These lines show six zones of histological change: (*a*) the

primary articular cartilage remains intact; (*b*) a zone of deep-staining cartilage "mother-cells" shows active mitotic division; (*c*) a zone of flattened cartilage cells arrange in "poker-chip" fashion or parallel columns; (*d*) a zone of degenerating cartilage cells lie in broad spaces, the areolae, produced by dissolution of the cartilage matrix; (*e*) a zone of calcification of the cartilage spicules formed from the remnants of the old matrix and acting as a temporary framework for (*f*) the deposition of true bony spicules laid down by the osteogenic buds (Fig. 13).

When a secondary center of ossification appears in the epiphysis, the cartilage becomes converted into a plate which provides for continued growth until maturity is reached, when it becomes completely ossified (14th to 16th year for girls; 17th to 20th year for boys).

In the repair of fractured bones, it is generally held that the periosteum is the essential tissue. Some theories however deny this and consider the true function of the periosteum to limit bone growth by pressure since osteoblasts are wanting in the mature membrane. The osteoblasts of repair are recruited from the undifferentiated fibroblasts of the injured zone. Four days after fracture, all osteocytes within one millimeter from the break are dead. An osteoid matrix forms which soon calcifies and "knits" the dead bone. If endosteum intervenes in the break, it generally produces a "callus" of granulation tissue which will not calcify.

The blood supply to the bone is thought to be of primary significance in repair. Three sources have been described for long bones: (1) the periosteal supply is a capillary network distributed to the outer third of the cortex; (2) a metaphyseal supply enters by small vessels to the spongy bone in the ends of the shaft; (3) the major supply is by way of the nutrient artery. Free anastomoses occur.

In the deposition of bone it is of interest to know that enzymes, hormones and vitamines are of great importance. An enzyme, phosphatase, is essential to precipitation of phosphate

from the blood. Vitamine D of cod-liver oil "cures" the bow-legs of rickets. The hormone of the parathyroid gland controls the calcium level of the blood through its action on the stored calcium of bone. Overproduction of the hormone from an anterior lobe of the pituitary body may lead to gigantism by continued bone growth. Reciprocally, undersecretion may lead to dwarfism.

Bone normally undergoes senile change at the age of thirty. Resorption may be particularly marked by loosening of the teeth during pregnancy if calcium is deficient in the diet.

In conclusion, bone should be considered something more than a "dead" supportive skeleton. Bone is an active physiological "organ" undergoing histological changes throughout life. In the course of evolution it is of interest to note that bone reaches structural perfection in "white-man" (Foot).

JOINTS

Bones constitute the fundamental elements of all joints. Three varieties of joints are recognized: (1) synarthroses or immovable joints; (2) amphiarthroses or slightly movable joints; (3) diarthroses or freely movable joints. The first class is illustrated by the sutures of the skull, where the interlocking bones are held together firmly by fibers of connective tissue. The second class, represented by the intervertebral joints, show a fibro-cartilaginous disk interposed between the bones. The diarthrodial joint, represented by the "hinge," "pivot," "ball-and-socket" and the "gliding" joint, is much more complex and important. The ends of the two bones are free to move. They are capped by yielding articular cartilages, lubricated by a jelly-like synovial fluid, and bound by the fibrous articular capsule. They may be further strengthened by ligaments that may serve to "check" movement. Some joints are further complicated by interarticular cartilages, the menisci.

The capsule surrounding the joint cavity comprises two

layers: the outer dense, fibrous, stratum fibrosum, and the inner loose fibrous, stratum synoviale. The latter, the synovial membrane proper, is a delicate membrane bearing blood vessels, lymphatics, and encapsulated nerve endings. In certain joints, fat pads and fibrocartilages may develop. The nature of the lining cells of the joint is much disputed. One opinion is that a simple squamous mesenchymal epithelium is present; the alternate view holds that an incomplete lining of flattened fibroblasts exists. Small fingerlike processes of the synovial membrane project into the cavities of many joints. These are the synovial villi. It is thought that they control the pressure of the fluid within the joint, which is secreted by the membrane. Occasionally the villi may become converted into cartilage as "joint mice" or "joint rice."

Chapter VII

MUSCULAR TISSUE

Contractility is possessed in some degree by all protoplasm, but muscle is especially differentiated to effect movements by shortening in one direction only. The functional unit is the muscle fiber. Three varieties are recognized—smooth, striate and cardiac. Smooth muscle and cardiac muscle are not under the control of the will. Hence they are often referred to as involuntary. The striate skeletal muscles are voluntary.

Striate muscle is much more rapid in its reaction than either of the other two types. An entire contraction is completed in 0.04 second, while that of cardiac is 0.3 second and smooth muscle 3 or more seconds. Structurally, striate muscle is the more complex.

SMOOTH MUSCLE

The smooth muscle fiber is a single cell, spindle shaped, 6 to 12 micra in diameter and 0.03 to 0.1 mm. long (Fig. 14). The nucleus is rod-shaped, centrally placed and deeply staining. The cytoplasm is composed of two elements—the long fine fibrillae (not visible in the living cell) imbedded in a more fluid sarcoplasm. A very delicate cell membrane is present, but not a true sarcolemma.

Smooth muscle may occur as single fibers (e.g., the myo-epithelial cells of the sweat glands); in small bundles (erector muscles of the hair); in interlacing networks (prostate and uterus); in long continuous bands or in encircling bands (muscle coats of the intestine). In these bands and bundles, the cells lie so close together that their boundaries are not always visible. They are held together by intercellular cement, by intercellular

bridges, and by a fine reticulum of collagenous and elastic fibers. The larger bundles are united by connective tissue septa in which the blood vessels and nerves course (Fig. 48).

Smooth muscle is sometimes difficult to distinguish from reticular connective tissue. Mallory's connective tissue stain is an aid in identification. Connective tissue stains blue; muscle, red.

Smooth muscle in the gross, has a pale yellow or gray color. It is soft, elastic and easily torn. The blood supply is scanty as compared to striate. Nerve fibrils from the sympathetics form plexuses on the surface of the muscle. It is questionable as to whether every fiber receives an independent nerve fibril. There is evidence that the stimulus for contraction is conducted

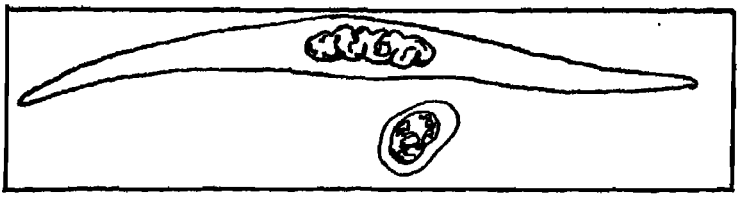


FIG. 14. Longitudinal and cross section of a smooth muscle cell. Drawn from the fibers in the media of the umbilical artery.

from muscle to muscle. Nerves have not been demonstrated in the muscular wall of the umbilical artery beyond one inch from the navel, yet these muscles actively contract throughout the course of the vessels.

STRIATE MUSCLE

Striate or striped muscle is so called because of the lines and bands that cross the fiber (Fig. 15). The fibers are long, attenuated cylinders, 10 to 150 micra in diameter and 10,000 to 45,000 micra (10 to 45 mm.) in length. They are multicellular masses or syncytia, containing as many as eight thousand nuclei. They rarely branch. In life they are combined into the massive named muscles of anatomy and are popularly known

as the "flesh" of the body. They are white in fish and frogs; pink or red in man, due to the presence of myohemoglobin, a close chemical relative of the coloring matter of the blood.

The single fiber shows four essential parts; the nuclei, sarcolemma, sarcoplasm and the myofibrils. The sarcolemma (G. *sarx*, flesh; *lemma*, husk) is a thin, clear elastic surface

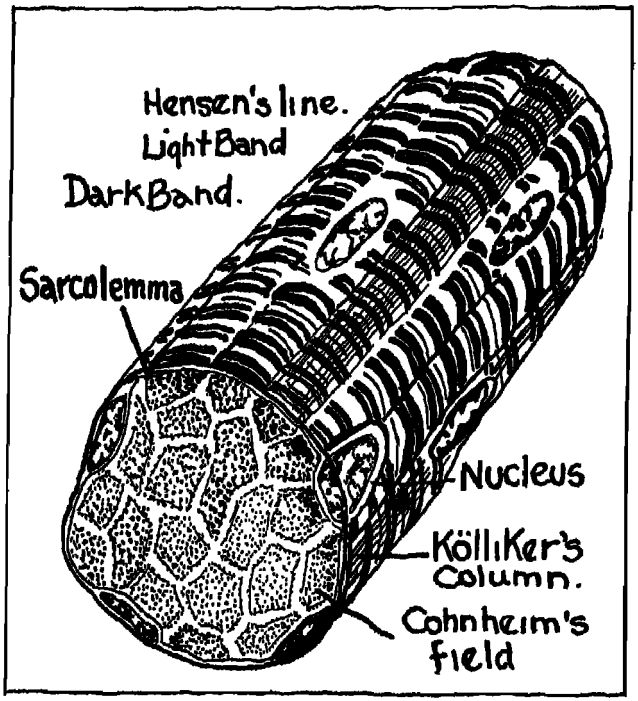


FIG. 15. A stereogram of a portion of a single striate or voluntary muscle fiber.

membrane. In the majority of striate muscles, the nuclei lie adherent to its inner surface, but in some small muscles they may be deep in the fiber. The myofibrils are extremely fine (1 to 2 micra). They course the entire length of the fiber. They lie in and are separated from one another by the more fluid colloidal sarcoplasm. They may be uniformly distrib-

uted throughout the fiber or they may lie in small bundles, known as sarcostyles or Kölliker's columns. Cross sections of such columns are called Cohnheim's fields (Fig. 15).

The cross striations are alternating light and dark bands. These are readily seen in fresh muscle and were first described by Leeuwenhoek. These bands are sufficient for identification of striate muscle. A more detailed description, however is required as the structural basis on which theories of contraction have been based.

When the fibers are split and the fibrillae exposed, it is seen that they are marked by the same cross bands. In Rollet's system, the dark bands are designated the Q bands and the light as the J bands. Each J band is traversed by a dark line, Z. This is Krause's membrane and is supposed to extend across the entire fiber and anchor in the sarcolemma. The dark band in turn is divided by a light band, H, the disk of Hensen, which in turn is again subdivided by a line M, the membrane of Heidenhain. The detail may vary according to the state of contraction of the muscle. It is generally held that there is an interchange of fluid between these various elements during contraction. Scott has recently shown that the ash produced by micro-incineration methods is rich in calcium, in the Q band and absent in the J band.

In spite of their unusual length, the individual muscle fibers rarely pass the entire length of a muscle. The fibers are bound together by a series of connective tissues. The fine fibrils that immediately surround and bind the individual fibers is called the endomysium. The coarser connective tissues of the fibrous type that bind the fibers into bundles or fascicles constitute the perimysium. The fibro-elastic sheets that bind the fascicles together make up the epimysium (Fig. 16).

The larger blood vessels, lymphatics and nerves course in the fibrous layers, while the capillary plexus which surrounds every muscle fiber is supported by the endomysium. Krogh

has estimated 2000 capillaries per square millimeter of skeletal muscle in man; a point of considerable interest in relation to the active metabolism of this tissue.

Striate muscle has a double nerve supply. Naked fibrils from the sympathetic system are supposed to control tonus and metabolism of the fibers; medullated fibers from the cerebrospinal system, ending in motor end-plates (Fig. 26), control contraction. When the nerves to a muscle are cut, degeneration of the muscle occurs.

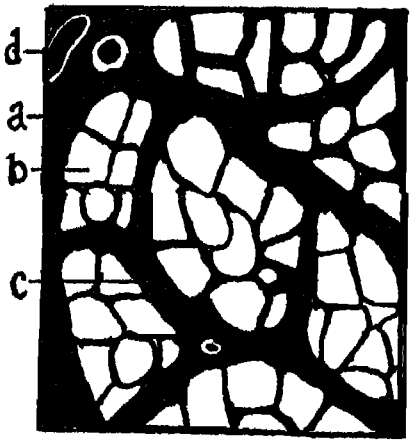


FIG. 16. Cross section of a voluntary muscle stained with Mallory's triple stain, to show the connective tissue coats. *a*, the epimysium; *b*, the muscle fiber; *c*, the septate perimysium; *d*, blood vessels. The endomysium is the fine sheath that encircles each individual fiber.

With few exceptions, striate muscles show a fixed attachment, the origin, and a movable attachment, the insertion. They are connected to bone, cartilage, ligaments, skin or mucous membrane, by the intra-fascicular connective tissue which may be either loose or condensed into a tendon. Two types of tendinous connection have been described. In one, the muscle fiber ends bluntly and the endomysium fuses directly with the fibers of the tendon, with an accumulation of fibroblasts on the sarcolemma. In the second type, the myofibrils seem to ex-

tend through the sarcolemma and become continuous with the fibrils of the connective tissue. Since both muscle and connective tissue have a common origin from mesenchyme, this variation in termination is not surprising.

CARDIAC MUSCLE

Cardiac muscle has one character in common with striate muscle. It, too, is striate. It is like smooth muscle in that it is involuntary; it is made up of "single cell" units in which the nuclei are centrally placed. These cells fuse end to end, however, to form a true syncytium which is further complicated by lateral branching (Figs. 28, 29). A sarcolemma is present. In transection, the fibers are angular; the myofibrils are radially arranged; and a clear zone of sarcoplasm immediately surrounds the nucleus, which in old hearts may contain brown granular pigment.

Cardiac muscle shows one peculiarity. At irregular intervals, corresponding in part at least to the premised ends of the cells, are transverse bands which stain more deeply (or not at all) than the ordinary dark band. Occasionally, they take a "stair-step" course across the fiber and may lie at the level of the nucleus. The significance of these intercalated disks is not known. They have been considered to be growth zones; irreversible "fatigue" bands, etc.

Chapter VIII

NERVOUS TISSUE: I

The substance of nervous tissue contains two genetically related parts: (1) the nerve cells and their processes; (2) the neuroglia cells, their fibers and their secretory products. To these two should also be added the invasive vascular tissues and the covering membranes of the brain, cord and peripheral nerves.

The special function of the nerve cell (neurone) is the detection, conduction and co-ordination of stimuli for the purpose of effecting rapid, purposive reactions, such as movements and secretions. The function of the neuroglia cells and their products is nutritive, supportive and insulative. The vascular tissues and the connective tissues are more than nutritive organs, since they play an important rôle in controlling the general nervous reactions through cerebrospinal pressure and through endocrines.

The neurone or nerve cell consists of a cell body (perikaryon) and its processes (Figs. 17, 18, 94, 95). Two types of processes are recognized—(1) the axon, (2) the dendrite. The cell bodies are spherical, pyramidal, or stellate and vary in diameter from 4 to 150 micra. No distinct cell membrane is present. The nucleus is large, central, spherical, achromatic, and generally marked by a conspicuous nucleolus. The cytoplasm of the perikaryon contains massive, discrete granules which stain deeply with basic dyes;—the tigroid substance or Nissl's granules. These are important since they vary with the functional states of the cell (Figs. 17).

Certain techniques show a series of very fine "neurofibrils" traversing the perikaryon and extending into the processes (Fig. 17).

The processes of the neurone are generally extremely delicate, profusely branched and unbelievably long. The Golgi method of chrome-silver impregnation produces a silhouette by which the detail of the ramification may be studied (Fig. 94). The

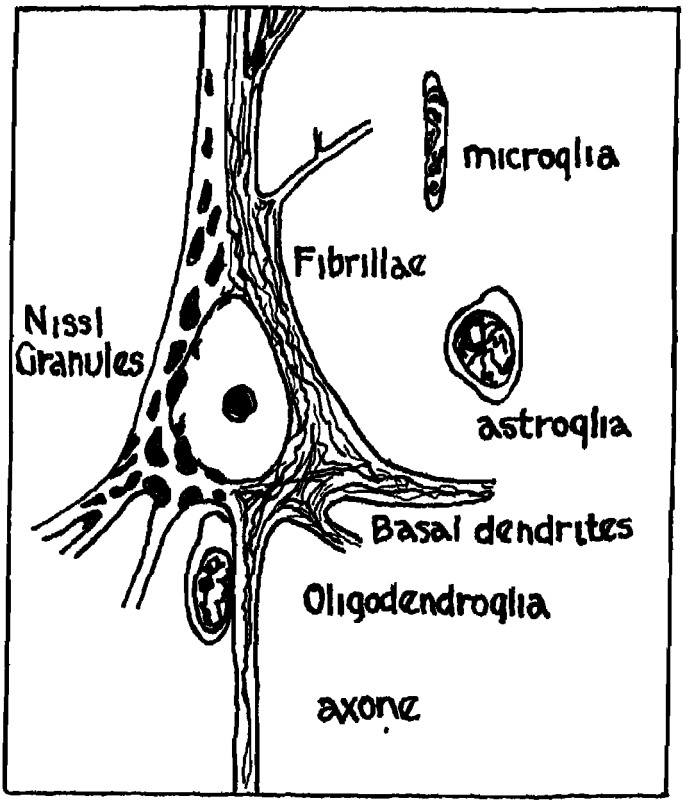


FIG. 17. Semi-diagrammatic drawing of a pyramidal cell from the cortex of the cerebrum of the guinea pig. The left half is drawn to show the tigroid substance as stained by the Nissl method; the right half shows the neurofibrils brought out by the Bielschowsky method.
Three types of neuroglia cells are also represented.

axon is usually single, 1 to 2 micra in diameter, and in some cells as much as three feet in length. It has its origin from the perikaryon, in the axon hillock, a small swelling devoid of tigroid substance. The axon gives off a few lateral branches, the

collaterals. It terminates in a fine brush-like arborization, the telodendria (Fig. 18).

The dendrites are generally multiple, thick, blunt, short and varicose, with irregular branching.

In the living nerve, the impulse flow is centripetal (toward the cell) in the dendrites, and centrifugal in the axon—the law of functional polarity. The rate of flow is some 30 meters per second.

Nerve cells are classified functionally as sensory, motor or associative. A combination of a sensory (afferent) cell and a

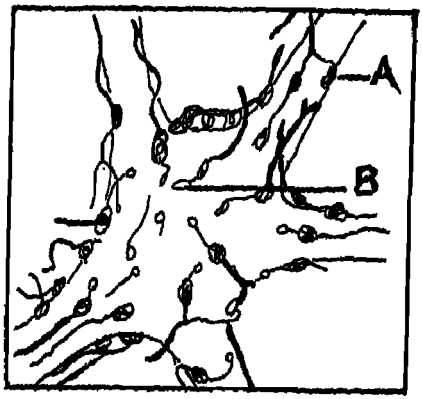


FIG. 18. Neuropodial synapses of terminal arborizations of axones and their collaterals about the cell body and dendritic processes of a motor cell in the spinal cord. *A*, large terminal bulbs; *B*, fine terminal rings. Stained by the reduced silver method of Cajal. (After Cajal.)

motor (efferent) neurone form the neural basis of the reflex act, such as a spinal reflex (Fig. 90). "Associative" neurones may be introduced into the system to bring (1) a sensory cell into relation with more than one motor neurone; (2) a motor neurone in relation to more than one sensory neurone. This permits in "chain relexes" a certain degree of modification in behavior such as inhibition, enhancement, etc.

The point of "transfer" of stimulus between two nerve cells is called the synapse. Older theories premised a continuity of neurofibrils from cell to cell. Current opinion denies this and substitutes a "contact" between cells (Fig. 18).

The most frequent type of synapse is between the telodendria of one cell and the dendrites of the next cell. The telodendria may, however, synapse on the perikaryon. Structurally the telodendria may show varicosities, knobs, rings, gemmules.

The hereditary pattern of the nervous system seems to have developed on Cajal's law of economy of space, economy of material and economy of reaction time.

The popular terms "white matter" and "gray matter" apply to the gross appearance of the parts of the brain and cord (Fig. 91). The whiteness is due to the presence of myelin, a neutral fat, which lies in the sheaths that cover the nerve processes. The histological detail of white matter shows cylinders of myelin supported by an interlacing reticulum of fibrils and an occasional glial cell. On the other hand, gray matter consists of nerve cell bodies, their naked processes, neuroglia fibers, occasional neuroglia cells. Collectively, this interlacing network is known as neurophil. In addition to the layers of gray matter in the cerebrum and cerebellum, and the central column in the spinal cord, large isolate accumulations occur as "nuclei" of the brain such as the caudate, lenticular, thalamus, red, olivary, etc. (Fig. 93).

Neuroglia cells have an origin from ectoderm in common with the nerve cells. Many varieties have been identified including the ependymal cells, the astrocytes or mossy and spider cells, the oligodendroglia. Their positions are interfascicular, pericellular or perivascular. They give rise to the glial fibers and it is generally conceded that they also produce the myelin of the brain and cord. The capsule cells of the cerebrospinal ganglia and the "sheath of Schwann" cells of the peripheral nerves are "first cousins" of the glial cells (Figs. 17, 19, 20).

A special race of microglia are found in the brain and cord that are thought to be wandrants from the blood stream and mesodermal in origin. They are considered to be the phagocytes of the brain whose function it is to digest and remove the remnants of dead brain cells.

Peripheral nerves have the same glistening whiteness of the

brain and cord, due to the myelin sheath of axon or dendrite of which the nerves are composed. The peripheral sheath is more complex than that in the cord. It consists of three parts, the axolemma, the myelin sheath and the sheath of Schwann (Fig. 19). The axolemma is a delicate membrane that surrounds the axis-cylinder or nerve process. Outside of this is

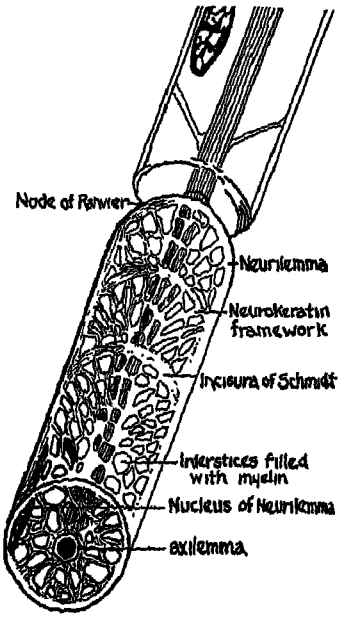


FIG. 19. Stereogram of the sheath of a medullated nerve, showing the central axis cylinder; the axilemma, the myelin sheath, the neurilemma or sheath of Schwann; the node of Ranvier. Note particularly the position of the nucleus of the sheath of Schwann. The sheath of Henle is not represented.

the myelin sheath, 2 to 20 micra in thickness. The sheath of Schwann or neurilemma is a delicate nucleated membrane covering the myelin sheath. The myelin sheath is interrupted at the nodes of Ranvier, bringing the neurilemma and axilemma in apposition. Each internode of the sheath of Schwann bears a single nucleus. The myelin is supported by a fine reticulum of neurokeratin extending from the neurolemma to

the axilemma. It may show funnel-shaped bands, the "clefts of Schmidt."

Unmyelinated fibers from the sympathetic system, are sheathed by Schwann cells, intimately fused. The nuclei are

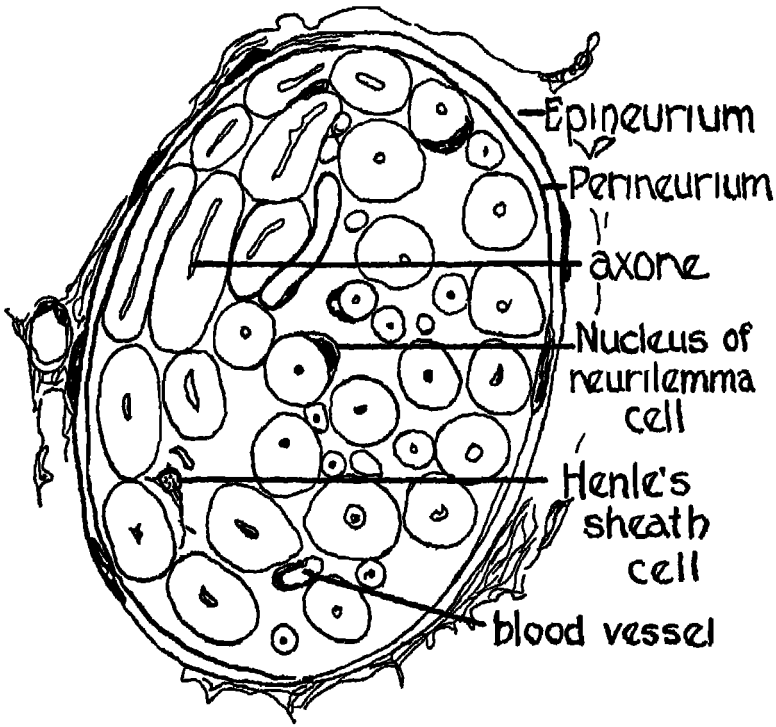


FIG. 20. Camera lucida drawing of a small nerve showing the connective tissue coats. The epineurium is the loose outer fibrous coat; the perineurium is the dense laminated sheath; the endoneurium (Henle's sheath) consists of the connective tissue fibers that surround the individual nerve fibers.

irregularly placed and no nodes of Ranvier are apparent. These fibers are also known as Remak's fibers.

The nerve processes and their intimate sheaths are bound together in fascicles or bundles by connective tissue of mesodermal origin. The fine fibrillar membrane immediately surrounding Schwann's sheath is the endoneurium or sheath of

Henle. It is continuous with a tough, fibro-elastic, laminated membrane, the perineurium, which surrounds the fascicle. The separate fascicles are bound together to form the "nerve" by a loose, irregular fibro-elastic tissue, the epineurium, in which course the nutrient blood vessels (Fig. 20).

Collections of nerve cells may lie outside the cerebrospinal or "central" nervous system, namely in the cerebrospinal and sympathetic ganglia. The cells of the spinal ganglia are large, spherical, unipolar cells whose processes constitute the dorsal roots of the spinal nerves (Fig. 90). Since sensation to the part is lost when these roots are cut, these cells are considered "sensory" (Bell-Magendie's Law). (The cell bodies of the "motor" or ventral roots lie in the "anterior horn" of the gray matter of the cord.) Each "sensory" cell of the ganglion is covered by a membrane of "capsule cells," close relatives to the sheath of Schwann cells.

Sympathetic ganglia are widely distributed—in the two ganglionated trunks; in the celiac, cardiac, renal plexuses; in the myenteric plexus of the intestine—with their efferent processes coursing in the sympathetic trunks, in the gray rami communicantes to the spinal nerves or directly in the visceral nerves, to blood vessel, gland or viscus. Their afferent fibers pass by the visceral nerves and the white rami to the dorsal roots of the spinal nerves to enter the spinal cord, and synapse about the preganglionic cells in the lateral columns. The cells are usually large, multipolar, spherical or "comets," or small unipolars—either "encapsulated" or irregularly covered by the "interstitial" cells of Cajal (Fig. 55).

Chapter IX

NERVOUS TISSUE: II. COVERING MEMBRANES. PERIPHERAL NERVES. END ORGANS

The covering membranes of the brain and cord are three in number: the dura, the arachnoid and the pia. The dura, because of its dense, firm, fibrous character is frequently referred to as the pachymeninges (G. *pachys*, thick; *meninx*, membrane) while the other two constitute the leptomeninges (*leptos*, delicate).

The dura is two-layered. In the skull the outer layer forms the periosteum, and carries the branches of the meningeal arteries and the meningeal nerves. The inner layer is reflected into the major fissures of the brain as the falx and the tentorium. Within it course the dilated venous sinuses (Fig. 21). In the spinal canal, an epidural space separates the outer "periosteal" layer from the inner "dural" layer (Fig. 90).

The arachnoid (G. *arachne*, cobweb; *eidos*, like) is a delicate, areolar tissue, partly adherent to the dura, and partly to the pia, by a series of strands, pillars or trabeculae which traverse the so-called subarachnoid space. Arachnoid villi project through the inner wall of the dura into the superior sagittal sinus as the Pacchionian granulations, where they constitute an important organ of fluid exchange between the subarachnoid space and the venous system (Fig. 21).

The pia (L. *pia*, tender; *mater*, mother) is a very delicate fibrous membrane, highly vascular, and adherent to the surface and entering the substance of the brain and cord on the blood vessels. As the outer vascular layer of the telae choroideae, it literally carries a plexus of blood vessels into the ventricles of the brain (Fig. 22). Perforated by the medial foramen of

Magendie and the lateral foramina of Luschka, a pathway is established for the flow of cerebrospinal fluid from the fourth ventricle to the subarachnoid space, which in turn is in hydro-

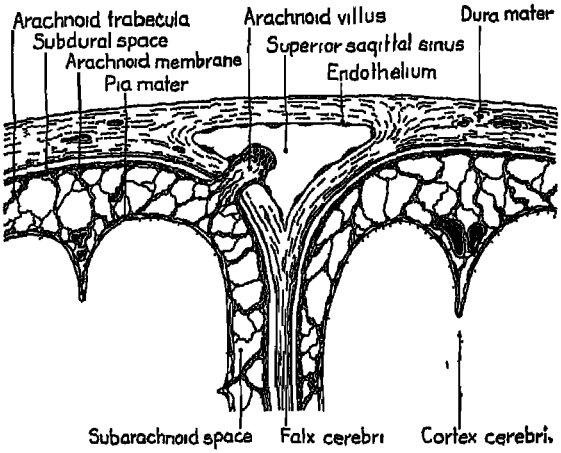


FIG 21 Schematic diagram of a coronal section of the meninges and the cerebral cortex to show the relation of the arachnoid villus to the dural sinus (After Weed)

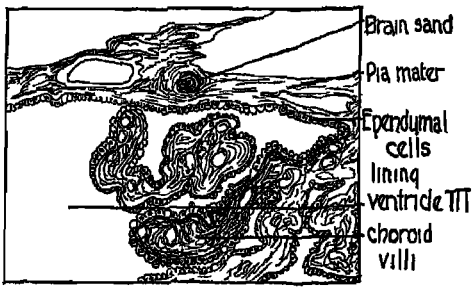


FIG 22 Section through the human choroid plexus showing the villi, the ependymal cells and the pia "Brain sand," commonly seen in the pineal gland, was present in the pia of this specimen

static relation to the venous system through the Pacchionian granulations.

The cerebrospinal fluid is a clear, colorless fluid. Its specific gravity is 1 004. Normally it contains from 3 to 5 cells per

cubic millimeter. The number increases in diseases of the brain, cord or meninges. It is either a dialysate or a secetory product from the telae into the cerebrospinal canal. From here it passes to the subarachnoid space to form a "water-cushion" around the brain and cord. It is normally maintained at 200 to 250 mm. water pressure.

PERIPHERAL NERVE ENDINGS. END ORGANS

Peripheral nerve endings are essentially identical for all cells. They are represented by free filar or varicose ramifications of the naked axis cylinder on or in cells of epithelial, connective tissue or muscular origin. Functionally they may be classified as sensory (receptors) or motor (effectors). Theoretically a double innervation is to be found in practically every tissue in the body, although it should be born in mind that some physiological processes are controlled through the chemical agency of hormones rather than by demonstrated nerves.

All sensory nerves do not mediate "sensation" such as pain, hot, cold, touch, taste, odor, sight, hearing, equilibrium. They function reflexedly at a level lower than consciousness, although they may occasionally "break through" as "referred pains."

The nature of the tissue to which the nerve is distributed determines largely the morphology of the ending. In stratified squamous epithelia, nerves coming from a subepithelial plexus enter the cement substance between the cells of the germinal layer and terminate as pericellular fibrils (Fig. 23). In glandular epithelium the fibers penetrate the basement membrane and form a terminal skein about the individual secretory cells. In hairs, fibrils encircle and enter both the connective tissue and epithelial sheaths to terminate among the cells in the root. Free nerve endings are abundant in the pulp of a tooth. It is possible that they even extend into the dentinal canals.

For the most part the connective tissue nerve endings are of

the special encapsulated type. Free netknots of a sensory nature occur however on many arteries and seem to be distributed to the adventitial fibers. Similar arborizing terminations have been demonstrated in the walls of the bronchial tubes. They are supposed to control the degree of distention of such tubes reflexedly. Such endings have been found in the wall of the carotid sinus, where they are considered to control respiratory and the heart rate.

Of the encapsulated ending, the Meissner tactile corpuscles and the Pacinian lamellated corpuscles are the common types.

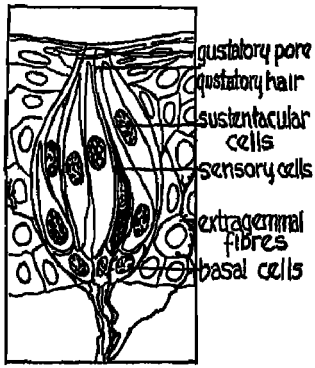


FIG. 23. Drawing of a taste bud from the circumvallate papilla of the tongue of an ox. Note the gustatory pore, the gustatory hairs, the neural cells and the sustentacular cells.

Meissner's corpuscles are oval bodies, 20 x 80 micra, composed of epitheliod cells arranged in a loose spiral (Fig. 24). One or more myelinated fibers enter the basal end of the body and arborize in flattened expansions about the cells. A loose connective tissue sheath bind the whole together. These corpuscles occupy the dermal papilla on the more sensitive areas of the skin. They are supposed to mediate the sense of fine tactile discrimination.

The Pacinian corpuscles are thought to be the organs of deep or coarse pressure. They occur commonly in the subcutaneous layer of the skin, but are also found in the mesenteries, in the

capsules of some glands, in the fibrous tissues about many joints, in the genital organs and urethra. They are elliptical in form and can be seen with the naked eye. Structurally the corpuscle consists of a central core of protoplasm surrounding an axis cylinder. This may end in a bulb-like expansion.

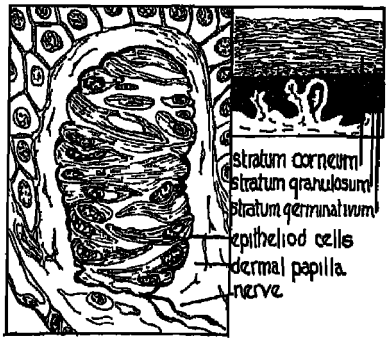


FIG. 24. Meissner's tactile corpuscle in a papilla of the skin of the human finger. Sketch to the right indicates the position relative to the epidermis.

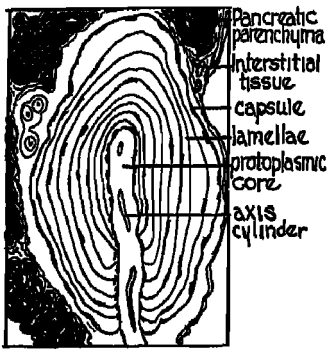


FIG. 25. Pacinian corpuscle embedded between the lobules of the pancreas, showing the central core, the axis cylinder, and the concentric lamellae.

Surrounding the core are some twenty to thirty thin concentric connective tissue lamellae or plates. In some of the corpuscles, a capillary plexus may enter the core along with the nerve. Schumacker considers the corpuscles to be sensory ending that regulate local blood pressure (Fig. 25).

Many variants of these two types have been described such as Krause's end bulbs, Ruffini's cylinders, organ of Herbst.

Nerve terminations on smooth and cardiac muscle are of the fibrillar type. The Remak fibers end in small rosaries, or wide meshed nets of varicose branches. Striate muscle has a double innervation. The medullated fibers end in round multinucleated granular motor end plates, as intraprotoplasmic arborization of nets, rings and bulbs. They do not penetrate the striate substance (Fig. 26). A sympathetic non-medullated

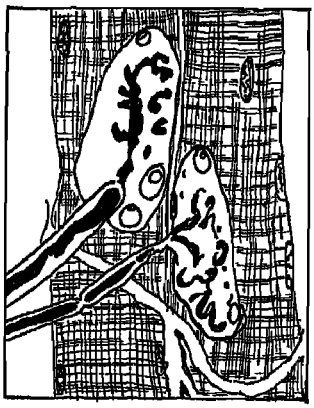


FIG. 26. Motor end plates on the intercostal muscles of a rabbit. At the interruption of the myelin sheath, the terminal arborization of the axis cylinder begins. A part of the capillary plexus crosses the two muscle fibers.

fiber has been demonstrated accompanying the main fiber, which is supposed to mediate trophic (metabolic) stimuli and to maintain tonus.

The muscle sense or "state of contraction" is invested in special sense organs, the neuro-muscular spindles of Kühne (Fig. 27). These spindles course in the muscle just like small muscle fascicles. Each spindle contains several striated muscle fibers 1 to 5 mm. in length. They are enclosed as intrafusal fibers, in a laminated connective tissue sheath or capsule, and bound lightly together by a loose axial sheath, in which courses the nerve fibrils, before they reach their varicose terminations

on the muscle substance. The muscle fibers are of the primitive type, showing centrally placed nuclei and pale striations.

Cajal has also shown typical motor end plates to the muscles of the spindle.

The neuro-tendinous spindle is another sensory end organ that is considered to give "positional" sense. The terminal arborizations of the medullated nerves follow a complex spiral course on the tendon that practically ensheathes ten or twenty fascicles. It is encapsulated like the neuro-muscular spindle.

In spite of the complicated structure of the organs of special sense, the relation of the nerve fibrils to the end organ remains comparatively simple. The olfactory endings are the most

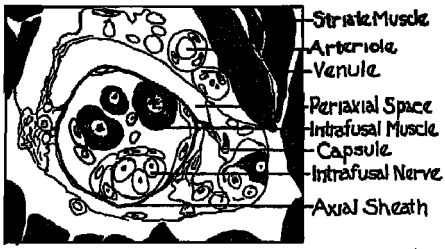


FIG. 27. Cross section of a neuro-muscular spindle embedded in the fibers of the adductor longus muscle of a young kitten.

primitive. In the superior region of the nasal mucosa, the epithelium consists of two elements; the bipolar sensory nerve cells, and the epithelial sustentacular cells. The slender peripheral process of the nerve cell reaches the free surface of the epithelium to end in a clump of stiff cilia, the olfactory hairs. These correspond to the dendrites of the typical neurone. A typical axon leaves the cell body, penetrates the basement membrane and courses as the "olfactory nerve" to the brain.

A more complex arrangement prevails in the "taste buds" (Fig. 23). These are flask-shaped bodies composed of a number of spindle shaped cells, extending through the depth of the stratified squamous epithelia on the tongue or epi-

glottis. They are composed of two elements, the gustatory cells and the sustentacular cells. The gustatory cells are long and fusiform, reaching from the basement membrane to the taste pore, through which their stiff bristle like ends project. The sustentacular cells are of two varieties—the fusiform upright cells and the stellate basal cells. The nerves distributed to the taste buds are dendritic processes of the ganglion cells of the seventh, ninth and tenth cranial nerves. They end in two patterns—(1) as arborizations about the gustatory cells (intragemmal fibers); (2) as free varicose terminations in the cement substance between the surrounding stratified squamous epithelium (intergemmal). *This second type of termination* is the only one found on the filiform and fusiform papillae, yet they mediate the sense of taste.

This same type of a fundamental arrangement exists in the ear, where the dendritic processes of the ganglion cells of the eighth nerve arborize about the ciliated cells of the organ of Corti, the maculae and the cristae (Fig. 89).

The special end organs for vision are the rods and cones, which may be interpreted as dendrites of bipolar cells whose axones synapse with other bipolar cells in the deeper layers of the retina. These in turn associate with ganglion cells whose axons make up the so-called optic nerve. The detail of this arrangement will be left for a later chapter (Fig. 86).

The student has probably begun to wonder how the detail of the various fiber tracts have been established since it is impossible to dissect out these microscopic elements with any degree of certainty. Three methods of approach have been utilized: (1) the association of dysfunction with known injury or "lesion"; (2) cytological studies on degeneration and regeneration of injured nerves; (3) embryological studies on the development of the complex tracts from relatively simple beginnings. The organized results of such studies have become incorporated as the special science of neuro-anatomy and its clinical associate, neurology.

Chapter X

THE HEART AND THE AORTA

The heart is a hollow conical muscular organ composed of four chambers: two thin walled atria and two thick walled ventricles. The inferior and superior venae cavae bring the venous blood to the right atrium whence it passes to the right ventricle. From here the blood is forced through the vascular bed of the lungs, is aerated and brought to the left atrium. It passes to the left ventricle to be distributed throughout the body by the aorta and its branches. The atria are separated from the ventricles by the tricuspid and mitral valves on the right and left sides respectively. Check valves in the pulmonary artery and aorta prevent regurgitation into the ventricles.

The heart lies within the pericardial cavity, in which it is free to move except for the fixation by the great vessels at its base.

The heart measures 12.5 cm. from the base to the apex; 8.7 cm. broad and 6.2 cm. thick. Its adult weight is 255–312 grams. Its average output is 75 cc. for each ventricle, although the pressures in the two circuits vary; 120/80 for the aortic; 40/20 for the pulmonary.

The same three coats extend throughout the heart; namely, the epicardium, myocardium and endocardium (Fig. 28).

The epicardium is a serous membrane which is continuous with the pericardium at the base of the heart. It consists of a layer of mesothelial cells supported on a dense fibro-elastic tissue in which are many small blood vessels, lymphatics and sympathetic ganglia (Fig. 28). It becomes fatty in obesity, especially in the coronal sulcus and about the branches of the coronary vessels. It is continuous internally with the septa

that serve as a perimysium about the muscle bundles, and it passes over into the dense fibrous tissue that forms the so-called "skeleton" of the heart.

The myocardium is composed primarily of continuous spiral whorls of cardiac muscle. The auricular outer coat is transverse and is common to both atria. The inner coat is longitudinal and independent in the two chambers.

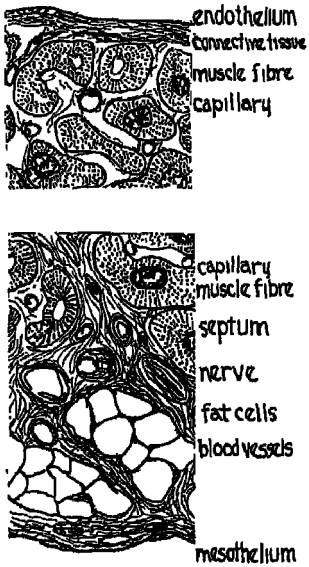


FIG. 28. Transection through the wall of the heart to show (above) the endocardium resting on the myocardium, and (below) the epicardium. Only a few muscle fibers are shown.

Except for the Purkinje fibers, the musculature of the atria and the ventricles is entirely separate, a point of great interest in theories of contraction (Fig. 29).

The ventricular coats are disposed in several layers; a superficial and a deep. They run at approximately right angles to each other. The superficial set has its origin in the fibrous ring about the atrio-ventricular valves. It winds around both ventricles in a spiral and terminates in the papillary muscles of

the opposite side. The deep set, originate in the a.-v. rings wind around the ventricle of the same side, pass through the septum to terminate in the papillary muscle of the opposite side in a figure of 8 course.

The inner wall of the ventricles takes on a cavernous trabeculate pattern due to the projecting papillary muscles and the chordae tendinae, the columnae carnae and the moderator bands.

The endocardium is composed of a lining endothelium which is continuous with that of the arteries and the veins, resting on a subendothelial layer of collagenous and elastic fibers. Few

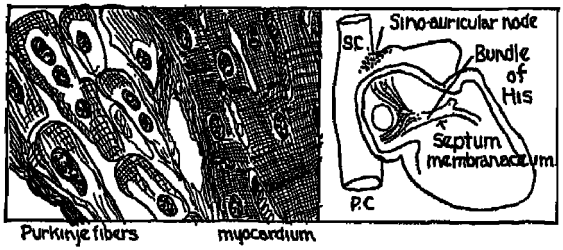


FIG. 29. Longi section through the endocardium and the bundle of His showing the Purkinje fibers. The adjacent myocardium presents comparisons. The sketch of the dissected heart indicates the position of this important conduction path.

smooth muscles may also be found. External to this is a subendocardial layer which consists of areolar tissue, and in which the peculiar muscle elements, the Purkinje fibers, course. Fat is rare except in disease (Figs. 28, 29).

The so-called "skeleton" of the heart comprises the connective tissue septum that separates the auricles from the ventricles at the level of the coronal sulcus, plus the fibrous portions of the interatrial and interventricular septa, the septum membranaceum. The former bears the annuli fibrosi or dense fibrous rings that form the support for the bases of the lappets of the valves. They are important in that they prevent stretching and incompetency of the valves. Between the

valves is the trigona fibrosa, marked by chondroid tissue, a portion of the cardiac skeleton which may calcify in aged individuals (Fig. 30).

The valves all have the same general structure. A central ground plate of chondroid tissue, having an origin in the fibrous ring, may show some collagenous and elastic fibers. Both surfaces of the plate are covered by endothelium. The fibrous chordae tendinae are attached to the ventricular surface of the

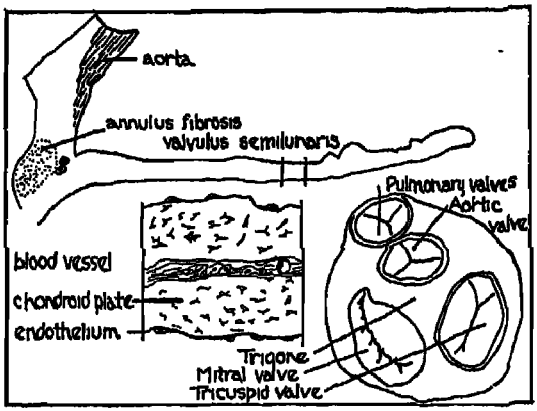


FIG. 30. The valves of the heart. The top figure represents a section through the cusp of the aortic valve of a calf. The middle figure is drawn from this same preparation at a higher magnification. The endocardial endothelium, the chondroidal plate and blood vessels in the valve are clearly seen. The lower figure shows the arrangement of the respective valves on the atrioventricular septum.

a.-v. valves, while the free margins of the semilunar valves form the noduli Arantii. The valves of the heart have recently been shown to have a rich vascular supply—an important point in theories which attempt to account for the method of establishment of the so-called "vegetations" or bacterial growth on the valves (Fig. 30).

The blood supply to the heart is very profuse. Practically every angle between the muscle fibers is occupied by a capillary. These are branches of the larger vessels that course in the perimysium and have their origin in the coronary arteries.

The coronaries arise from the aorta at the sinuses of Valsalva. The veins drain by way of the coronary sinus or directly by the venae minimae into the right auricle. The coronary circulation is under the vasomotor control of the sympathetics (dilators) and the parasympathetics (constrictors).

The nervous mechanism of the heart is complex. The extrinsic nerves consist of two or three rami of the vagus and branches from the superior, middle and inferior cervical sympathetics. The latter may fuse more or less completely with the first thoracic as the "stellate ganglion." Additional fibers are derived from the thoracics 2 to 5. The fibers for the most part arborize about the ganglion cells in Wrisberg's cardiac ganglion or about the isolated groups of sympathetic cells on the dorsal surface and the atrial septum of the heart. There are no ganglia in the ventricle, but extensive nerve fibers from both extrinsic and intrinsic origins pervade its musculature.

In addition to the nervous mechanism, another system of "conduction" exists as the fibers of Purkinje (Fig. 29). These are primarily muscle fibers or the cardiac type, differing from them (1) in the size of the fiber; (2) size of the nucleus; (3) pale incomplete fibrils (4) in the relative amount of sarcoplasm to fibrils. This system is extraordinarily extensive, arising in the crista near the opening of the superior vena cava; circling the foramen ovale; passing by way of the interatrial and interventricular septa to the papillary muscles of both right and left ventricles. The three most conspicuous parts are the sinoauricular node of Keith-Flack; the auriculo-ventricular node of Tawara; and the "bundle of His." The first node is considered the "pace-maker" since the cardiac contraction begins at this region. The bundle of His is the conduction bundle between auricle and ventricle. Injury to it may lead to a "heart-block" in which the auricles and ventricles beat with independent rhythms, as 1:2 or 1:3 instead of 1:1.

The extrinsic nerves, sympathetic (accelorator), and the right vagus (inhibitor) are distributed to the "pace-maker."

The left vagus goes to the a.-v. node and is supposed to control the strength of contraction.

While this is the generally proposed theory of the control of the heart beat it should be indicated that it is not altogether satisfactory. Gross lesions of the conduction system may show no functional disturbance as recorded by the electrocardiograph, while marked disturbances may show no gross lesions. According to the myogenic theory, the capacity for rhythmic contraction is inherent in the heart musculature.

THE AORTA

While the heart is the actual "force-pump" of the vascular system, the so-called "elastic" arteries, including the aorta, innominate, subclavians, common carotids and pulmonaries, serve as the "recoil" tissue which provides for a continual blood flow through the capillary bed during the diastolic or rest period of the cardiac cycle. This period occupies practically two-thirds of the entire "beat." The force of the heart is expended on (1) the direct displacement of the blood towards the periphery in the "pulse wave" and (2) the distention of the contractile tissue in the aorta.

The aorta arises from the left ventricle, where its inlet is protected by the semilunar valve. The ascending portion is 5.5 cm. in length and 3 cm. in diameter. The transverse portion is 4.5 cm. in length, while the descending portion extends to the level of the fourth lumbar vertebra and bifurcates as the common iliac arteries. Here its diameter is 1.75 cm. The total length is 32.5 cm. and the estimated capacity is 150 to 190 cc. Approximately 60 cc. of blood is added to its content with each beat of the heart, hence its walls are stretched 6.6 per cent.

The aorta presents the same three coats seen in all arteries: namely, the intima, media, and adventitia (Fig. 31). The intima consists of a lining layer of endothelium, resting on a thin layer of fibro-elastic tissue with fibers irregularly disposed

and a "mucoid" ground substance. This is supported on a definite lamina of elastic tissue, corresponding to the so-called internal elastic membrane of the muscular artery. The media consists of thirty to seventy concentric lamellae, 2 to 5μ in thickness, and composed of coarse elastic fibers circularly arranged. The lamina are partially fused. The prevailing interspaces, 6 to 18μ in thickness, are occupied by collagenous

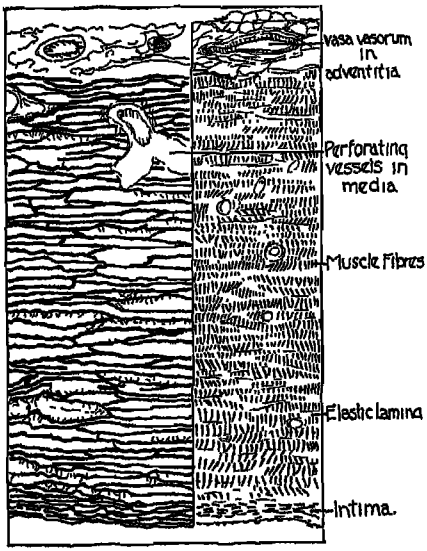


FIG. 31. Cross section through the wall of the aorta. Left, stained with orcein to show the elastic lamina; right, stained with hematoxylin and eosin to bring out the muscle fibers. The elastic laminae of "vital rubber" are the "rebound" tissues that convert the variable ventricular force into an even regular pressure in the arterioles. Note the small vascular channels within the wall of the aorta—significant in theories of aneurism and arterial sclerosis.

fibers, fibroblasts, some blood vessels and numerous smooth muscle cells. The latter do not constitute a continuous circular lamina as in muscular arteries, but are singly disposed, radially, oblique, circularly and longitudinally. From the irregular pattern of the whole, it is not clear as to whether the elastic fibers stretch or merely "iron out" when the vessel is distended. The function of the muscle is also problematic.

It may provide against overdistention or possibly impart "tone" to the membrane. It probably does not take part in the rhythmic contraction, since its contraction time is much too slow to follow the pulse.

The adventitia comprises a thin coat, rich in elastic and connective tissue, the fibers of which are longitudinally disposed. This coat is supposed to prevent overdistention of the vessel. It carries the large nutritive blood vessels, the nerves, occasional ganglia and Pacinian corpuscles. The depressor nerve, distributed to the arch of the aorta reflexedly controls blood pressure.

The nutrient blood vessels, vasa vasorum, penetrate the media at right angles and pass to the outer two-thirds of that coat. They are particularly important, for it is thought that syphilitic infections weaken their walls, bring about degenerative changes and result in local "ballooning" or aneurism of the aorta.

The nutrition of the intima is equally important. It has been shown that various dyes, fats, mucoids may diffuse through the endothelium from the blood stream, and under pathological conditions lead to softening and calcification and fibrosis in this and the deeper layers, causing "hardening of the arteries." The relative elasticity (per cent volume increase per millimeter rise in blood pressure) of the aorta, however, is a function of aging. At 5 years it is estimated at 0.47; at 20, 0.33; at 80, 0.17. "A man is as old as his arteries" is a common saying in medicine.

Chapter XI

THE VASCULAR BED. ARTERIES, CAPILLARIES, VEINS, LYMPHATICS

Arteries are classified as conducting (elastic) and distributing (muscular). The elastic arteries have the same general structure as the aorta; the distributing arteries have the same three coats with the media developed into a thick muscular tunic which by contraction can vary the diameter of the lumen of the vessel. A distinct single internal elastic membrane is generally present, while a thick external elastic membrane occurs as the inner layer of the adventitia (Fig. 32).

In section, muscular arteries generally show a "crinkling" of the intima due to postmortem contraction of the muscular coat.

Many special varieties of arteries have been described on functional grounds. Arteries anastomose freely, as a safety mechanism against functional occlusion, but some few are called "end" arteries because their terminal distribution is discrete (e.g., central artery of the retina).

Sensory and motor nerve fibers in the adventitia, reflexedly control, through the vasomotor centers in the brain stem, the state of contraction or "tone" of the vessels, thereby regulating local pressure and vascular supply to some extent.

Arterioles are the smaller branches of arteries. They range in size from 25 to 100μ (Cowdry) to 300μ (Maximow). The wall is relatively thick as compared to the lumen, due to the presence of circular muscle. They pass over into the capillaries, from which they may be distinguished by the muscle, which is lacking in the latter. Some authorities recognize a precapillary arteriole as an intermediate stage (Fig. 33).

The capillaries are the terminal distributing tubes of the vascular bed. All important metabolic exchanges are made through their wall between the tissue cells and the blood stream. Whether the capillary wall acts as a simple diffusion membrane or is somewhat selective, is a still muted question. The blood

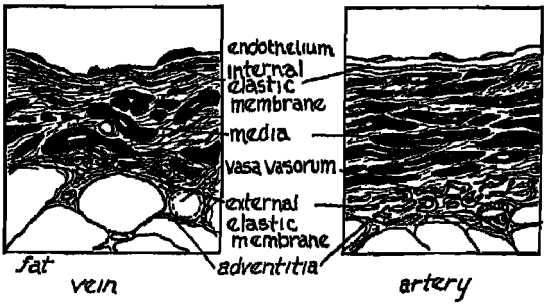


FIG. 32. Section of the wall of a branch of the coronary artery and the coronary vein. Drawn side by side for comparison. Stained with iron-hematoxylin.

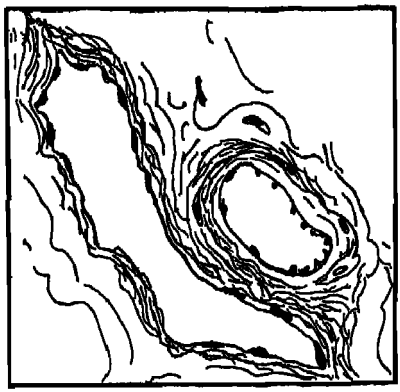


FIG. 33. Sections through walls of small arteriole and venule.

pressure in the arterial end of the capillary is greater than the osmotic pressure of the plasma; at the venous end it is less.

Capillaries are minute, microscopic tubes, 5 to 30μ in diameter and 0.5 mm. long. "Occult" or collapsed capillaries have been described. The wall of the capillary may consist

of a single endothelial cell rolled into a tube, fusing with others of its kind, end to end. More commonly, however, several cells, held together by serrated borders or "lock-joints" comprise the tube. In transections, the nuclei bulge into the lumen (Figs. 28–33).

As a rule muscle does not occur in the capillary wall, but certain "pericytes" or Rouget cells have been described as partially encircling the tube. Three opinions prevail as to the mechanism of "contraction" and "dilatation" of capillaries: (1) purely passive as regulated by the pressure and flow under control of the arteriole; (2) contraction of the Rouget cells (3) independent contractility of the endothelial cells. The mechanism seems to be partly under the control of the vasomotor nerves and partly by chemicals such as adrenalin, histamine.

While the capillary wall forms a continuous tube, white blood corpuscles are able to adhere to its surface and pass through the intercellular cement by ameboid movement (diapedesis). The process takes from one-half to two hours. The temporary openings close after the migration. The red corpuscles never leave the capillary bed unless some injury to the wall permits an extravasation. E.G. "black-eye"; minute hemorrhages into the skin in many febrile diseases.

Capillaries occur in all tissues except epithelia and cartilage. Krogh estimates that the total capillary length in man would reach around the world $2\frac{1}{2}$ times. He calculated 1350 per square millimeter in a muscle; 3230 per square millimeter in the heart. Cragie counted 430 per cubic millimeter in the cortex of the brain at birth; and 1470 at one year of age. Howell estimates the general cross section of the capillary bed to be 800 times that of the aorta. The hydrostatic result is a tremendous drop in pressure and reduction in rate of flow, comparable to an analogous illustration where a river, confined to the narrow limits of a rocky gorge spreads out through a wide, level, swampy plain.

In some tissues, such as the liver, adrenals, parathyroids, the capillary bed may lose its regularity and become irregularly and widely dilated as "sinusoids." In the spleen these sinusoids seem to communicate directly with the so-called "tissue" spaces (Figs. 52, 56, 84).

Growth of capillaries is not confined to the embryonic period. New capillaries continue to form in some organs throughout life by blind tubular extension from the pre-existing capillaries. This is particularly true in any healing process, where they are among the first invaders into the repair zone.

Capillaries are continuous with venules. The latter differ from the former in point of size, addition of a delicate fibrous coat and an occasional stray muscle cell (Fig. 33).

Veins have essentially the same histological structure as arteries except that the coats are not as thick nor the layers as clearly defined. In section they may be identified by the thin wall, generally somewhat collapsed and a lumen filled with clotted blood. Postmortem contraction of the arteries fill the veins. Veins of medium sized caliber, particularly in the extremities, possess valves, or semilunar pockets which prevent the flow of blood away from the heart. Structurally they are made of intima, reinforced with elastic fibers (Fig. 32).

THE LYMPHATICS

The lymphatics constitute a collateral vascular system, outgrowths from the veins. They were originally discovered as the lacteal vessels of the intestines by Asellius in 1627. Absorption, as noted by Hunter in 1784, is still considered their primary function.

The system consists primarily of a series of "blind" capillaries, 30 to 60μ in diameter, which accompany the blood capillaries into practically every organ of the body, except the deeper portions of the brain, coats of the eye and cartilage. The system drains by larger vessels through a "chain" of lymph nodes into the thoracic duct and hence into the left

subclavian vein. That of the right side of the head and neck and right arm drain into the right lymph duct and hence into the right subclavian.

The exact nature of the "blind" ends of the capillaries is still in dispute. The present tendency is to consider the system "closed" normally but opening into the "tissue spaces" in inflammation. The tissue spaces are clefts which exist between the fibers and cells of all connective tissues.

Two points of view prevail with respect to the relation of the serous cavities and the lymphatics. According to one opinion, the mesothelium of the diaphragmatic peritoneum, the visceral pleura, etc., present "stomata" or little holes which communicate directly with the underlying lymphatics. This is based primarily on the rapidity with which solid particles (India Ink) are taken up by the lymphatics when injected into the cavities. Others deny the existence of such channels and claim that the migratory phagocytes take up the material.

The origin of the fluid lymph is primarily from the blood stream by dialysis or filtration from the blood capillaries, through the tissue spaces. Increase in capillary pressure may lead to increase lymph flow. The rate of absorption of lymph is rapid. Injected material reached the end of the thoracic duct in 10 seconds from the sole of the foot of the dog (Drinker). Pressure in the lymph vessels is a variable; 1.8 cm. water pressure at rest; 68 cm. in activity; and 120 cm. in inflammation. Flow from the thoracic duct varies from 10 to 14 cc. per ten minutes at a pressure of 10 to 25 mm. mercury. Flow is increased by massage, passive movement, activity, increase in venous pressure, decrease in blood proteins, and in injury to the blood capillaries that result in increased permeability. "Lymphatic block" may lead to edema or "water-logging." The lymphatics are thus important agents in maintaining the "water-balance" of the body.

Since the lymphatics and the blood vessels have much the same structure, the identification of the former in tissue sec-

tions, is based on the absence of red blood corpuscles within their lumens. White blood corpuscles and fibrin may be present. Capillary valves are present in the lymphatics.

The larger "collecting" lymph vessels have the same three coats as an artery when they reach the diameter of 0.5 mm.

The lymph nodes, or "glands," are encapsulated structures ranging in size from microscopic to 2 cm. They present a firm cortex of a nodular character and a loose corded medulla. The softer tissues are supported by septa of fibrous tissue and a

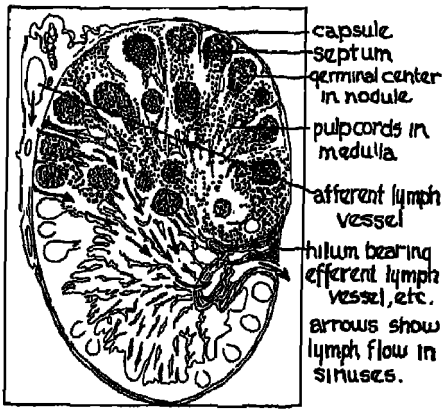


FIG. 34. Semi-diagrammatic sketch of a section through a lymph node. The arrows indicate the direction of flow of lymph through the node.

fine meshwork of reticular fibers. The interstices constitute a series of lymph channels through the node (Fig. 34).

The nodules are formed of spherical accumulations of lymphocytes. Each one presents a "germinal center" in which the cells are pale staining, and epithelioid in character. Many mitotic figures occur, index of a rapid cell production. The nodules produce lymphocytes which gradually separate from the germinal center by growth pressure to form the medullary cords. The matured cells break free and become floating cells in the fluid lymph of the medullary sinus.

The nodes receive several afferent vessels from neighboring

nodes. These open into the subcapsular sinuses, which are in free communication with the medullary sinus by way of the perinodular sinuses. The medullary sinus drains by an efferent vessel to the next node in the "chain." A nutrient artery enters, and the vein and efferent vessel leave the node, in a fibrous sheath at a small depression, the hilus, or hilum. Loose fibrous tissue binds the capsule to the surrounding structures.

Non-encapsulated surface nodes occur in the tonsils, Peyer's patches and the appendix, while the spleen and thymus are considered special lymphoidal organs. Their structure will be considered in later chapters.

In conclusion, it should be stated that the lymphatics present an important pathway of spread of cancerous growths and a route of dissemination of infections. The nodes act as "filters" and may for a time localize these pathological processes, a reaction commonly manifested by "swelling" of the glands.

Chapter XII

THE BLOOD

Blood is the circulating medium of the body. It is maintained at a constant temperature of 98.6°F. Its volume is estimated at 5.5 liters. Its specific gravity is 1.055. It is viscous and has a slightly alkaline reaction. It is composed of two parts, the fluid plasma, 65 per cent, and the formed elements, 35 per cent. The plasma contains globulins, albumins, chlorides, carbonates, phosphates and calcium. The formed elements are of three kinds—the red corpuscles, the white corpuscles and the platelets.

RED CORPUSCLES (ERYTHROCYTES)

The red corpuscles were first seen by Swammerdam (1658), Malpighi (1665), and Leeuwenhoek (1673). The red corpuscles constitute practically 100 per cent of the formed elements—5,000,000 per cubic millimeter as compared to 8000 white cells. En masse, the red corpuscles give the blood its color, but singly they are buff, due to the presence of hemoglobin, a complex protein with an empirical formula of $C_{758}H_{1203}N_{195}S_3FeO_{218}$. The amount of hemoglobin in the blood is 13.5 to 17.5 grams per 100 cc. It constitutes from 40 to 50 per cent of the weight of the corpuscle. Oxygen is carried in loose chemical combination by the hemoglobin, which gives the cell its prime function. The rôle of the erythrocyte in the "rubor" of inflammation has never been determined.

The erythrocyte is a biconcave disk, with a thickness of 2.5μ and a diameter of 7.5μ (Fig. 35). It is frequently used as a "yard stick" or micrometer, to estimate the size of surrounding cells. In sections of tissue, the fixing reagents may give

it a "cocked-hat" appearance. It is remarkably plastic and passes even the smallest open capillaries without difficulty. Its movements are purely passive, being carried along by the force of the blood stream. It consists of a delicate amorphous

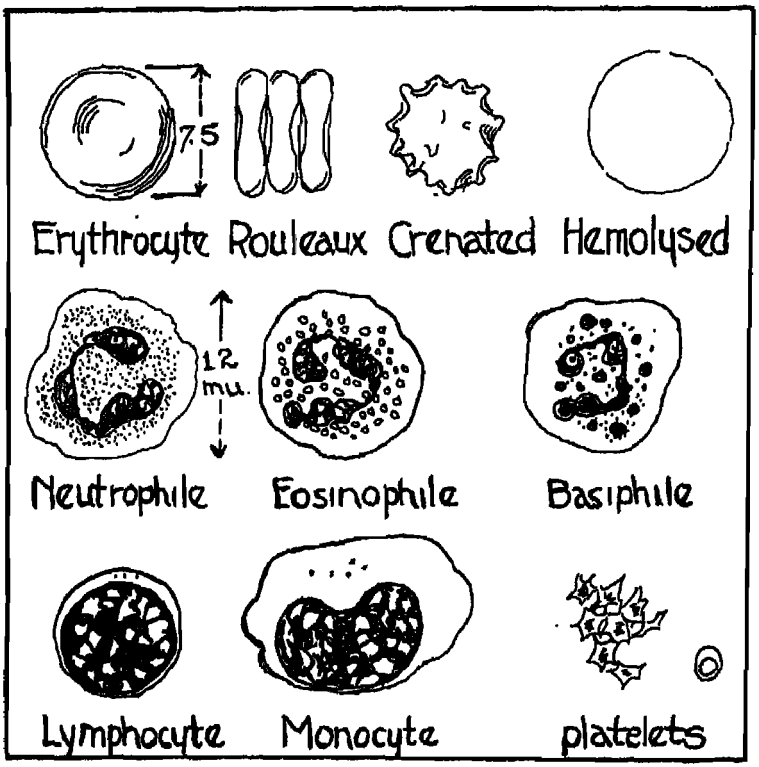


FIG. 35. Cell types in human blood. The top row shows the erythrocyte *or red blood cell as normal, rouleauxed; crenated, or hemolysed.* The middle and lower row show the types of leucocytes or white blood cells as they appear after staining with Wright's stain. The tinctorial effects are described in the text.

stroma (2.26 per cent by weight) which forms a semipermeable surface membrane rich in lipoids. The bulk of the corpuscle is water, in which the colloidal hemoglobin is "dispersed." Its staining reaction is acidophilic except when the hemoglobin content is low.

In freshly drawn blood, the red cells have a tendency to adhere side by side (Fig. 35) in rouleaux or "poker-chip" fashion. In blood that has been allowed to dry slightly, the cells "crenate" or assume a "prickled" form (Fig. 35) due in part to the extraction of water by the now "hypertonic" plasma. The cells preserve their normal shapes in "isotonic" solutions such as "physiological salt solution" with a concentration of 0.85 per cent. "Hypotonic" solutions, such as distilled water, "hemolize" the cells. The hemoglobin goes into solution and leaves the slightly swollen stroma as a "shadow." Various acids, poisons and bacterial toxins may destroy cells by the wholesale. Foreign blood may hemolize cells or "agglutinate" them so that they stick together, a point of prime significance in the practice of transfusion. Today bloods are "typed" and "matched" before this procedure is carried out.

The normal red blood cell count (R.B.C.) in man is 5,000,000 per cubic millimeter for the male and 4,500,000 for the female. This is of course, subject to wide variation. In polycythemia, counts of 12 million are not uncommon; while recovery from counts as low as 780,000 in severe anemias, has been recorded. The loss of two liters of blood by hemorrhage is serious but not necessarily fatal.

The "length of life" of the red cell has been estimated at 30 to 100 days. The durability of these cells, buffetted about at the rate of 30 meters per second in the aorta, is attributed to the fact that they are "dead," since they have no nuclei. It is estimated, from the chemical relation of bilirubin and hemoglobin, and the amount of bilirubin excreted daily, that about 1.5 per cent of the red cells are destroyed daily. To maintain a balance, a like number of new cells must be formed to take their place. These have been identified as the "reticulocytes" —red cells that show a fine granular punctation, or a filar wreath in the stroma, when stained with cresyl blue. They normally constitute 0.5 per cent of the total red count, but increase to 15 or 30 per cent in the days following severe hemor-

rhages. They return to normal when the blood level is restored. The origin and destruction of red cells will be discussed in the next chapter.

WHITE CORPUSCLES (LEUCOCYTES)

The white corpuscles of man were first described by Hewson, Professor of Anatomy of the University of Pennsylvania, 1765. Numerically they occur in blood to a negligible extent—only 8000 per cubic millimeter, or little more than one tenth of one per cent, as compared to the reds. This is no indication, however, of their significance. Their relative numbers rise quickly in infections and they constitute one of the most important means of diagnosis and prognosis in disease. Functionally they represent the most important defense mechanism of the body against microscopic invaders.

They constitute the bulk of the white matter in pus. They pass from place to place in the current of the blood stream, but the seat of their activity is generally in the connective tissues. Lewis has estimated that the tissues of the healthy rat may contain 855,000,000 macrophages (monocytes); a number several thousand times greater than that for the circulating blood.

They differ primarily from the reds in the possession of nuclei; ameboid movement; lack of hemoglobin; and presence of cytoplasmic granules. Some of them pass through other tissues with apparent ease, such as the capillary wall, nerve sheath, etc. Even the early workers (Hassall, 1855) noted that they adhere to the sides of the capillary tubes, out of the general current. Their numerical fluctuations are independent of that of the reds.

They present five different types; a classification established after the introduction of a method of staining with eosin and methylene blue. In point of numbers and significance the order is as follows: neutrophiles, lymphocytes, monocytes, eosinophiles and basophiles (Figs. 35, 36, 38).

These five types may be identified in freshly drawn blood,

but their detailed structure is more apparent in "blood smears" fixed and stained with Wright's stain (Fig. 36).

The neutrophiles are ameboid, phagocytic, 9 to 12μ in diameter. The nucleus, rich in reticular chromatin, is lobated. The three, four or five lobes are connected by delicate strands. The number of lobes is considered indicative of age of the cell. The cytoplasm is finely granular (Figs. 38-21). The granules

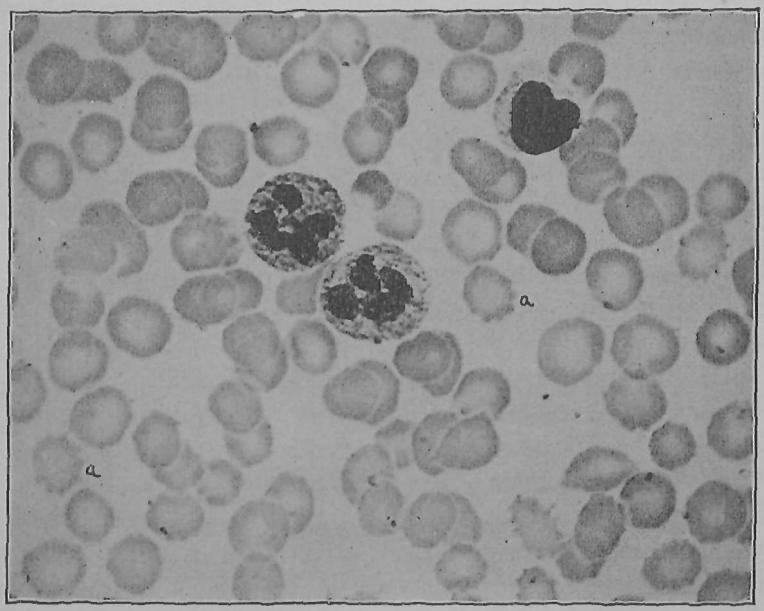


FIG. 36. Photomicrograph of a blood smear stained with Wright's stain. *Among the numerous erythrocytes are two polymorphonuclear neutrophiles* and a single "transitional" lymphocyte. Some of the erythrocytes are crenated. (After Bailey.)

are purple in color, indicating a balance in reaction between the acidophilic (eosin) and the basophilic (methylene blue)—hence the name (L. *neuter*, neither; G. *philos*, love). The neutrophiles constitute 60 to 70 per cent of the total white cell count. They increase rapidly in number in acute infections, and by phagocytosis and bacteriolysis combat the extension of the disease.

The lymphocytes are small round cells, 7 to 10μ, slightly ameboid but non-phagocytic. The nucleus is single, spherical, vesicular. The cytoplasm consists of a thin shell or "hallow" around the nucleus. It stains a pale "sky-blue" and only rarely are granules seen (Figs. 35, 36). These cells constitute 20 to 25 per cent of the white count, but in infancy the numerical relation between neutrophile and lymphocyte, is reversed. Lymphocytes increase in number in chronic diseases of long standing. Their function is still purely speculative. It is thought that they produce "ferments" which pass into the surrounding medium and act as bacteriolytic agents.

The monocytes are large cells, 14 to 20μ, actively ameboid and phagocytic. The nucleus is single, generally bean-shaped and vesicular. The cytoplasm is more voluminous than that of the lymphocyte. Its staining reaction is "sky-blue" with few granules (Fig. 35). The relative number of monocytes is 6 to 10 per cent. They are the active macrophages of the blood stream and are related to or identical with the histiocyte of the connective tissues. So-called "transitionals" exist, that are difficult to classify as lymphocyte or monocyte They increase in number in malaria and typhoid.

The eosinophiles are large cells, 12 to 14μ, actively ameboid. The nucleus is lobated. The cytoplasm is filled with coarse round granules, that stain brilliantly with eosin. They make up from 2 to 4 per cent of the white count. Their function is unknown, although they increase in number in such diseases as hook-worm, tape-worm, trichiniasis, and in true bronchial asthma and a variety of skin diseases (Fig. 38, *14*).

The last class include the basophiles. This cell is 8 to 10μ, nucleus lobated, cytoplasm marked with large coarse granules which stain deep blue to black. They occur as 0.5 per cent in the white count. Their function is obscure (Fig. 38, *8*).

Neutrophiles, eosinophiles and basophiles are sometimes grouped together as the "granulocytes" or again as the "polymorphonuclears." They have little in common except their

origin from the marrow. The term "poly" is frequently used for "neutrophile" on hospital charts. The geneology of the white cells will be discussed in the next chapter.

THE PLATELETS (THROMBOCYTES)

The platelets have been known for a long time, but were first accurately described by Hayem, 1841. They are very small, 1 to 3μ, possess no nuclei, are circular disks in freshly drawn blood, but soon "explode" and form star-shaped bodies (Fig. 35). A central granular substance is present. Platelets occur normally in concentrations of 250,000 per cubic millimeter of blood. They are thought to be essential in the mechanism of "clotting." They occur in normal numbers in "hemophilia" (hereditary bleeders).

The following outline may be used as a point of departure for more detailed studies on the mechanism of clotting. A ferment, prothrombin, plus the substance of the "exploded" platelets, produces thrombin. Thrombin has the capacity to convert the "soluble" fibrinogen of the plasma, into insoluble "fibrin." Fibrin "comes down" in the form of needles or fibers, which enmesh the corpuscles and produce the red clot, or thrombus. Calcium of the plasma is essential to the reaction. The fibers of the clot contract and the expressed fluid is the "serum."

Anticoagulants are citrates, oxalates, leech extract, etc. The reaction may be delayed by cold.

Intravascular coagulation is supposed to be prevented by an "antithrombin." On injury however, more thrombin is liberated than can be "neutralized," and coagulation occurs. The purpose of clotting is self evident.

Clotting may occur in the living body when the internal vessels have been injured. This is of prime significance, because such clots may break lose from their site of attachment and become "emboli" in the open circulation that come to lodge in terminal arteries and produce blocking or "occlusion,"

which cuts off the circulation to a part such as the brain or heart, with serious results.

Clotting also occurs within the body after death. It is sometimes important to know when a given clot formed, in order to determine the cause of death. This can be done by a study of the clot, and the distribution of the cells within it. Fibrin appears in histological section in three forms, fibrillar, granular and hyaline.

Chapter XIII

MARROW

Although Newmann referred the origin of the blood corpuscles to the marrow in 1868, the concept of marrow as an organ is only gradually developing. It is rarely realized that collectively, the marrow is practically as great in amount (1419 grams) as the liver (1500 grams). It is not confined to the long bones, but is present in every bone in the body. Two types are generally recognized, the "red marrow" in the cancellous bone and the "yellow marrow" in the shaft of the long bone. Marrow is constantly undergoing change, becoming cellular in hyperplasia, and fatty in hypoplasia. If the changes are too rapid a "gelatinous" form may be produced.

Histologically, marrow presents six major elements: (1) a delicate reticulum of supportive cells; (2) fat cells, after the fifth year; (3) "blood islands" or patches of formative cells which give rise to the red and white corpuscles (4) isolate giant cells which give rise to the platelets; (5) vascular bed and its contained circulating corpuscles; (6) intercellular fluid and coagulum. Since all of these are contained within fixed spaces with rigid walls, their quantitative variations materially affect one another (Fig. 37).

By examination of sections of marrow and marrow smears, the genealogies of the red blood cells and some of the white blood cells have been established, since graded developmental series can be identified.

The red cells series include (1) hemocytoblast, (2) megaloblast, (3) normoblast, (4) reticulocyte, (5) erythrocyte. The hemocytoblast (Fig. 38, *1*) is a basophilic cell with a large vesicular nucleus. It is difficult to distinguish from a young

"lymphocyte" and is considered to be the same in the "unitarian" theory of hematopoiesis or blood formation. The megaloblast is characterized by the beginning of the deposition

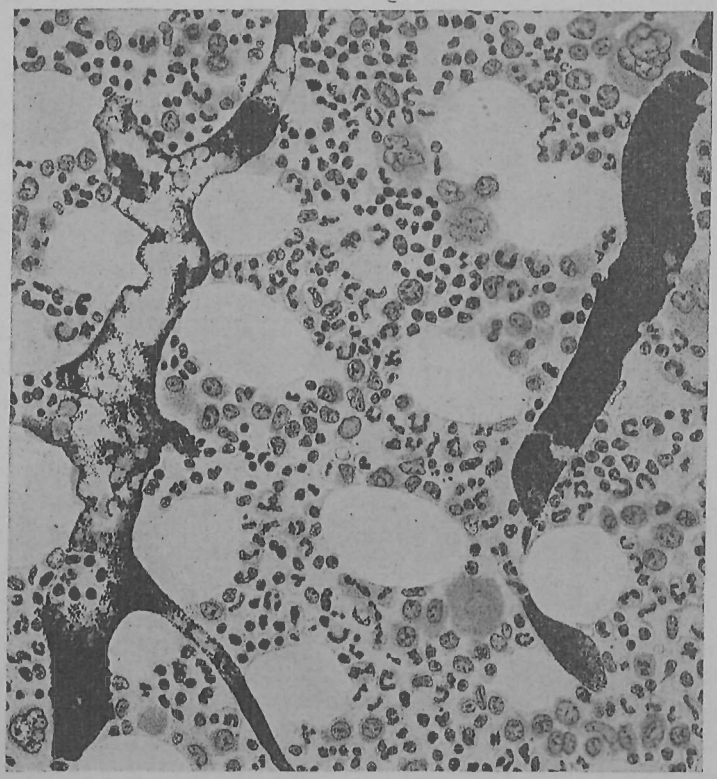


FIG. 37. Camera lucida drawing, ×500, of the cellular marrow of the rabbit. The venous sinuses are injected with India ink. The large clear spaces are occupied by fat cells. The round solid black nuclei belong for the most part to cells of the erythroid series; the vesicular nuclei mark the leucoid areas. Many polynuclear megakaryocytes are seen. (From Drinker, Drinker and Lund.)

of hemoglobin, which gives the cytoplasm a purplish, lilac or gray color (Fig. 38, *27*) when stained with Azur II-eosin. The nucleus shows a "cart-wheel" or "checker-board" arrangement of chromatin. Mitosis is frequent.

The normoblast presents a pycnotic, condensed or "bird-shot" nucleus with the typical eosinophilic staining reaction of the erythrocyte, although in various anemias, when the hemoglobin content of the blood is low, the cytoplasm may be basophilic (Fig. 38, *29*).

The erythrocyte has already been described as a non-nucleated, biconcave disk. The problem of the mechanism of the disappearance of the nucleus of the normoblast is of wide interest. Three main opinions have been held: (1) karyolysis or solution, (2) karyorhexis or fragmentation, (3) extrusion. The last theory is the one most generally accepted, since "naked" nuclei are frequently met with in marrow. There is cumulative evidence that the chemical dissolution of the "extruded nuclei of the normoblasts" gives rise to the major portion of the endogenous uric acid.

The reticulocyte has been identified as the "young" erythrocyte. It is identified in fresh blood by the presence of a basophilic substance stained by cresyl blue. It appears first in a coarse "wreath," a fine fillar form and lastly as a number of fine granules. The reticulum is not the remnants of the nucleus, since it can be demonstrated in the normoblast while the nucleus is still intact.

The geneology of the granulocytes include (1) hemocytoblast = myeloblast, (2) myelocyte, (3) granulocyte. The stages are comparable for neutrophiles, eosinophiles and basophiles; identification being based on the character of the granules. According to the polyphyletic (G. *polys*, many; *phyle*, tribes) theory,

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FIG. 38. Diagram to illustrate the genetic relationships between the immature cells of the bone marrow and the mature cells of the circulating blood. (Unitarian theory.) *1, 2, 3*, hemocytoblasts (stem cells). *4–8*, basophil line: *4*, promyelocyte; *6*, myelocyte; *8*, granulocyte. *9–14*, the eosinophil line: *9*, promyelocyte; *11*, myelocyte; *13*, metamyelocyte; *14*, granulocyte. *15–21*, neutrophil line: *16*, promyelocyte; *17*, myelocyte; *20*, metamyelocyte; *21*, granulocyte. *22–31*, erythrocyte series: *22*, procerythroblasts; *23–27*, erythroblasts (megaloblasts) with increasing amounts of hemoglobin; *28, 29, 30*, normoblasts (at *30*, an extruded "naked" nucleus); *31*, erythrocyte. *32–33*, megakaryocytes—parent forms of the platelets. (After Maximow-Bloom, Textbook of Histology, courtesy of W. B. Saunders Company.)

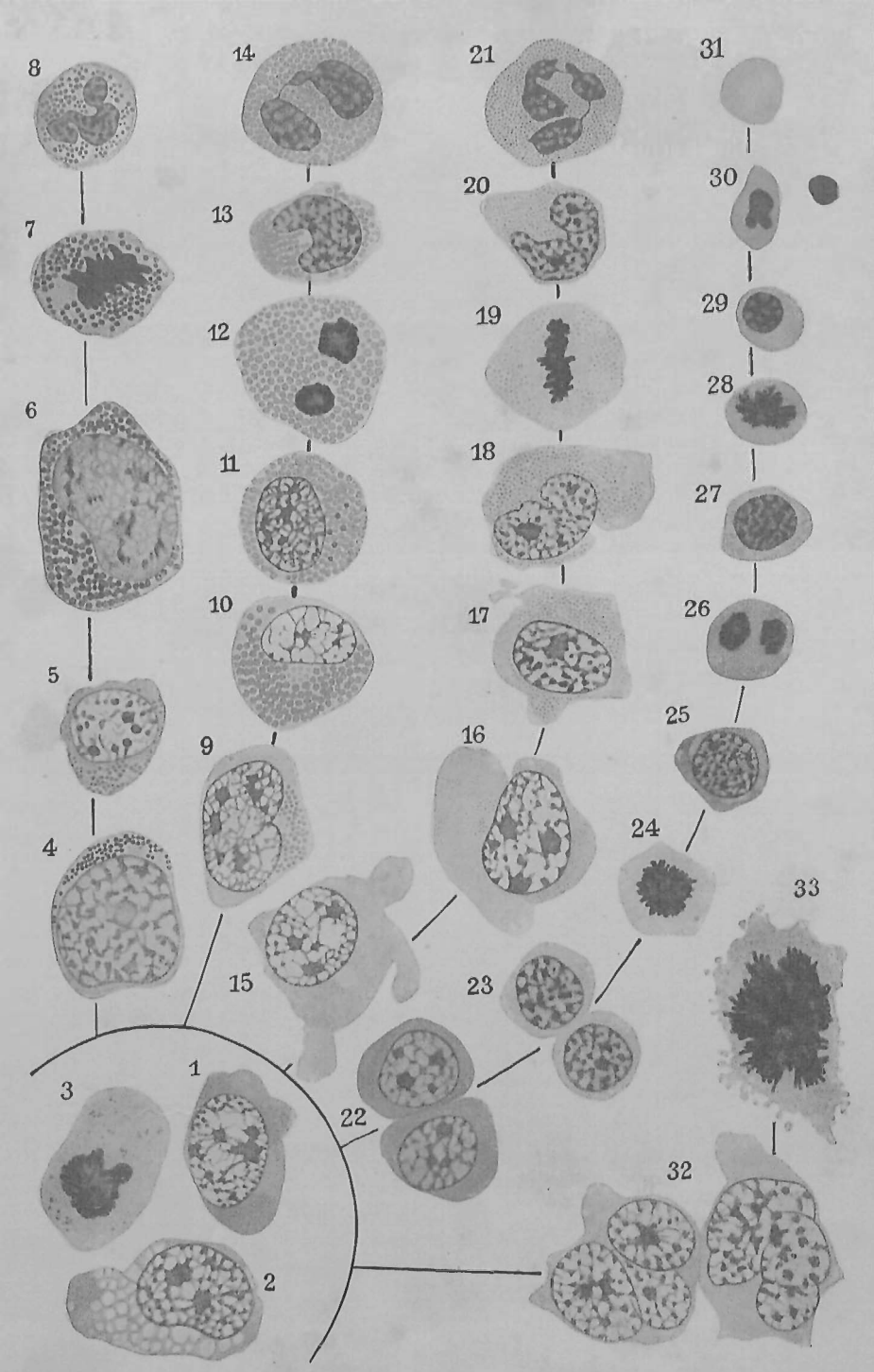
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Fig. 38

the red cells and the white cells have an independent origin, and the hemocytoblast and myeloblast are different in their potentialities.

The myeloblast is a large basophilic cell with a vesicular nucleus possessing four or more conspicuous nucleoli. Its characters grade into those of the myelocyte, a cell which may be specifically identified by the granulations. Three stages are arbitrarily recognized: Myelocyte A, with ten granules and two nucleoli; Myelocyte B, with many granules, reniform nucleus and no nucleoli; Myelocyte C, with mature granulation and a nucleus showing the beginning of lobation (Fig. 38, *9, 11, 13*).

According to Wright, the platelets of the circulating blood are derived from giant multinucleate megakaryocytes (Fig. 38, *32*). These are scattered at random throughout the marrow. They may be confused with osteoclasts except for position. In sections, they frequently give the appearance of extending ameboid processes through the walls of the venous sinuses. These processes fractionate as platelets.

In certain anemias, an increase in number of megakaryocytes has been correlated with an increase in number of platelets.

Degenerative forms of megakaryocytes have also been identified. They are replaced by young and active forms recruited from the hemocytoblasts. Megakaryocytes rarely enter the blood stream in severe marrow injury.

The geneology of the monocytes is somewhat obscure. They are considered to arise from (1) myeloid tissue, (2) from endothelium, (3) from macrophages, (4) from lymphocytes, and are referable to the marrow, spleen, liver and general connective tissues. Sabin, Cunningham, Doan claim to recognize monoblasts on the basis of "rosettes" of granules vitally stained. Clark and Lewis both claim a direct transformation of macrophages into monocytes. Maximow derives them from the hemocytoblast (lymphocyte) and distinguishes them from the larger macrophages in their inability to store vital dyes.

Maximow further claims that the hemocytoblast is identical with the large lymphocytes of the lymph nodes, thus deriving all blood cell types from a single source.

The mechanics of delivery of mature red and white corpuscles from the marrow presents an unsolved problem. The erythroid and leucoid marrow is distributed (Fig. 37) in more or less discrete islands. About 70 per cent of the cellular tissue is leucoid by count while the erythroid represents about 30 per cent. Quantitatively, this would give about 325 cc. of red marrow and 1064 cc. of white marrow—an interesting relationship when compared to the cells in the circulating blood, which contains some 1935 cc. of red cells and 3.8 cc. of white cells. The white marrow is thus a tremendous reserve store for white cells which can be called out on demand as in an acute infection when the W.B.C. may rise from 8000 to 40,000 in twelve hours. The demand for red cells is never so pressing. The normal rise after severe hemorrhage rarely exceeds 200,000 per cubic millimeter per day, and is not initiated until about three days after the blood loss.

The leucoid "islands" in the marrow occupy an extravascular position. Due to the ameboid activities of the white cells, it is generally premised that they reach the open circulation of the marrow sinuses by diapedesis. Red cells lack this capacity, hence it is thought that they arise intravascularly and are pushed into the blood stream by "growth pressure." Crops of maturing reticulocytes can be "flushed" out of the marrow by large doses of caffeine; but marked rises in blood pressure fail to loosen and wash out the normoblasts, from the endothelial "bayous."

It is of interest to note that there is an independent delivery of white and red cells. So far, the nuclear extracts, nucleotides, are the only therapeutic agents that have been successfully used to increase the number of circulating white cells. Hemorrhage, oxygen want, liver extract and ventriculin are known red-cell stimulants under certain conditions. No depressants

are known, but benzol is used to destroy white cells in leucemias and phenylhydrazine is used as a hemolytic agent in polycythemia.

The chronology of hematopoiesis is of importance. Blood islands in the yolk sac serve as the source of cells during the first three weeks of life. The liver assumes this function from that time until the seventh month. The spleen is an accessory organ of red cell production from the second month until birth after which it becomes hemolytic. Marrow begins to develop in the clavicle at the sixth week. In case of stress on the marrow any or all of these organs may become hematopoietic by vicarious resumption of this process.

It is the function of the reticulo-endothelial system to dispose of the worn out red cells. A blood pigment, hematoidin, chemical isomere of bilirubin, is normally found in the macrophages of the spleen and bone marrow and lymph nodes. Chemically, it represents about 4 per cent of the hemoglobin molecule. As bilirubin it is excreted in the bile. The fate of the "globin" radicle is unknown. Hemosiderin, an iron containing compound derived from hemoglobin, is the coloring matter of a "black eye."

Chapter XIV

THE SKIN

Skin is more than a tissue; it is an organ of the body. Its functions are many. It forms a covering surface, practically impervious to bacterial and virus invasion; it prevents dehydration; it regulates body heat through its vascularity and through evaporation of sweat; it mediates sensation; it serves as a storehouse for fat; it manufactures vitamines and reacts locally in many allergic diseases. It comprises an area of 10,000 to 20,000 square centimeters. Its thickness varies from 0.03 to 5 mm.

Skin covers the body in its entirety except for the conjunctiva, cornea and tympanum. It is continuous with the mucous membranes at the orifices of the body.

Skin is semitransparent and elastic. Its color varies with its vascularity, with the amount of racial pigment, and with the amount of individual pigment as freckles, tan, albinism. It is generally moist, warm and oily. On the palm and sole of the foot it presents a definite individual pattern of "fingerprints." Fixed and temporary lines of cleavage follow the fiber bundles along the lines of attachment. Its degree of smoothness and distention varies with edema, dehydration, age, endocrine dysfunction and diet. Deep seated infections leave permanent scarring.

Skin is composed of an outer epithelial layer, the epidermis, and an inner connective tissue layer, the dermis. The subcutaneous tissue binds the skin to the underlying fascia, muscle and bones (Fig. 39).

The epithelium rests on a series of simple dermal papillae or "pegs" and descends deeply into the furrows between them. These papillae vary in height from 0.2 to 0.4 mm., and occur

approximately 100 to the square millimeter. They may atrophy in old age. Their height and form is of great significance in diagnosis of various skin diseases. Two primary types of epidermis are recognized. Thin skins show (1) a basal layer; (2) a "prickle cell" layer; (3) a corneous layer. Thick skins show two additional layers (4) a granular layer; (5) a hyaline layer (Fig. 24).

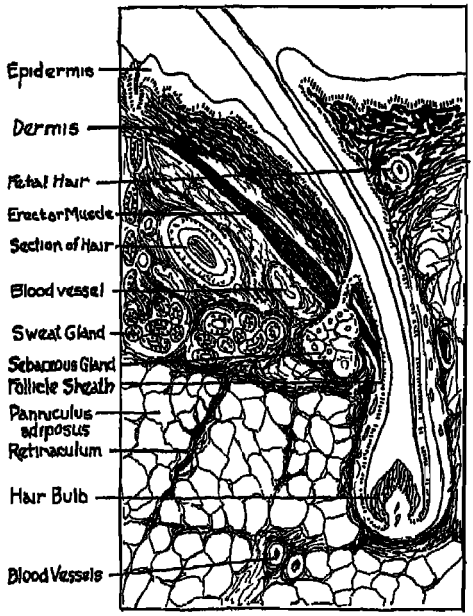

FIG. 39. Vertical section through the scalp (slightly diagrammatized)

The stratum cylindricum or basal layer, is composed of a single row of cells resting on a basement membrane. This layer contains the bulk of the racial pigment, melanin, disposed as fine granules within the cytoplasm and particularly around the nuclei.

The stratum spinosum or "prickle-cell" layer is composed of two to twenty irregular rows of polyhedral cells which interlock with a series of intercellular bridges. Interlacing tonofibrils of unknown origin have also been demonstrated as binding elements.

These two layers are referred to as the stratum germinativum since frequent mitoses (0.4 to 2 per cent) indicate that growth occurs in each. Pathologists, however, have found a fundamental difference in behavior of tumors (cancers) arising from the two layers.

Overlying the stratum spinosum, at a uniform depth from the surface, is the stratum granulare. This is only one to two cell layers thick. The cells are flat, nuclei prominent, and the cytoplasm is filled with coarse, deep-staining granules of keratohyalin.

The hyaline layer or stratum lucidum, is approximately as thick as the granular layer. Its cells are flattened, indistinct, and the nuclei are normally not visible. A high refractive index gives the layer its name, due to the presence of eleidin, a substance intermediate between the keratohyalin of the granular layer, and the keratin of the corneous layer. Keratin is an albuminoid rich in sulphur. Rift in the layers in blister formation, comes between the lucidum and the granulosum.

The stratum corneum is the outermost layer. It varies in thickness, particularly in callus formation. The cells are dead flat plaques of keratin. They slough off or "desquamate" from the surface or peal off in sheets, "exfoliate," after severe sunburn. The superficial layers blacken with osmic acid, due to the presence of paraleidin, a product of fatty degeneration. In the fetus this forms a part of the protecting coating of waxy, vernix caseosum. Cornification is not entirely due to exposure to air, since it will occur on internal surfaces and in the skin of the fetus in utero. The character of the desquamation, however, differs on dry and moist surfaces, and is sometimes a valuable clew to students in the identification of sections from unknown tissues.

In passing it should be mentioned that migratory leucocytes enter the basal layer of the skin and forms so-called "dry pus." They are generally of the neutrophile variety, but in specific diseases such as pemphigus, they are eosinophiles. The so-called cells of Langerhans are questionable constituents.

The corium, derma vera, or true skin, consists of two indistinct layers: the pars papillaris and the pars reticularis. It is composed of fibrous tissue in which the bundles are irregularly distributed to form a closely knit web. Some few fine elastic fibers are present. The cell types are fibroblast, histiocytes, plasma cells, and an occasional fusiform, pigmented melanophore. The papillae are classified as vascular or sensory, according to whether they contain a capillary tuft or a touch corpuscle of Meissner. The corium contains the blood vessels, small nerve trunks, ducts of the sweat glands and the bulbs of the fetal hairs. In special regions as the scrotum and nipple, smooth muscle may be present; and in the face the insertions of the muscles of expression may reach this layer.

The subcutaneous layer or hypodermis, is composed of coarse fibro-elastic tissue, extending from the corium to the fascia subcutanei. In various areas it forms definite fatty pads, the panniculus adiposus. The lobules are separated by vertical retaining bands, the retinaculae cutis. The subcutaneous layer contains the larger blood vessels, nerves and end organs of deep pressure, and the coiled ends of the sweat glands and adult hair bulbs. In it course the larger lymph channels, draining the tissue spaces, the site of subcutaneous injections (Fig. 39).

The skin contains glands of two varieties: the sweat or sudoriparous glands, and the sebaceous glands. Sweat glands are generally distributed over the skin, except on the lips and glans penis. Their average number is 2700 to the square inch. Their excretions have a volume of 800 cc. daily. They are simple tubular glands with coiled blind ends which lie in the superficial part of the subcutaneous layer. Their pores are just visible under the hand lens on the finger tips. The lining cells of the ducts, one or two layered, are continuous with the stratum cylindricum of the epidermis, while the lumen takes a spiral course through the more superficial corneum to open on the surface. The secretory portion of the gland consists of the same low cuboidal epithelium resting on a basement membrane and supported by a delicate sheath of connective tissue. An

incomplete row of "basket cells" is interposed between the membrane and the epithelium. In the large, branched axillary glands, these cells simulate smooth muscle and hence are known as myoepithelium. The glands are abundantly supplied with a capillary bed and regulatory nerves.

The sebaceous glands are branched saccular glands associated with the hair follicles except in the skin of the face. Their macroscopic pores are evident on the skin of the nose particularly when blocked with secretion (black-heads). The acini are short and flask-shaped, and open directly into a wide-mouth duct that empties into the upper third of the hair follicle. The basal layer is continuous with the stratum germinativum of the follicle. The lumen is filled with large polyhedral cells which progressively undergo fatty vacuolization and finally disintegrate as the secretion of the gland. Contraction of the erector muscles of the hair squeeze the secretions into the follicles. The secretion is chemically allied to wool-fat or lanolin. The wax glands of the ear are modified sebaceous glands.

HAIR

Contrary to biblical sayings, the hairs on the head are roughly numbered. They approximate 1000 to the square inch, being more numerous for blonds and least for red hair. The hairs are cellular cylinders, approximately 0.15 to 0.32 mm. in diameter. The length is variable. The mature hair consists of a shaft, root and a bulb. The free shaft presents an outer scaly cuticle and an inner cellular cortex which differ in degree of keratinization. The larger hairs contain a more cellular pigmented medulla in their proximal parts (Fig. 39).

The hair root, sheathed by the follicle, contains the same layers as the shaft. It is invested by (1) an inner epithelial sheath derived from the epidermis and (2) a connective tissue sheath of dermal origin. The epithelial sheath is subdivided into an inner and an outer root sheath. The inner sheath, applied to the lower two thirds of the root, presents three layers: (*a*) cuticle, (*b*) Huxley's layer, (*c*) Henle's layer; continuous

with the corneum of the skin. The outer root sheath is continuous with the stratum germanitivum. These layers become intimately fused in the bulb or growing point of the hair, and because of the amount of pigment present, are difficult to distinguish in this zone. The bulb caps a connective tissue papilla which bears the nutritive capillary plexus.

The connective tissue sheath presents three membranes; an inner vitreous or hyaline "basement" membrane, a middle vascular layer and an outer fibrous layer. The smooth muscles of the hair (arrectores pilorum) are inserted into the outer coat and by contraction make the hair "stand on end."

Scalp hairs have a life of two to five years, while eyebrows last from three to five months. They are replaced by new hairs, outgrowths from the old sheaths.

NAILS

Nails are horny plates derived from the stratum lucidium of the epidermis. They present a root, body and free edge. The underlying skin layers constitute a nail bed while the lateral borders are the nail wall. The semitransparent nail plate consists of hard, densely packed cornified cells, occurring in strata. Its pale base is the lunula. The nail walls have the typical structure of true skin. They turn under as the nail folds, particularly at the root. Here the corneous layer spreads onto the free surface of the nail as the eponychium or "cuticle." The stratum lucidium and stratum granulosum penetrate the groove, but the latter disappears at the outer border of the lunula, and the nail rests directly on the stratum germanitivum.

In the nail bed, the derma is fused directly with the periosteum of the bony phalanx. Its surface is studded with tall papillae at the base; is smooth under the lunula and is longitudinally ridged beyond. At the free edge, the horny layer of the skin is adherent to the nail as the hyponychium.

The nail grows out from the base at the rate of $\frac{1}{32}$ inch per week.

Chapter XV

THE MOUTH. LIPS. TEETH

The mouth is bordered by the lips. The first portion, including the vestibule and alveolar ridge, develope from a primitive oral pit. Hence the epithelial lining, including the enamel organs, is ectodermal in origin, and is continuous with the epidermis. The transition from skin to mucous membrane is marked by (1) increase in the height of the papillae, (2) disappearance of hair, sweat glands and sebaceous glands, (3) disappearance of pigmentation in the stratum cylindricum, (4) absence of cornification, and (5) the appearance of labial mucous glands. The membrana propria of the mucosa is continuous with that of the corium; the submucosa is continuous with the subcutaneous layer and has the same essential structures. In the lip, the striate fibers of the orbicularis muscle may anchor in the corium. The lip is a mammalian structure. In the lower forms the scales of the skin grade imperceptably into the teeth.

THE TEETH

The teeth are mastigatory organs, set in alveoli or sockets in the jaws. In the mammals, their forms and numbers are fixed. In man, two sets occur: the deciduous or "baby teeth" and the permanent teeth. The formula may be represented as follows $\frac{2\ 1\ 2\ 2\ 1\ 2}{2\ 1\ 2\ 2\ 1\ 2}$ for the deciduous set and $\frac{3\ 2\ 1\ 2\ 2\ 1\ 2\ 3}{3\ 2\ 1\ 2\ 2\ 1\ 2\ 3}$ for the permanent set; or 2 incisors, 1 canine, 2 molars in each half jaw for the deciduous and 2 incisors, 1 canine, 2 premolars and 3 molars for the permanent set. The baby teeth are all cut by the beginning of the third year and are normally shed by

the twelfth. The first permanent tooth to be cut is the inferior molar in the fifth to sixth year; followed by the central inferior incisor in the seventh. The "wisdom" teeth generally appear from the eighteenth to the twenty-fifth year.

Structurally, a tooth presents a crown, a neck and a root (Fig. 40). The root may have from one to three fangs. The body of the tooth is a cylinder of dentine, enclosing a pulp

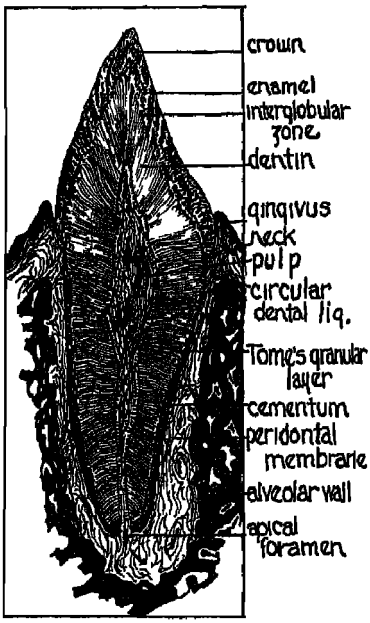

FIG. 40. Ground section of the human incisor showing a portion of the bony wall of the socket and the retaining membrane.

cavity which is open by the apical foramina at the tip of the fangs. The dentine of the crown is capped by enamel; that of the root is sheathed by cementum. The neck is protected by an overlap of cementum on enamel, and serves as an attachment of the gum and the circular dental ligament. The tooth is held in the alveolus rather firmly by the peridental membrane, a fibrous sheath that extends from the cementum to the wall of the alveolus. This allows for a slight amount of dis-

placement by gradual pressure, a process that is utilized in the practice of orthodontia, or "straightening" of the teeth, although permament effects are produced by modeling of the alveoli.

The histological detail of teeth has been made out by study of the ground sections, by embryology, and in part by decalcification. The latter method is not applicable to the enamel since it contains but a mere trace of organic matrix.

In longitudinal and in transverse sections, the dentine shows a whole series of very fine radiating lines, the dentinal canals, very similar to the canaliculi of bone. These canals, 2 to 3μ in diameter have their origin in the pulp cavity. They take a straight or spiral course to terminate in a series of irregular interglobular spaces of Czermak at the enamo-dentinal junction, and a somewhat similar series of structures in the granular layer of Tomes at the cemento-dentinal junction. The immediate wall of the tubule is more compact than the intertubal cement substance, and has been called the dentinal sheath of Neumann.

In longitudinal section, two series of lines are seen: the contour lines of Owen and the incremental lines of Schreger. These have been variously interpreted as growth lines representing periods of poor calcification or as artefacts made by the intersection of the spiral dentinal tubules with the line of cut (Fig. 40).

Chemically, dentin is 28 per cent organic and 72 per cent ash —the latter consisting of calcium phosphate, carbonate, trace of fluoride and some magnesium carbonate. Enamel is the hardest tissue in the body, containing less than 2 per cent organic material. Cementum has the composition of bone, with which it is histologically similar except that the lamina are placed parallel with the surface of the tooth and show no Haversian canals. All three layers are devoid of blood vessels.

The enamel is non-cellular. It is derived from a calcification of the cuticle produced by the epithelium of the enamel organ.

It shows a striation in section due to the arrangement of the cylindrical enamel prisms. These are 3 to 5μ in diameter and some of them course the entire thickness of the cap. Short secondary prisms have been described as filling the interstices between the primaries. Each prism is considered to be the product of a single ameloblast (Fig. 41) or enamel cell. The separate prisms are held together by a cement substance which differs slightly in hardness from the prisms. "Cracking" is thought to take place along these lines. The general course of

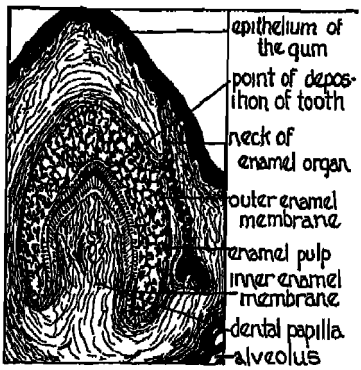

FIG. 41. Longitudinal section through the developing tooth of a 4 months human fetus. Note particularly the zone of deposition of the dentin and the enamel, between the papilla and the inner enamel epithelium.

the prisms is perpendicular to the dentinal surface, but many irregularities exist, particularly on the complex molars. The relations are of importance in securing a firm base for fillings.

In longitudinal section, two series of lines are visible; the radial lines of Schreger and the contour lines of Retzius—interpreted as refraction lines and growth lines respectively.

The pulp cavity is filled with pulp; a fibrous connective tissue divisible into three layers—the outer odontoblasts, the fibrous layer of Weil and the inner cellular pulp containing blood vessels, lymphatics and nerves. The odontoblasts arrange themselves in an epithelioid layer on the inner surface of the dentine after the fashion of osteoblasts (Fig. 41). They send long

processes through the dentinal canals to anastomose in the interglobular layer of Owen and the granular layer of Tomes. In addition small basal processes penetrate the membrane of Weil or pass laterally to adjacent odontoblasts. Nutrition of the dentine is supposed to be carried on by these processes. Incidentally they may become pathways of extension of infection from the pulp to the dentine. Odontoblasts control the deposition of dentine. They may be active throughout life and eventually lead to an obliteration of the pulp cavity. Enamel is never replaced in case of injury, since the cellular layer, capable of producing it is left imbedded in the gum at the time of eruption of the tooth.

The enamel organs for the deciduous teeth all appear between the seventh and eighth week of fetal life; those of the permanent incisors, canines, premolars in the sixteenth week and the first molar in the fifteenth week. The second molar buds arise three months after birth and those of the third molars are delayed until the third year.

The enamel organs bud off from a labio-dental shelf of ectodermal epithelium which grows into the underlying connective tissue of the gum-site (Fig. 41). The organ is a cup-shaped bud. Its outer wall is continuous with the basal layer of the epidermis by a so-called cord or neck. Its inner surface rests on the pulp-papilla. Between the outer and inner enamel epithelium is a loose reticulum of stellate pulp cells, comparable to the corneus layer of the skin. The inner enamel membrane becomes the layer of ameloblasts. The mesenchyme cells of the papilla that lie in juxtaposition to the ameloblasts become the odontoblasts. The dentine and enamel form in the basement membrane between them. The process is initiated at the extreme tip of the papilla, as a layer of predentine. Korff's fibers from the odontoblasts produce an organic matrix which becomes calcified as the dentinal globules. As the dentine extends down the slope of the papilla, the odontoblasts recede. Enamel is laid down on the outer surface of the

dentine, and as this layer thickens, the adamantoblasts (ganoblasts) recede (Fig. 41).

The connective tissue around the developing tooth differentiates as a fibrous sac, enclosing the dental follicle. The bony wall of the alveolus forms about it on all but the gingival or gum surface. At birth, the tips of the deciduous teeth are complete, and as the root forms, the crown is gradually forced upwards through the gum. The fangs continue to grow for two and a half years.

The enamel organs for the permanent teeth, with the exception of those for the first molars, bud from the posterior walls of the necks of the precursors. The follicles lie dormant for several years, resume growth and by pressure atrophy loosen the deciduous teeth.

Since enamel and dentine is laid down in the fourth month, the diet of the mother is of prime importance in its effect on the deciduous teeth. Similarly the diet during infancy has its effect on the permanent teeth.

Experiments indicate that Vitamines A, B and D, parathormone and calcium are all important agents in tooth formation. Softening and loosening of the teeth occur commonly in pregnancy and in scurvy.

Chapter XVI

BUCCAL CAVITY AND PHARYNX. TONGUE. TONSILS. SALIVARY GLANDS

That portion of the mouth between the lips and the alveolar ridge is termed the vestibule, while that part behind the ridge extending to the soft palate and glosso-palatine folds is the buccal cavity or cavum oris. The latter is bounded laterally by the cheeks, above by the hard palate and below by the tongue. It communicates posteriorly with the pharynx by way of the faucial isthmus. Its general lining is a typical mucous membrane with a stratified squamous epithelium. That of the hard palate is thrown into folds or rugae and is bound firmly to the periosteum by a fibrous submucosa. It contains many small palatal glands. The soft palate is a double reflection of mucosa on a septum of fibro-muscular tissue. The submucosa of the cheek may contain a layer of fat, which forms a sucking pad in the infant. The tongue is a muscular organ overlaid by a specialized mucous membrane. A submucosa is generally considered to be absent.

The tongue presents two parts—an anterior free portion or body and a fixed basal portion or root. These two regions differ both structurally and developmentally. The line of demarkation is the sulcus terminalis which follows the V shaped row of large circumvalate papillae. At the apex of the V, a slight depression, the foramen cecum, marks the point of origin of the median thyroid.

The most conspicuous characteristic of the dorsum of the tongue is the presence of the papillae. These are minute elevated processes. Three varieties occur—the filiform, fungiform and the circumvallate. The filiform are threadlike 1 to

3 mm. in height. They are composed of the vascular central core of tunica propria overlaid by the epithelium. In case of "coated tongue," when desquamation is incomplete, the epithelium may pile up like "shingles on a steeple." These papillae are without taste buds, but they mediate the sense of taste through free nerve endings in the epithelium (Fig. 42).

The fungiform papillae are elevated, cylindrical and flat topped (hence the name). The epithelial surface is smooth, but the core may show secondary papillae. The fungiform are distributed to the back and sides of the tongue and are dispersed among the filiform.

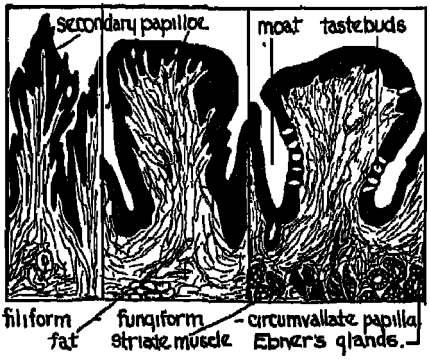

FIG. 42. Composite figure to illustrate the three primary types of papillae found on the human tongue.

The circumvallate are cylindrical, flat and slightly depressed. They vary in number from 7 to 15. Each one is surrounded by a mote or furrow, 1 mm. deep and 2 mm. in diameter. Taste buds occur on the papillary wall of the mote. The serous glands of Von Ebner, which lie deep in the tongue, open into the motes (Fig. 42).

Papillae undergo atrophy in many digestive disturbances such as pellagra, pernicious anemia, sprue; and "tongue prints" are frequently made to determine the progress of the disease.

Sensory branches of the Vth nerve mediate the sense of touch; branches of the VIIth and IXth, the sense of taste.

The dorsum of the base of the tongue is not papillated, but it is pitted by the crypts of the lingual tonsils. This portion really belongs to the oropharynx.

The under surface of the tip of the tongue is smooth. In the median line is a prominent fold, the frenulum, which connects the tongue with the mandible and the floor of the mouth. It projects inward as the median septum of the tongue. On either side of the frenulum is an irregular fold, the plica fimbriata. The lingual veins are visible through the mucosa. The ducts of the submaxillary, sublingual and the anterior lingual glands of Nuhn, open in this region.

The musculature of the tongue consists of a double set—the intrinsic and the extrinsic. The intrinsic include the verticalis linguae, the transversalis linguae, the longitudinalis superior and the longitudinalis inferior. The extrinsics include the vertical genioglossus and hyoglossus; the longitudinal styloglossus and chondroglossus, and the transverse glossopalatinus. The fibers are all striate loosely bound and often branching. They are innervated by the hypoglossal nerves which pass independently to the two halves, a point of importance in neurology.

THE PHARYNX

The pharynx is a tubular passage, some five inches long, communicating with the mouth, the nasal cavity, the larynx and the esophagus. It is anatomically divisible into a nasopharynx, an oropharynx and a laryngopharynx. It is lined by a mucous membrane bearing a stratified squamous epithelium in all but its nasal portion where it grades to the ciliated columnar. The mucosa rests on a pharyngeal aponeurosis, which is backed by striate muscle and a loose tunica fibrosa except in that portion at the base of the skull where an elastic pharyngobasalaris membrane attaches it firmly to the occipital bone.

The palatine tonsils lie in the tonsillar fossa between the glosso-palatine arch and the pharyngo-palatine arch. The

tonsil is almond shaped, 10 x 15 x 20 mm. and its free surface projects into the pharynx. The mucosa is variously pitted by 10 to 20 slit-like crypts, which are irregularly tubular. The tunica propria is a loose reticular tissue impregnated by many lymphocytes. Typical lymph nodules with germinal centers, lie immediately behind the epithelium. The submucosa is dense and fibrous and forms a fairly discrete capsule. Septa divide the structure into lobules. Some few mucous glands may be present. The pharyngeal aponeurosis and superior constrictor muscles lie immediately behind the capsule (Fig. 43).

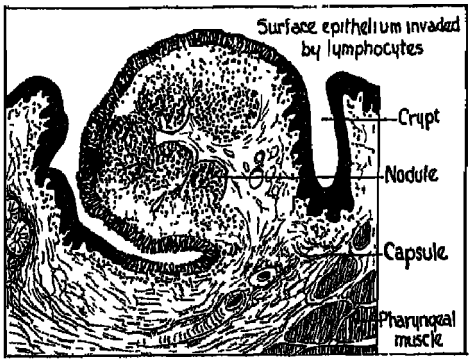

FIG. 43. Section through the palatine tonsil of the dog. Note particularly the migration of lymphocytes from the nodules through the surface epithelium.

The most conspicuous histological feature of the tonsil is the "worm-eaten" character of the epithelium overlying the nodules. A constant emigration of lymphocytes pass through the interstices, to become the free "salivary corpuscles" of the mouth. This phenomenon was discovered by Stohr in 1882 but its significance is still unknown. It is generally assumed to be a protective mechanism against bacterial invasion.

The lymphatic drainage of the tonsil is of importance. Afferent vessels from the mouth, pharynx and nasal cavity pass by an extensive plexus to the follicles. Efferent vessels drain into the upper deep cervical lymph nodes at the angle of the

mandible. Inflammatory hypertrophy of the tonsils is common in childhood. Atrophy occurs after puberty.

The adenoids, or pharyngeal tonsils, the lingual tonsils and the tubal tonsils constitute the so-called tonsillar ring of the laryngologists.

THE SALIVARY GLANDS

The salivary glands comprise the three named glands, parotid, submaxillary and sublingual and numerous small glands scattered throughout the mouth and pharynx. The

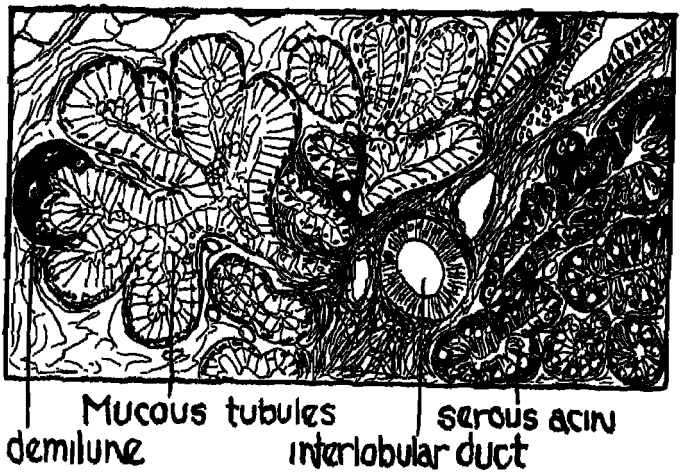

FIG. 44. Section through a lobule of the submaxillary gland of man. Note the mucous and serous acinin and the demilune of Heidenhain.

salivary glands are compound alveolar glands in which two types of acini are found—the mucous and the serous (albuminous). The mucous cells are cuboidal or pyramidal, and cloudy. The nuclei are basal. With H-E stain they remain clear and unstained (Fig. 44). The serous cells are highly refractive, transparent, with central nuclei. The cytoplasm stains deep purple. In the "mixed" glands, both types of acini occur in separate lobules. Occasionally individual acini may show cells of both types. In some cases single serous cells

may lie between the epithelium and the basement membrane, forming the "crescents of Gianuzzi" or "demilunes of Heidenhain." Basket cells have been described.

In general structure, the gland presents the epithelial parenchyma and the interstitial connective tissue. The glands show a variable number of lobes subdivided into lobules. A connective tissue capsule sends septa between the lobes and lobules and a fine reticulum serves as a bed for the alveoli. The main excretory duct subdivides into interlobar ducts, interlobular ducts and intralobular ducts. The latter terminate in the blind acini.

The intralobular duct is made up of a single layer of cells of the secretory type. They frequently show radial striations. It is generally assumed that the water from the blood plasma passes to the saliva at this point. Intercalated ducts of low flat epithelium and narrow lumens are found between the intralobulars and the acini in the parotid and submaxillary.

The parotid gland is mainly serous. Considerable fat may develop in the interstitial tissue. Stenson's duct, composed of two layered columnar epithelium, opens into the vestibule opposite the upper second molar tooth.

The sublingual and submaxillary glands are "mixed." Bartholin's ducts and Wharton's ducts open near the frenulum of the tongue. The blood supply is voluminous; the lymphatics few. Secretory innervation is by the sympathetics and parasympathetics.

Developmentally, the salivary glands are generally considered to be ectodermal ingrowths from the lining of the stomodeum. This point, however, is frequently disputed since the oral plate, separating the oral pit from the pharynx, disappears before exact delimitation is possible. Hence they are frequently termed endodermal.

Chapter XVII

ESOPHAGUS. STOMACH

The esophagus is a tubular muscular organ, some nine inches in length, connecting the pharynx and the stomach. It lies behind the trachea in the posterior mediastinum. It shows three constrictions, one at the level of the cricoid cartilage, one at the bifurcation of the trachea and one at the diaphragm. It consists of the four coats typical of the digestive tract; mucosa, submucosa, muscularis and fibrosa. The latter differs from the serosa of the abdominal viscera in that there is no peritoneal reflection over its free surface (Figs. 45, 59).

The mucosa is .5–1 mm. thick. It bears a thick, smooth, non-cornifying, stratified, squamous epithelium. In the ninth week of fetal life, however, the epithelium is ciliated columnar, and metaplastic islands of this type are not uncommon in the adult. The papillated tunica propria is reticular in character. A typical muscularis mucosa begins at the level of the cricoid cartilage.

The submucosa is thrown into a series of 5 to 8 longitudinal folds which practically obliterate the lumen. These are "ironed out" in swallowing.

The muscular coats are an inner circular and an outer longitudinal. Neither is as discrete as those of the intestine. In the upper third of the esophagus these muscles are striate and voluntary; in the middle third, they are mixed and in the lower third they are purely smooth and involuntary. This distribution materially affects the rapidity with which food passes through the respective parts. In the upper third it is literally "shot" through by contraction of the striate muscle; in the lower third it is moved along by peristalsis. The inferior

pharyngeal constrictors serve as a sphincter at the upper end of the esophagus. While a true cardiac sphincter does not exist in man, the oblique angle at which the esophagus enters the stomach forms a potential valve. The cardia opens under 8 cm. water pressure from the esophageal side, and 30 cm. from the stomachic, providing a mechanism for controlled vomiting or regurgitation.

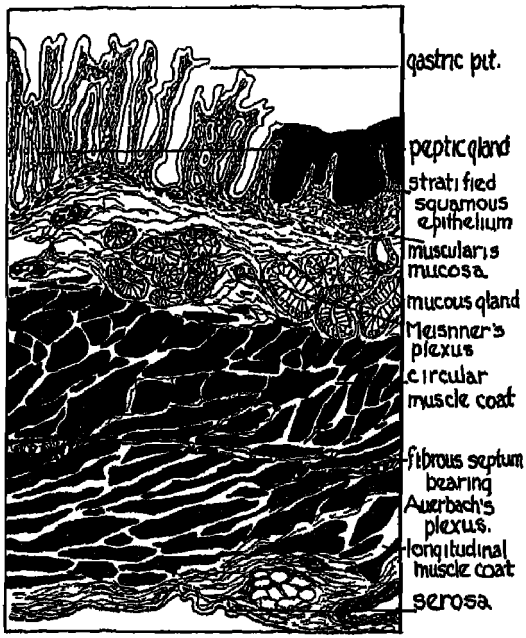

FIG. 45. Longitudinal section through the junction of the esophagus and stomach. Note the abrupt change in the character of the surface epithelium.

The esophagus is innervated by the vagus and the sympathetics. The intrinsic nerves consist of a typical Auerbach's plexus lying between the circular and the longitudinal muscles, and a Meissner's plexus (without ganglia) in the submucosa. The level at which these plexuses begin corresponds closely with the occurrence of smooth muscle; i.e., 3 to 4 cm. below the inferior border of the larynx. There is some indication that

cardiac spasm is a function of the number of ganglion cells in Auerbach's plexus at the cardia.

The glands of the esophagus are found in two regions; one (Fig. 45) at the level of the cricoid cartilage and the other at the cardia. These are racemose mucous glands. Their ducts show dilatations or ampullae just before they penetrate the muscularis mucosa.

THE STOMACH

The stomach (L. *ventriculus*; G, *gaster*) is a J-shaped sac, composed of a body with an enlarged upper end or fundus and a smaller constricted portion or pylorus. These two parts have been characterized by Alvorez, as the "hopper" and the "mill." The junction between the two is at the cardiac angle or incisura angularis. The pyloric portion, turned to the right, shows a dilated antrum (diameter 4.5 cm.) followed by a constricted pyloric canal closed by a pyloric sphincter (diameter 1.5 cm.) The stomach presents two borders—the lesser curvature, 10 cm. long, and the greater curvature, 30 to 40 cm. long. Since the stomach is rotated during embryological development, the right side is the posterior surface and the left is the anterior. The lesser curvature serves for the attachment of the lesser omentum and the greater curvature bears the greater omentum.

The normal capacity of the stomach is one liter. Its daily secretions amount to 1500 cc. The radiographic appearance depends upon the degree of distension and local contraction, characterized by such terms as "cow-horn," "drain-trap," "fish-hook" and "hour-glass."

The stomach shows the four typical coats of the alimentary tract (Figs. 45, 47). The mucosa is from 1 to 2 mm. thick, is inelastic and loosely attached by the fibro-elastic submucosa. When the stomach is contracted, these layers are thrown into folds or rugae. These ridges may form a narrow grooved channel along the lesser curvature, termed the "gastric canal," which sets it off somewhat independently from the rest of the

stomach. The mucosa shows in addition small quadrangular areas, 1 to 4 mm. broad, which are not obliterated by stretching. These are the mammillae. The gastric pits or foveolae open into them. In the fundus, the pits occupy but one-fifth of the depth of the mucosa; in the pylorus, they extend half the depth. The gastric glands open into the pits. It has been estimated that at birth there are some 268,770 of these glands; at 10 years, 2,828,560; and 14,000,000 in the adult.

Two main types of gland are found; the fundic (peptic) and the pyloric. In addition, a few glands of the esophageal variety extend into the stomach (Fig. 45) for a distance of 5 mm. from the cardia. These cardiac glands are of unknown significance. A few typical intestinal glands may be present in the stomach of the adult.

The fundic glands, 0.2 to 0.5 mm. long, are the principle secretory glands of the stomach (Fig. 46). They are simple tubular glands composed of a single layer of columnar epithelium. Three types of cells have been recognized with certainty; the chief neck cells, 20 to 30 μ tall, continuous with the lining epithelium of the pits; the chief body cells forming the body and fundus of the gland; and the parietal cells. The first are mucous secreting; the second are zymogenic and produce the pepsinogen; the third secrete the precursors of the hydrochloric acid (Fig. 46).

The zymogenic cells show a series of fine granulations on the free border which increase and disappear in the secretory phase. These granules are considered to be the precursors of the enzyme pepsin. The general staining reaction with hematoxylin eosin is slightly basophilic. This is in sharp contrast to the parietal cells. The latter are large ovoid cells with clear achromatic nuclei. They are pressed into a subepithelial position—hence the name, but in the fetus these cells are in the epithelium. The staining reaction is sharply eosinophilic. The secretion is considered to reach the lumen of the gland by a set of intra- and inter-cellular canaliculi. Various micro-

chemical tests indicate that the hydrochloric acid is eliminated first as a chloride.

The distribution of the peptic glands is throughout the fundus of the stomach down to the incisura on the body.

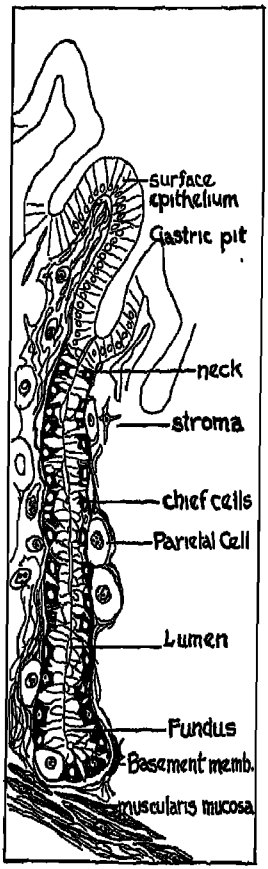

FIG. 46. Camera lucida drawing of one of the peptic glands of man. Note the parietal and the chief cells.

The pyloric glands are composed of a single cell type of the mucous variety and hence allied to the surface epithelium.

A muscularis mucosa is present in two layers. It is supposed to take the tension off of the mucosa in undue distention of the

organ. The submucosa has the same structure and function that it has in other parts of the system.

The muscular coats of the stomach were first described by Willis in 1674. They consist of an outer longitudinal, middle circular and an inner oblique coat of smooth muscle. All are irregular and not distinctly laminate as in the intestine. The oblique fibers begin at the cardia and sweep across the body. The circulars start on the fundus and gradually include the body to become markedly thickened as the pyloric sphincter (Fig. 47). Long fibers are irregular except on the lesser curvature. Al-

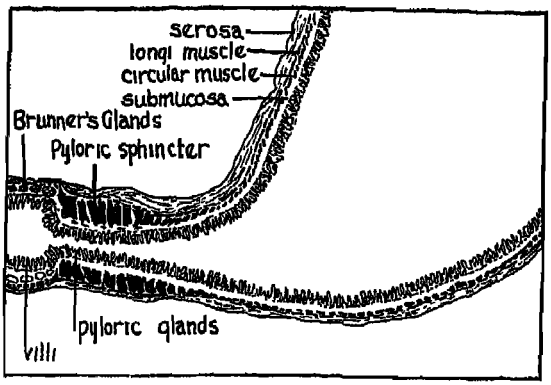

FIG. 47. Longitudinal section through the pylorus of a new-born child. Note the remarkable thickening of the circular muscles to form the sphincter.

verez believes that the several segments of the stomach are independently contractile. Waves start as ripples at the cardia and pass downward and outward at the rate of 3 to 4 per minute. They deepen at the antrum, but do not pass beyond the pylorus. There is some evidence of a discontinuity of muscle by connective tissue septa where the pylorus joins the duodenum. The emptying time of the stomach is normally 3 hours.

Two theories have been proposed to explain the propagation of these waves. Alverez considers the stomach purely autonomous since it will carry on its function when the vagi and

splanchnics are cut, although McCrae claims that section of both vagi is fatal. It is more generally held that peristalsis is controlled by the myenteric plexus (Auerbach's), which is widely distributed between the longitudinal and circular coats and particularly concentrated in nodal points at the sphincter (20,000 ganglion cells per square centimeter at the pylorus). The vagus, passing through the esophageal plexus is motor to the sphincter; the splanchnics and coelic plexus are inhibitory.

Meissner's plexus of sympathetic cells and fibers is located in the submucosa. Preganglionic parasympathetic fibers are supposed to control secretion of HCl, while sympathetic fibers control the enzyme secretion. The amount of HCl secreted is approximately 6 cc. per day; while the concentration is 0.4 per cent. About 3 per cent of normal individuals produce no HCl although achlorhydria (absence of HCl) is a significant find in pernicious anemia, pellagra and other diseases.

The vascular supply to the stomach is profuse. It is derived from many sources. The larger vessels pass by way of the mesenteric borders to the submucosa and from here are distributed to the mucosa and muscular layers. The principle interest in the blood supply aside from its normal function is the vascular spasm theory of the cause of gastric ulcer, as opposed to the hyperacidity and pylorospasm theory.

Lymphatic drainage from the stomach is profuse. The pathway is important as regards metastases from cancer of the stomach. The chain of nodes on the lesser curvature drain to the coelic glands; those from the fundus to the splenic nodes before entering the cisterni chyli.

Within recent years, Castle has discovered that the stomach elaborates an intrinsic principle, ventriculin, which acts on an extrinsic factor (vitamin B_2') in ingested beef muscle to become an important hematopoietic agent in pernicious anemia. This is absorbed from the digestive tract and stored in the liver. The stomach is not absolutely essential for life, since patients with total resection have lived for four years. But all have eventually developed a severe anemia.

Chapter XVIII

THE SMALL INTESTINE

The small intestine is a coiled tubular abdominal viscus, some 21 feet in length. The first portion or duodenum (L. *duodeni*, twelve) is twelve "finger-breaths" in length and 4 cm. in diameter. The jejunum (L. *empty*) is approximately 8 feet long and the ileum (G. *ileo*, I roll up) is 12 feet. The intestine is supported as in a sling by the mesentery, suspended from the dorsal abdominal wall. This provides a connective tissue bed for the blood vessels, lymphatics and nerves. The mesentery of the duodenum becomes obliterated by fusion with the peritoneum—hence the duodenum is retroperitoneal, i.e., lies behind the peritoneum. The terminal duodeno-jejunal angle is supported by a fibro-muscular ligament of Treitz, a surgical landmark. The duodenum receives the common bile duct and the ducts of the pancreas.

The division of the jejunum and ileum are not so readily recognized. Group characters are made use of in identification. The jejunum has a thick coat and a large diameter (3.5 to 4 cm.); the arcades of the arterial vessels are larger and the vasa recta are longer than in the ileum; lymph nodes are fewer and fat tabs are rare. Valvulae are few in the ileum while the lymphoidal patches of Peyer are marked (Fig. 48).

The general histological character is the same for all three divisions. The typical four coats are present: mucosa, submucosa, tunica muscularis and serosa. The mucosa differs from that of the stomach in the possession of (1) villi, (2) cuticle, (3) goblet cells, (4) crypts of Lieberkühn and (5) plicae circulares. The transition from pylorus to duodenum is abrupt (Fig. 47).

The villi are small fingerlike projections of the tunica propria overlaid by the surface epithelium. They are from 0.2 to 1.0

mm. high and range from 10 to 40 per square millimeter. They occur in several forms: foliate, clavate and filiform. The central core contains a loose reticular tissue continuous with that of the tunica propria. A central blind lymph capillary or "lacteal" is present, as is also a vascular capillary tuft. A few smooth muscle fibers extend from the muscularis mucosa into the core. These are supposed to have a "milking" action on the villus (Fig. 49).

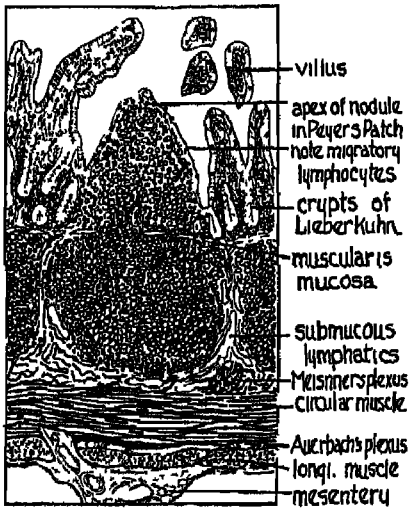

FIG. 48. Portion of the cross section of the ileum of the dog, showing one of the nodules in a Peyer patch. Note the absence of villi over the nodule and the migratory lymphocytes passing through the epithelium.

The surface epithelium is made up of tall columnar "absorptive" cells, interspersed with occasional goblet cells (unicellular mucous glands). A thin striated cuticle covers the entire surface, interrupted only by the perforations over the goblet cells. The cells all stand on the basement membrane, but a series of small intercellular spaces are frequently seen at their bases which have been variously interpreted as absorption channels of a lymphatic nature or as fixation artefacts.

The crypts of Lieberkühn are simple tubular glands of the

intestinal mucosa. They have a length of about 450μ. They open into the interspaces at the bases of villi. The epithelium is simple columnar, and is continuous with that of the villi. The cuticle and goblet cells gradually disappear at the neck of the glands, and the chief cells become simple mucoid similar to the pyloric glands, although the staining reaction is more basic (Fig. 48).

Two special cell types have been described from the fundus of the gland: the Paneth cell and the argentophil or chromaphin cell. The Paneth cells bear large, coarse and eosinophilic granules; the granules of the chromaphin cells are smaller and specifically stained with silver nitrate. The significance of

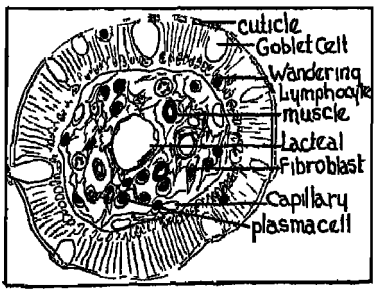

FIG. 49. Cross section of a villus

neither of these cell types has been determined, although it is generally assumed that the various enzymes of the intestine are secreted by Lieberkühn's glands.

Absorption is thought to take place through the epithelium of the villi. Proteins are taken up as amino acids; the carbohydrates as glucose. These pass by way of the blood stream to the liver. The fats are split into fatty acid and glycerol and are absorbed by the lacteals to drain into the thoracic duct. Recent studies indicate that vitamin B is essential for proper absorption. Stainable fat droplets have been found in the epithelial cells, beneath the cuticle, around the nucleus and in the intercellular spaces and lacteals, constituting "absorption

by streams." These droplets have been identified as Gage's chilomicra, found in the circulating blood.

The plicae circulares or valvulae conniventes of Kirchring are circular or crescentic folds of mucosa, reaching a height of 8 mm. They are permanent and not completely obliterated by distension.

A conspicuous feature of the small intestine is the accumulation of lymph nodules beneath the epithelium. They are solitary in the duodenum and jejunum but assume macroscopic proportions (1 to 4 cm. in extent) in the ileum, where they are known as Peyer's patches, agminated or aggregated follicles. They belong to the mucosa, but may extend through the muscularis and become partially submucosal. The villi are wanting over their free surfaces. Germinal centers may be present. An outstanding feature is lymphocyte migration through the surface epithelium— a process, the significance of which, is as obscure as it is in the tonsil. Bunting has made counts on the number of migratory lymphocytes, circulating lymphocytes and those entering the blood stream through the thoracic duct. External migration seems to be part of the mechanism that maintains the lymphocyte level (Fig. 49).

One hypothesis is that the migrant lymphocytes act as bacteriolytic agents in the alimentary tract, but Burgett has shown that a resected loop of intestine, closed at both ends, never becomes sterile. Bacillus coli persisted for four months in such a loop. Migration also occurs within the intestine of the fetus before the flora of the tract is established; hence the rôle of the lymphocyte is still obscure.

The submucosa has the same general structure as in other parts of the digestive tract. Surgically it is of importance in that it gives a firm tough membrane for the placement of sutures. Blood vessels, passing from the mesenteric border to the submucosa, break up as Heller's plexus and send fine branches to the mucosa and muscular coats. The veins drain into the portal vein to pass to the liver. Valves are present. The sympathetic plexus of Meissner is conspicuous.

The muscular coats comprise an outer longitudinal and an inner circular, the relative thickness of which, differs with the degree of contraction. They are both innervated by Auerbach's plexus (Fig. 48). Contractions are of two types: (1) local segmental or kneading movements, and (2) peristaltic "rush" or progressive movements by which the bolus of food is moved along. Reverse movements are common, particularly in the duodenum, where regurgitation of alkaline secretion is forced through the duodenal ampulla or "bishop's cap" into the pylorus, to neutralize the acid chyme. Occasional telescoping with obstruction may occur. Motility and abdominal pressure may lead to herniation at the weak sites of the abdominal wall such as the inguinal canal or umbilicus.

The serosa is a tough outer serous membrane continuous with the peritoneum. It can be readily stripped from the muscular coat, although it is extremely thin. In inflammation it may form adhesions with the peritoneum and bind the gut to the abdominal wall (Fig. 48).

Histological preparations of the intestines and other organs such as the gall bladder, pancreas and adrenals, must be made shortly after death because of the fact that enzymes rapidly digest the epithelium. This process of self-digestion is known as autolysis.

It is sometimes necessary to determine by histological means, the region from which a specific section was taken. The general characters that distinguish the three parts of the small intestine from one another are as follows: the ileum bears Peyer's patches (Fig. 48); the duodenum bears the submucous glands of Brunner (Fig. 47); the jejunum is without either of these marks.

Chapter XIX

THE LARGE INTESTINE

The large intestine constitutes the last segment of the digestive tract. It is approximately 5 feet long and has a variable diameter from 3 to 8 cm. It shows the following parts: cecum, appendix, ascending colon, transverse colon, descending colon, rectum and anus. Except for the terminal portion, where a fibrosa replaces a serosa, it shows the same four coats of the small intestine, but its macroscopic appearance is different, since the longitudinal muscular coat is formed into three discrete bands, the tenia coli. These are shorter than the full length of the remaining coats, which are thrown into a series of sacculations or haustra, partially separated by the transverse plicae semilunares. Fatty tabs, the appendices epiploicae, are formed within the serosa (Fig. 50).

Histologically, the large intestine differs from the small in the absence of villi (Fig. 50). The glands are all of a uniform type—simple tubular crypts of Lieberkühn, that lie in close approximation. Since their prime function is the secretion of mucus to make a tenacious cement substance for the feces, goblet cells extend deep into the glands. Paneth cells are few in number or absent. Enzyme action is probably slight. Water absorption is the most characteristic function as the intestinal content is dehydrated and moulded into "stools." Bacterial putrefaction is of import in "gas formation" and "autointoxication." Absorption of predigested foodstuffs, however, is practical, as shown by rectal feeding. Furthermore, materials such as bile pigment, secreted in the small intestine, may be re-absorbed from the fecal content of the large bowel. Normally the rectum is empty, the descending

colon serving as a storehouse for feces awaiting a convenient time for evacuation.

Four regions deserve special study: cecum and ileo-cecal valve, appendix, rectum and anus.

The cecum is a cul-de-sac, defined as that part below the entrance of the ileum. It is entirely invested by peritoneum. The ileum enters the colon at right angles (Fig. 50). The wall

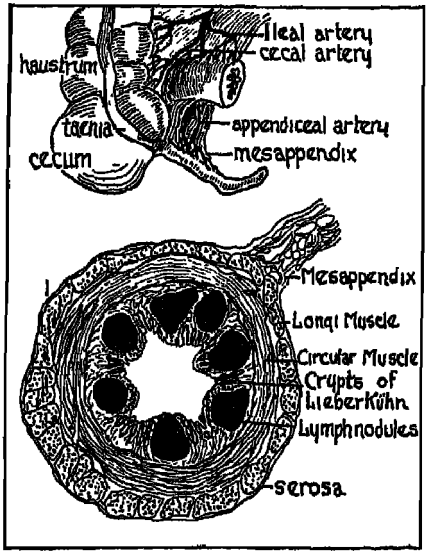

FIG. 50. Sketch to show the anatomical relation of the appendix to the cecum and the ileum. Below, a cross section through the appendix.

is produced into two valve-like folds or labia surrounding a slit-like orifice. These are prolonged to the right and left as the frenulae valvulae coli. The musculature is interrupted by connective tissue septa—a significant point in the mechanism of the propagation of the peristaltic wave. The circular musculature forms a sphincter which guards the ileum from regurgitation.

The cecum lies in the right iliac fossa (underneath the watch pocket). The ascending colon, with which it is continuous,

passes upward on the right side to make a right angle bend under the liver. As the transverse colon, the intestine passes below the stomach; forms a splenic flexure; descends on the left side to the left iliac fossa to make a sigmoid bend to reach the median line as the rectum (straight portion).

The appendix is a blind tube attached to the original apex of the cecum. It has a diameter of 0.8 cm. and a variable length of 8 cm. It is pendulous, twisted, or coiled, either upward or downward. It has no true mesentery, but a falciform fold, the mesappendix, is continuous with the lower layer of the mesentery of the ileum, through which it receives a branch of the ileocolic artery. It is a point of some surgical significance that it may receive part of its blood supply from the submucous plexus in the cecum.

Histologically, the appendix has the same fundamental structure (Fig. 50) as the large intestine. There are no villi. Each transection shows from eight to ten lymph nodes which separate the crypts of Lieberkühn widely. The muscular coats are not as discrete as in the small intestine. The longitudinal coat is complete and at the base gives rise to the tenia coli. A distinct muscularis mucosa is not present. Meissner's and Auerbach's plexuses are not as definite as in other sections of the intestine. The extrinsic nerve supply is still a subject of speculation. The thoracolumbar sympathetic is generally accepted as arising from the last three thoracic segments and the first two lumbars, but the source of the parasympathetic is obscure. Reflex vomiting in appendicitis indicates that the vagus is involved.

Argentophil cells are of some interest in the appendix since they give rise to so-called carcinoid tumors. Paneth cells are rare. Eosinophilic invasion of the mucosa is common. Fecal concretions are frequently found in the lumen. Fibrosis with thickening of the wall and obliteration of the lumen is characteristic of the appendix after maturity.

The rectum is similar in structure to the colon except that

the muscle coats are discrete. There are no tenia and no haustra. The rectum is divided into three sections—an upper peritoneal portion, a middle infraperitoneal portion and a lower anal canal. A fibrosa replaces the serosa in the lower segments. In the upper portion three or four folds or valves of Houston are present as incomplete transverse crescentic elevations of the submucosa and mucosa.

The anal canal is marked by ten to twenty longitudinal folds —the columns of Morgagni. These are fused at their outer

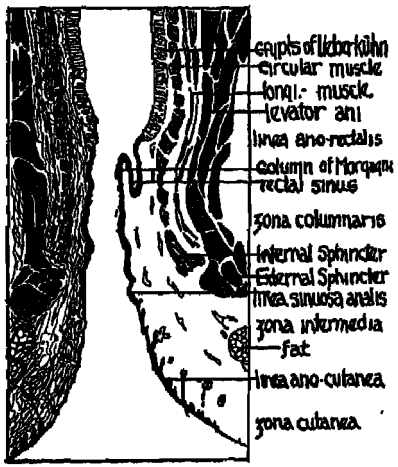

FIG. 51. Longitudinal section through the anal canal of the full-term human fetus.

bases to form the anal valves (Fig. 51). Above them lie the rectal sinuses, frequent sites of fistula in ano. The anal canal shows three zones—zona columnaris, zona intermedia and zona cutanei. The upper border of the zona columnaris is marked by the linea ano-rectales, a discrete line where the crypts of Lieberkühn stop, and the epithelium become stratified squamous. The middle zone constitutes the so-called white line of Hilton, lying about 2 cm. above the anal opening. It is separated from the upper zone by the linea sinuosa analis (Hermann) and from the lower zone by the indistinct linea ano-

cutanei, marked by the presence of hair follicles. The lamina propria becomes conspicuously thickened in the columnar and middle zone by the prominent hemorrhoidal veins in the submucosa. The two coats of smooth muscle of the rectum continue as low as the anal valves where the circular coat thickens as the internal involuntary sphincter. The levator ani (striate) encases the longitudinal coat. An external voluntary sphincter surrounds and occludes the orifice of the anus. It is covered by the superficial fascia continuous with the subcutaneous tissue of the skin. Fatty pads are present and smooth corrugator muscle fibers lie imbedded in the skin. Special circum-anal glands of Gay lie in the cutaneous zone.

It is of interest to note that the intestine is third in frequency as the site of cancer in the male, and that the greater proportion of these are confined to the lower segment of the large intestine.

PERITONEUM, MESENTERY AND OMENTUM

The abdominal cavity is lined throughout by peritoneum, a double reflection of which forms the mesenteries, continuous as the serosa of the stomach and intestine and as the capsule of the liver and spleen, etc. It is a thin layer of loose connective tissue covered on the free surface by a layer of mesothelial cells. The peritoneal cavity is a potential or capillary space between the parietal and the visceral layer which permits movement and volume changes of the viscera. A small amount of serous fluid is always present, the serous exudate. This contains some few cells derived from the tissue of the serous membrane. Transudation from the serosa and peritoneum into the peritoneal cavity is common in diseases of the peritoneum, obstruction of the portal circulation, disease of the liver, obstruction of the inferior vena cava, heart failure and Bright's disease. The cavity is filled with fluid (ascites) due to back pressure from the vascular bed.

The greater omentum developes as the dorsal mesentery of the stomach. It is formed of a double fold of mesentery, the

cavity of which has become obliterated by secondary fusion and by attachment to the mesocolon. The omentum is an organ of importance in disease of the gastro-intestinal tract, because of its response in inflammation. It may "plug" a ruptured ulcer, appendix or infected tube. It may "wall-off" and localize sites of peritoneal infections. The adult omentum may present a lace-like appearance because of the holes that are formed in it by continual stretching. Fat accumulates in the fibrous network and so called "milk spots" of macroscopic size are occasionally present which represent aggregations of wandering leucocytes. The omentum is an important route of intra-abdominal absorption through its lymphatic drainage.

Omental "patches" are frequently used in surgery in the repair of the stomach or intestine.

CHAPTER XX

THE LIVER

The liver is a compound tubular gland in the lower vertebrates, but in the mammals it has taken on a secondary corded arrangement with no definite terminal tubules. The intralobular lumens are reduced to canaliculi.

The liver is the largest gland in the body—1450 to 1700 grams. It is reddish in color; firm in consistency but friable and easily ruptured. It presents four surfaces—a convex superior, convex anterior, a triangular posterior and a concave visceral. It is divided roughly into two lobes, the right and left, by the falciform ligament. The Spigelian (caudate) lobe lies near the midline on the posterior surface, bounded on the right by the fossa lodging the inferior vena cava, and on the left by the fissure of the obliterated ductus venosus. The quadrate lobe is in the midline of the visceral surface, with the fossa for the gall bladder to its right.

The adult liver is surrounded by peritoneum except at the bare area where it is supported from the diaphragm by the coronary ligament. The right and left triangular ligaments are lateral extensions. The round ligament is the fibrous remnant of the umbilical vein and is enclosed in the falciform. The lesser omentum is the primitive ventral mesogastrium, extending from the stomach to the liver. Under the peritoneum is the fibrous capsule of Glisson. It sends septa into the substance of the liver to support the major branches of the blood vessels.

The lobes of the liver are composed of minute lobules which give the organ a mottled appearance. These are polyhedral or pyramidal in form with general dimensions of 0.7 mm. In the

pig they are entirely separated by connective tissue septa, but in man only the angles are fibrous. The lobules are anatomic and functional units (Fig. 52).

Within the lobule, the hepatic cords are radially arranged around a central vein. The cords anastomose irregularly, but

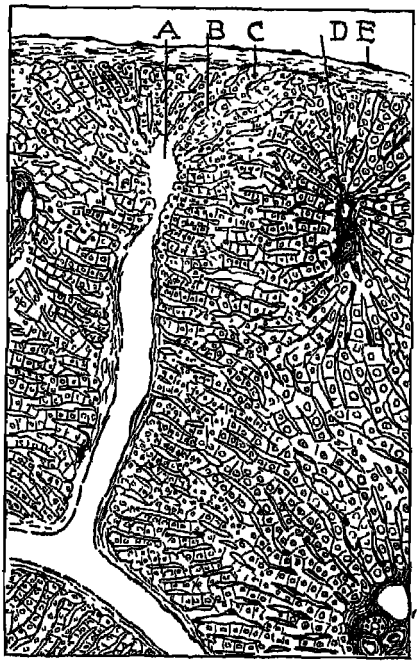

FIG. 52. Oblique section through a lobule of the human liver. *A*, the upper end of the central vein, supplied by the sinusoids, *B*, lying between the cell cords, *C*. The periphery of the lobule is indicated by the fibrous portal canal at *D*, enclosing a branch of the portal vein, the hepatic artery, and the bile duct. This particular lobule lies immediately under the capsule, the mesothelium of which is shown at *E*. The central vein is a contributing branch to the sub-lobular, which in turn drains into the hepatic veins.

lie in planes that parallel the base of the lobule. The cords are from one to two cells thick and enclose the fine canaliculi or bile ducts between them (Fig. 53). At the periphery of the lobule, these canaliculi connect with the lumens of the finer radicals of the bile ducts by the canals of Herring (1871) formed

from small hepatic cells. The flow of bile is centripetal; that is, from the center of the lobule to the periphery.

Between the hepatic cords are the sinusoids or dilated capillary spaces 15 to 45μ wide. These receive their blood supply from two sources; the portal vein and hepatic artery (Fig. 52). The purpose of this double blood supply is still the subject of controversy. The portal vein brings blood with its absorbed nutritive material such as amino acids and glucose, from the intestine to the liver for storage or further metabolism (Ber-

FIG. 53. Section through the margin of a lobule showing Herring's canal connecting the bile canaliculi with the bile ducts. A Kupffer cell bearing granular pigment is seen in the upper sinusoid.

nard, 1848). The hepatic artery is thought to supply the necessary oxygenated blood to the hepatic cells. Injection experiments show a free anastomosis near the periphery of the lobule (Olds and Stafford, 1930). From 13 to 31 per cent of the flow is by way of the hepatic artery as shown by clamping (McLeod and Pearce). Incidentally, the pressure falls from 140 to 70 mm. when the artery is occluded indicating that the production of a head of pressure may be the purpose of the hepatic supply.

The vascular drainage of the lobule is centrifugal, passing

from the periphery by the sinusoids to the central vein. This vessel increases in size from the apex to the base of the lobule to become tributary to the sublobular vein. The sublobulars join to form the hepatic veins that drain into the inferior vena cava.

This arrangement of vessels has a marked effect on the appearance of the lobule. In spite of the fact that the hepatic cells are all quite similar, three functional zones have been recognized—a peripheral, intermediate and a central, based on distribution of glycogen, fat and pigment (Forsgren). Stagnation of blood in chronic passive congestion may produce a "false lobulation" by destructive changes on the "central" cells. Toxic agents in phosphorus and chloroform poisoning and in severe anemias affect the three zones differently.

The divisions of the circulatory system may be readily recognized, however, since the branches of the portal vein, hepatic artery and bile duct always accompany each other as a "hepatic trinity," in the connective tissue between the lobules. This grouping is called the "portal canal." It is accompanied further by a lymph vessel and a branch of the vagus and sympathetic nerve. The sublobular vein also lies in the connective tissue septa, but it has none of the associated structures.

The hepatic cells are large, polyhedral cells (20 to 35μ). The nucleus is large, spherical, central, vesicular, sparse in chromatin and generally shows a discrete acidophilic nucleolus. The cytoplasm may show pale eosinophilic granules; fatty vacuolization or diffuse yellow pigmentation. Cell boundaries are not clear. Marked increase in size occurs during digestion due to glycogen storage. Ten per cent of the weight of the liver may be glycogen. Bile canaliculi are ordinarily not evident except by Golgi silver impregnation technique.

The cytology of the sinusoids presents some disputed points. Current opinions are (1) that no endothelium is present; the hepatic cells being bathed directly by blood; (2) that the endothelial lining is incomplete; (3) that endothelium lines the

sinusoids throughout and that a potential lymph space exists between it and the hepatic cells (Rich). The endothelium is considered to rest on a fine fibrillar reticulum devoid of fibroblasts.

Two varieties of cells line the sinusoids—typical endothelium and stellate Von Kupffer's cells (Fig. 53). The latter are phagocytic and belong to the reticulo-endothelial system. Their supposed function at this site is to digest worn out erythrocytes and deliver blood pigment to the hepatic cells for secretion as bilirubin. Some investigators make no distinction between these and the endothelial cells, claiming that the latter may become phagocytic on demand. The liver is not essential, however, for the production of bilirubin. Mann showed that it continued to form in dehepatized dogs. "Yellow jaundice" results when the destruction rate of erythrocytes exceeds the rate of bile elimination or when the bile ducts are blocked by a gall stone or other obstruction.

In view of the single cell type, the liver shows a versatility of function. It excretes bile acids, bile pigment, cholesterol, lecithin; it stores amino acids, fats, glycogen, and a hematopoietic agent; it forms fibrinogen and completes the metabolism of urea; it is an active detoxicator and phagocytic organ and forms one-fourth of the body lymph. Sugar is released from the stored glycogen to maintain a blood level of 0.1 to 0.2 per cent.

The liver is absolutely essential to life. Dehepatized dogs die in forty-eight hours (Mann). While frequently injured, the liver possesses a remarkable capacity for repair. Seventy per cent of the liver of the rat may be removed, and the remaining portion will regenerate within four weeks (Higgins). Clara has shown mitoses in both hepatic cells and Kupffer cells after chloroform poisoning.

EXTRA HEPATIC BILIARY SYSTEM

The drainage system of the liver includes the hepatic duct, the cystic duct, the gall bladder, the common bile duct, ter-

minating in the duodenum at the papilla of Vater. The biliary ducts in the portal canals are characterized by a low cuboidal epithelium. The larger ducts of the extra-hepatic system have the same type. In the latter the tunica propria rests on a smooth muscle coat. In the hepatic duct the muscles are for the most part longitudinal (Mann); in the cystic, circular; in the common duct, three irregular coats. The common duct courses obliquely in the wall of the duodenum for 2 cm. Here its outer coat forms a retractor for the papilla and its inner circular coat forms the sphincter of Oddi. The lumen is am-

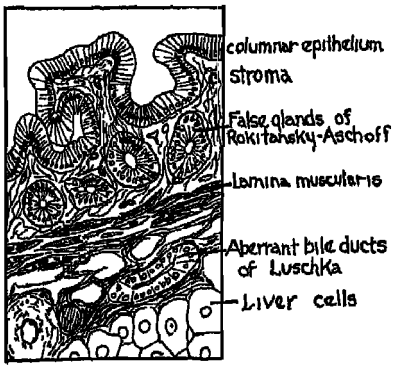

FIG. 54 Section through the wall of the gall bladder, showing the false glands of Rokitansky-Aschoff and the "true glands" of Luschka

pullated and receives the terminal end of the main pancreatic duct. Embryonic bile ducts (sacculi of Beale) have been described particularly in the mucosa of the hepatic duct.

The gall bladder is a blind, pyriform sac or lateral outgrowth of the main system. Its capacity is 20 to 30 cc., while the daily output of bile from the liver is 800 cc. The function of the gall bladder is the storage and concentration of bile. Its inspissating capacity is about 10. When fully distended the wall is 0.75 mm. thick; when contracted, about 2 mm. When contracted the mucosa is thrown into a series of folds or rugae and in section may show "protruberant villi." Three coats are generally described; mucosa, muscularis and fibrosa. The

latter is fibro-elastic. Over the greater portion it is covered by peritoneum, but on the hepatic surface it is continuous with the capsule of Glisson (Fig. 54).

The musculature is irregular, showing "penciling" on section. On distention the fibers form a loose meshwork of extreme thinness. The so-called "false glands of Rokitansky Aschoff" are outpouchings or "herniations" of the mucosa through these meshes. In contradistinction to these are found the "true ducts" of Luschka located within the wall of the gall bladder but communicating with the cystic duct. Halpert considers the latter to be aberrant bile ducts. They are present at birth.

The mechanism of emptying of the gall bladder is still problematic. Boyden has shown, by radiography, a partial emptying two and one-half hours after a meal of egg yolk and cream, although some authorities maintain that collapse is due to resorption.

No specific characteristics mark the epithelium. The cells are tall columnar non-cuticulate and mucoid. The general staining reaction is weakly eosinophilic. Fat, stainable by Sudam III, has been found within the cells. The main interest lies in the relation of these cells to the formation of gall stones, of cholesterol or calcium. Atrophy is common when biliary block is due to a stone in the common duct (Courvoisier's Law).

Chapter XXI

PANCREAS. SPLEEN

The pancreas is a compound alveolar gland. It presents a head, neck, and tail, extending from the concavity of the duodenum, by a retroperitoneal position to the vicinity of the spleen. It possesses two ducts—the principle duct of Wirsung (1643) which enters the duodenum in common with the bile duct; and the accessory duct of Santorini (1777) which opens near by. Anastomoses between the two ducts generally occurs at the neck. Embryologically, the two ducts mark the primordial sites from which the pancreas arose.

The gland possesses no distinct capsule; the interstitial connective tissue is loose and the lobules, primary, secondary and tertiary, are not compact. The color of the gland is reddish cream. Only the anterior surface is partly covered by peritoneum. The connective tissues may include numerous sympathetic ganglion cells and a few lamellar corpuscles, in addition to blood vessels and lymphatics. Fat cells may be present, even within the lobules (Fig. 55).

The parenchyma of the gland contains two elements—the zymogenic alveoli and the Islands of Langerhans. The exocrine system is not markedly different from the salivary gland. The pear-shaped terminal acini (Fig. 55) communicate with a system of interlobular ducts by the so-called intercalated ducts. No distinct intralobular ducts exist. The intercalated ducts are lined by low pavement epithelium. Single cells, allied to the duct system may partially block the acinus. These are the centro-acinar cells. The acinus is made up of a number of pyramidal cells, with apices toward the lumen and bases resting on a basement membrane. The nuclei are clear, vesicular and

centrally placed. The apical side of the cell is the secretory pole. It is filled with small eosinophilic zymogen granules, first identified by Bernard (1856). These decrease markedly during digestion and are stored again during rest. Since the digestive activity of the pancreatic juice is tripolytic, these granules give rise to lipase (fat splitter) trypsinogen (peptone splitter) and amylopsin (carbohydrate splitter). Approximately 750 cc. juice may be secreted per day. Secretion begins $1\frac{1}{2}$ minutes after food taking and may continue for 3 hours.

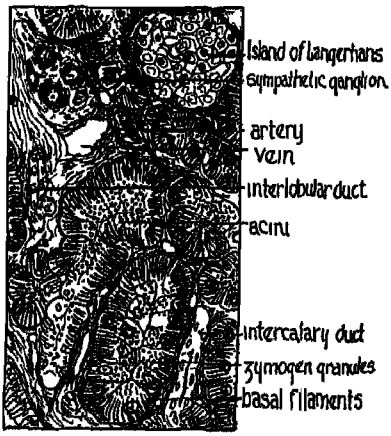

FIG. 55. Section through the margin of a lobule of the pancreas. Note the basal filaments and the zymogen granules in the secretory cells of the acini. An Island of Langerhans is shown, while a sympathetic ganglion occurs in the interlobular connective tissue.

Control is effected by acid chyme in the duodenum, by secretin and by the vagus.

The Islands of Langerhans were discovered in 1869. They represent small spheroidal patches of corded cells which are very pale staining with routine technique (Fig. 55). The patches are approximately 3 mm. in diameter. They vary in number— counts ranging in man from 206,000 to 1,760,000. They are generally within the lobule, but may be associated with the interlobular ducts or be isolate in the interstitial con-

nective tissue. Four types of cells have been identified in the Island, termed respectively A, B, C, D. A and B are the more prominent. Granules of A are insoluble in alcohol; those of B are soluble. Mallory's azan stains the types differentially (Bloom). The significance of the several types is not known, but the island as a whole produces an endocrine "insulin" that controls the sugar metabolism of the body.

Hypofunction of the islands causes a disease, diabetes mellitus, an emaciating condition resulting from the non-utilization of the blood sugar. Glycosuria, or sugar in the urine, is the chief laboratory finding.

The disease was known to the Romans. Minkowski produced it experimentally by the removal of the pancreas in dogs (1890). Extracts of whole pancreas did not protect against the disease because the enzymes destroyed the hormone. Ligation of the pancreatic ducts produce degeneration of the acini, but not of the islands. In 1921 Banting and Best successfully extracted "insulin" from such atrophied glands and made possible a "substitution therapy" for diabetes so that carbohydrate and fat may be completely metabolized in the body without glycosuria and ketosis.

The pancreas has some capacity to regenerate if the injury to the organ has not been too severe.

THE SPLEEN

The spleen is still the organ of mystery of Galen (Mysterii Plenum Organon). It is an elongated ovoid body, presenting a diaphragmatic, a gastric and a renal surface. It lies in the left hypochondriac region with its long axis parallel to the tenth rib. Its peritoneal reflection binds it only at the hilus and hence it is freely movable. The supporting ligaments are the gastrolienal, the phrenolienal and the phrenocolic.

It is the largest lymphoid organ in the body, measuring 4 x 7 x 12 cm., and weighs 200 grams. It differs from the lymph nodes in that it has no afferent vessels and no lymph sinuses.

From a developmental standpoint it belongs to the stomach. In man it arises as a thickening of the dorsal mesogastrium, but in the lung-fish, it lies within the stomach wall.

It is composed of soft, reddish brown cellular tissue, the pulp, enclosed and supported by a fibro-muscular capsule and internal trabeculae which divide it into poorly defined lobules. It has no duct. The splenic artery, main branch of the coeliac, divides into four or five branches before entering the hilum, while several large veins emerge to form the splenic vein, an "upstream" tributary to the portal which brings it into close relation with the liver.

The capsule and trabecular network are strongly muscular, providing a mechanism for rhythmic contraction of two types: (1) slow expansion and contraction associated with an obscure digestive function, and (2) rapid volume changes of one minute duration, correlated with blood pressure changes. In cats, it has been estimated that the spleen may "bank" or store one-sixth of the total blood volume of the body, to be "squeezed out" into the general circulation "on demand." Innervation is by the right vagus and the greater splanchnics.

The cellular pulp is of two types: white pulp, composed of a reticular network invaded by lymphocytes, and red pulp, colored by numerous erythrocytes in and around the venous sinuses. The most conspicuous part of the white pulp (and at the same time the identification mark of the spleen) is the Malpighian corpuscle, a typical lymph nodule, 0.2 to 0.7 mm. in diameter, penetrated by a "central artery." The two types of pulp are not sharply separated, but are confined to a degree to certain parts of the vascular bed (Fig. 56).

The interlobular branches of the splenic artery pass into the spleen in the trabeculae. After a short course, branches leave the septa and invade the pulp to become the eccentric "central arteries" of the splenic corpuscles. Fine arterial loops are given off to the germinal centers, while the main branches continue as the pulp arteries. These break up into ten or more

small straight arterioles, or penicilli (L. painter's brush) of Ruysch. For a portion of their course, the walls are thickened, fibrous and invaded by lymphocytes; hence the name "sheathed

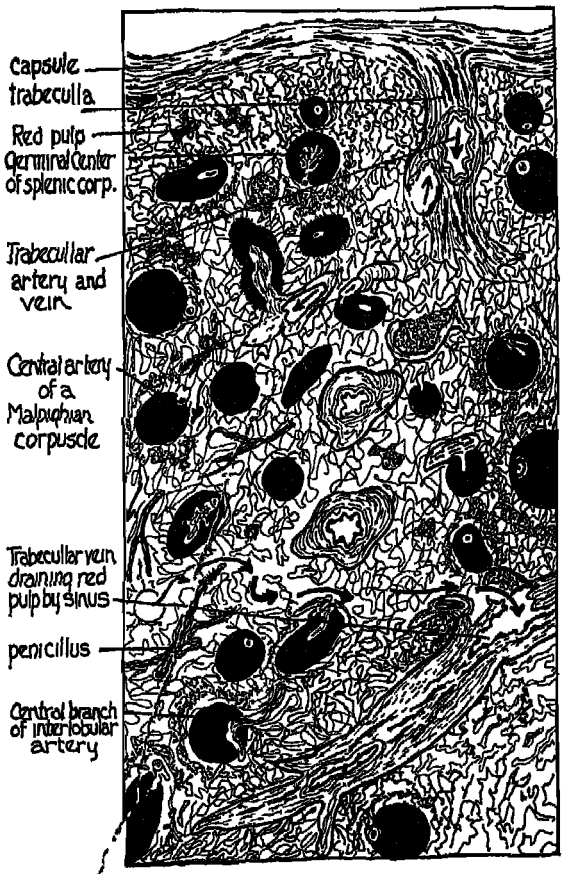

FIG. 56. Section through the human spleen to show the general topography. The general course of the circulation is indicated by a series of arrows.

arteries." Their lumens may be occluded. They may act as "check valves," against back flow when the spleen contracts (Fig. 56).

The exact nature of the channels that communicate between

the sheathed arterioles and the veins is subject to dispute. One opinion holds that the arterioles drain into venous sinuses, wide dilated spaces, lined by an atypical endothelium, composed of spindle-shaped contractile cells, arranged in circular and longitudinal fashion, but fenestrated so that the blood has ready access to the subepithelial pulp spaces. Maximow considers these cells to be fixed macrophages. Arterial ampullae of Thoma have also been described, which permit direct passage of blood into the "red pulp spaces." Reverse perfusion experiments of Nisimara and Steggerda, indicate that the "open system" may become "closed" under certain conditions.

The venous sinuses are drained by pulp veins or directly by atypical trabecular veins. The later anastomose to form the splenic veins at the hilum.

The splenic pulp (mud, Cajal) is supported throughout by a fine reticular meshwork. In the interstices are found free red blood cells and all of the varieties of white corpuscles. Free macrophages are common and show active phagocytosis of erythrocytes. Hematoidin and hemosiderin granules indicate an active hemolysis markedly increased with splenomegally (enlarged spleen) in malaria, lead poisoning and other hemolytic diseases. The sluggish current in the "back-water" of the splenic pulp, is conducive to a selective destruction of "worn out" red corpuscles. It is of interest to note that the spleen is erythropoietic from the second month until birth, when it becomes hemolytic. There is some evidence that the spleen produces a hormone that inhibits erythropoiesis to counteract the stimulating hormone of the liver.

Phagocytosis of débris and bacteria is also carried out by the reticulo-endothelial system of the spleen. It likewise must have some function in the production of immune bodies. Its entire work may be taken over by other organs, however, since splenectomy is commonly performed without harmful effects.

Chapter XXII

THE RESPIRATORY TRACT: I. NASAL PASSAGES. LARYNX. TRACHEA

The respiratory tract includes the nasal passages, pharynx, larynx, trachea, bronchi and lungs. The pleural spaces, chest wall and diaphragm, and the pulmonary vascular bed complete the system. The thoracic and diaphragmatic musculature constitute the motor mechanism. The remainder of the system is practically passive. The automatic nervous control is effected through the "respiratory center" in the medulla and the cord, and partially by the blood pressure in the carotid sinus.

NASAL PASSAGES

Four histological zones are recognized in the nasal passages: (1) true hair-bearing skin lining the vestibule; (2) the olfactory membrane extending over the superior concha and the corresponding area of the septum; (3) the Schneiderian membrane or respiratory mucosa lining the greater part of the passages; (4) a thin modified mucosa lining the paranasal sinuses (frontal, maxillary, sphenoidal and ethmoidal cells). The Schneiderian membrane is continuous with the mucosa of the Eustachian tube and the naso-lacrymal duct.

The respiratory mucosa was first described by Schneider in 1660. It consists of a covering epithelium and a tunica propria (Fig. 57). The epithelium from the vestibule to the turbinates is stratified squamous; from the turbinates to the Eustachian tube it is stratiform columnar ciliated, passing by a narrow transitional "mixed" ring into the stratified squamous of the nasopharynx. The stratiform epithelium is 50 to 70μ

thick, composed of a superficial layer of tall columnar cells that bear cilia, 5 to 10μ tall. The basal cells vary in height and are interspersed between the tapering basal ends of the colum-

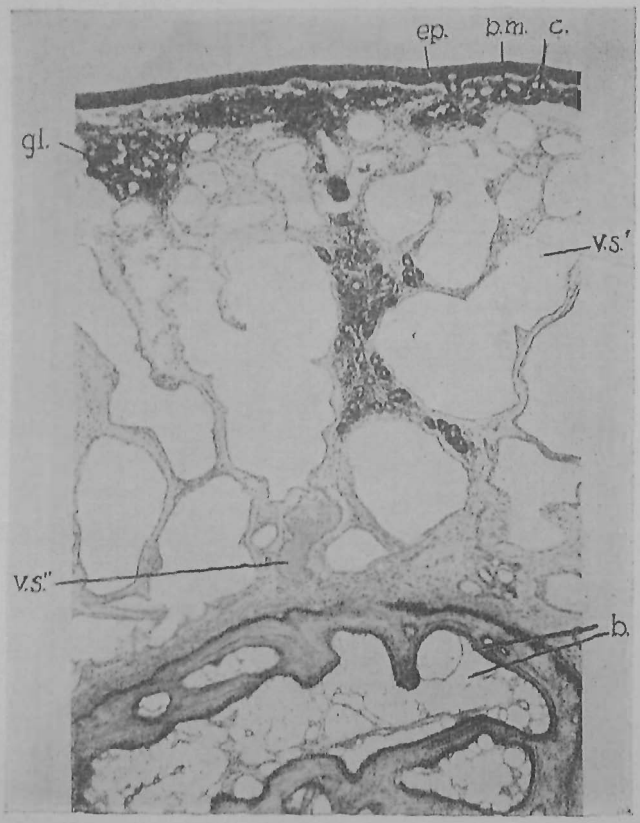

FIG. 57. Section through the mucous membrane of the middle concha showing the distended venous plexus. *B*, bone with medullary cavity; *bm*, basement membrane (clear); *c*, distended capillaries; *ep*, epithelium; *gl*, mixed glands; *vs'*, venous sinuses empty, and *vs''*, distended. (From Peterson.)

nar cells which reach the basement membrane. The basal cells are thought to be replacement cells, but Schafer claims that they do not take part in regeneration of the excoriated epithelium. Goblet (chalice) cells are common. The ciliary beat carries the secreted mucous sheet toward the pharynx for disposal.

The non-papillated tunica propria shows a deep compact and a superficial fibro-cellular layer. The latter is invaded by numerous wandering cells. A rich blood supply of intercommunicating sinusoids, with smooth muscle distributed in the trabeculae, gives the tissue a superficial resemblance to erectile tissue. Passive congestion and swelling is common. Polyps, resulting in nasal obstruction, are indicative of sinus infection.

Glands are numerous and mostly of the tubo-alveolar type. Secretion is estimated at 1000 cc. per day.

The olfactory mucosa, first described by Todd and Bowman (1857) is a yellow brown, waxy mucoid coat. Its epithelium differs from that of the Schneiderian membrane in that three types of cells occur: (1) bipolar nerve cells; (2) tall sustentacular cells; (3) basal cells. The bipolar nerve cells retain a very primitive position, unique among receptors. Their short bristle like "dendritic" processes are exposed on the free surface of the epithelium. Their axones pass by way of the olfactory nerve, through the cribriform plate, to synapse as glomeruli about the telodendria of the mitral cells of the olfactory bulb.

THE LARYNX

The larynx (G.) or organ of voice production, can be readily felt as the Adam's apple. It is that part of the respiratory tract between the pharynx and the trachea. It is tubular in form, 44 mm. long, 43 in transverse diameter and 36 mm. in the antero-posterior diameter. Its wall is made up of a series of cartilages, elastic membranes, intrinsic and extrinsic muscle. It is lined throughout by a mucous membrane. Two special lateral folds enclose the thyro-arytenoid ligaments as the vocal cords (Fig. 58).

The first division or vestibule is bounded in front by the flexible epiglottis and laterally by the aryteno-epiglottic folds. The posterior limit is marked by the "false" vocal cords. A shallow depression, the ventricle, lies between the false and the true vocal cords on either side (Fig. 58).

In addition to the elastic cartilage of the epiglottis, the

cartilages of the larynx are the hyaline thyroid, cricoid and arytenoid. The corniculates are minor elastic processes of the arytenoids and the cuneiforms are variable or absent. The thyroid is composed of two lateral plates fused in the midventral line. Anterior and posterior cornuae or horns extend from their lateral angles. The cricoid encircles the lumen of the tracheal junction in a "signet ring" fashion, with the "set" turned toward the back. The paired triangular arytenoids articulate with the upper border of the "set," and their processes extend across the lumen in support of the vocal ligaments.

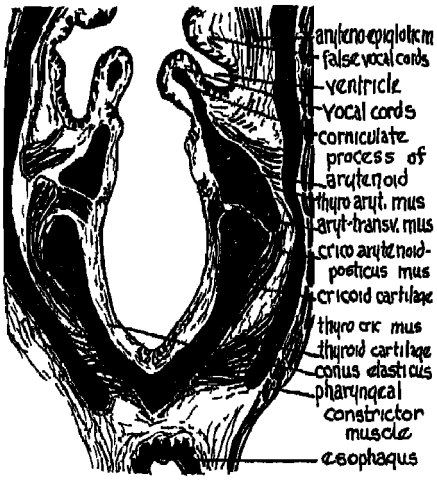

FIG. 58. Frontal section through the larynx of a guinea pig. Note the true and false vocal cords; the arytenoid, cricoid and thyroid cartilages and the various voluntary muscles which regulate the voice.

The anterior ends of these ligaments are fixed in the thyroid in close approximation. The posterior ends, widely separated in normal inspiration, may be brought together in close apposition by contraction of the transverse arytenoid muscle moving the arytenoid cartilages to the midline (Fig. 58). The aperature (rima glottis) is thus reduced to a mere slit and the expiratory air currents vibrate the sharp free edge of the cords to produce voice.

This action is opposed by the posterior crico-arytenoid

muscle. Variation in tension in the cords is brought about by "up and down" movements of the thyroid on the cricoid through the action of the crico-thyroid muscle; the thyro-arytenoid (vocal) muscle and by the lateral crico-arytenoids.

The epithelium of the larynx shows a number of transitions. It is stratified squamous on the epiglottis; stratiform on the

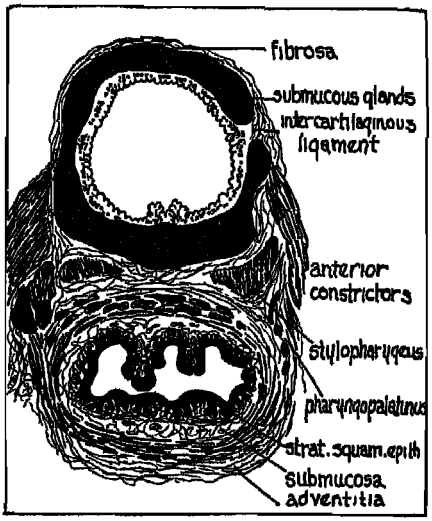

FIG. 59. Transection through the esophagus and trachea of a new-born human fetus. The cut passes through the extreme lower end of the cricoid cartilage and hence does not show the trachealis muscle.

false vocal cords and ventrical; stratified squamous on the true vocal cords, and stratiform again toward the trachea. Tubulo-acinar glands of the mucous variety are common except on the vocal cords. A special elastic membrane lends support to the mucosa.

The innervation of the larynx is by the superior laryngeal branch of the vagus (sensory) and the inferior laryngeal (motor). Injury with loss of voice is not uncommon in surgery of the neck. Diphtheria, angioneurotic edema and hysteria are important conditions that effect the larynx. New growths are not common.

THE TRACHEA

The trachea is a tube, 2 to 2.5 cm. in diameter and 11 cm. long. It is composed of three coats; a mucosa, submucosa and a fibrosa. The most conspicuous feature is the presence of 16 to 20 cartilaginous C-shaped rings that lend support to the softer portions. These are from 2 to 5 mm. in length and are bound together end-to-end by a fibro-elastic sheath, the annular ligament, continuous with the perichondrium of each segment. This membrane also completes the esophageal side of the tube. Bundles of smooth muscle pass through this sheath between the ends of the cartilages and some fibers pass down the length of the tube (Fig. 59). This trachealis muscle functions to decrease the diameter and length of the tube. Radiographic studies indicate that the trachea may shorten ½ inch, and in cats the volume may vary from 1634 cu. mm. on inspiration to 933 cu. mm. on expiration.

The epithelium of the trachea is of the stratiform ciliated variety, interspersed with some goblet cells. The tunica propria is fibro-elastic and contains numerous lymphoidal cells, occasionally condensed into a nodule. The tunica is non-papillated. According to some descriptions, the submucosa is indistinct except in the lower part of the trachea, where a definite elastic membrane exists. The submucosa lodges the larger blood vessels, lymphatics and the tracheobronchial mixed mucous tubo-alveolar glands. Their secretions form a "dust-catching" mucous sheet which is moved toward the larynx by cilia at a measured rate of 3.5 cm. per minute (Florey, Carleton and Wells, 1932) (Fig. 59).

The trachea bifurcates into a right and left bronchus. The right bronchus has a length of 25 to 34 mm.; the left, 41 to 47 mm. The transverse diameter of the right is 18 mm.; the left 16 mm. Their combined cross sectional area exceeds that of the trachea.

The structure of the bronchi duplicates that of the trachea. The right bronchus has 6 to 8 cartilages; the left, 9 to 12. Nerves are from the vagus, inferior laryngeal and sympathetics.

Chapter XXIII

THE RESPIRATORY TRACT: II. THE LUNGS

The lungs, two in number, are pyramidal or conical in shape, with the bases resting on the diaphram and the apices in the root of the neck. Each lung presents three surfaces—diaphragmatic, costal and mediastinal. The left lung shows a deep impress or cardiac notch. The hilus and root of the lung is on the mediastinal surface, 8 cm. high and 2 cm. wide. The entering structures, or root, include the stem bronchus, pulmonary artery, pulmonary vein, bronchial vessels, lymphatics and nerves, bound together by connective tissue and covered by a pleural reflection. The latter is continuous over the surface of the lung as the visceral pleura and over the thoracic, diaphragmatic and mediastinal walls as the parietal pleura. A potential or capillary space intervenes between these two layers, permitting free movements during inspiration and expiration.

The color of the lung varies according to its blood content, being reddish in the fetus, pink in the infant, and gray in the adult. The latter color is due to storage of inspired dust particles. In consistency the lung is soft and spongy. It cuts readily with the knife. It emits a crackling sound when compressed. The right lung weighs 625 grams; the left, 570. Their total volume when fully expanded approximates 5000 cc., or ten times the "tidal volume" of normal respiration. Forced expiration drives a "supplemental volume" of 1500 cc. from the lung, while forced inspiration draws in a "complemental volume" of 1500 cc. A "residual volume" of 1500 cc. cannot be expelled by the mechanics of breathing, but partial or complete collapse may be effected by introducing from 250

to 850 cc. of air into the pleural space—a procedure commonly practiced in putting the lung "at rest," to permit healing in tuberculosis.

The histology of the stem bronchi is similar to that of the trachea. They divide and redivide within the substance of the lung with slight structural change until the branches approximate a diameter of 0.2 to 0.5 mm. These are the terminal or respiratory bronchioles. They open into the so-called

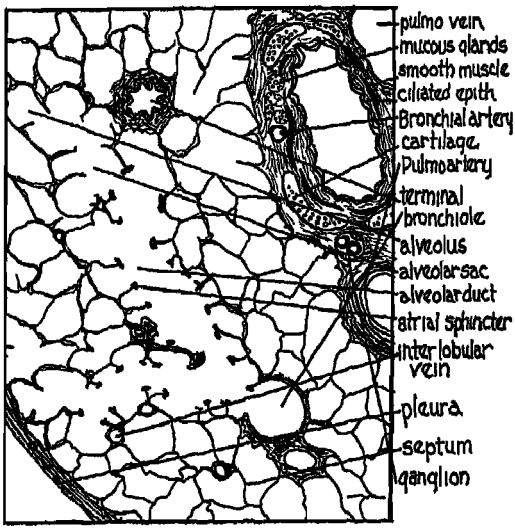

FIG. 60. Section through the lung showing one of the smaller bronchi, two bronchioles and the respiratory passages terminating in the alveoli.

alveolar ducts whose walls are beset by and continuous with (1) the atria, (2) the air sacs and (3) the alveoli. It is within the thin walls of these last divisions that the gaseous exchange between air and blood stream is carried out (Fig. 60).

The changes which occur in the bronchial tree from stem bronchus to bronchiole (Fig. 60) are: (1) the cartilage rings are replaced by a series of cartilage plates; (2) ciliated epithelium is reduced from stratiform to simple; (3) an incomplete circular muscle coat invades the tunica propria (4) the mucosa is

longitudinally folded. The terminal bronchioles are characterized further by the disappearance of cartilage, mucous glands and lymph nodes, but the cilia persist in order to assure outward passage of the mucous sheet and serous transudate. At the extreme ends, the cuboidal epithelium changes abruptly into the simple squamous of the alveolar ducts.

The macroscopic "lobules" of the lung are visible to the naked eye as small areas on the pleural surface, 1 to 1.5 cm. wide. They are outlined by the connective tissue septa. The superficial ones are pyramidal in shape; the deeper are polyhedral. These are, in reality, secondary lobules. The functional unit or "primary lobule" is microscopic in size. It consists of a terminal respiratory bronchiole and its associated structures, including 2 to 11 alveolar ducts, each bearing 3 to 6 atria, set with 2 to 5 air sacs and 5 to 20 alveoli.

There is still some confusion among histologists in the use of names for these subdivisions: thus, terminal bronchiole, respiratory bronchiole and alveolar duct have been used synonymously. The atria of Miller have been questioned. BNA (Basel nomina anatomica; international system of nomenclature) recognizes Bronchioli respiratorii, ductuli alveolares and alveoli pulmonum. To clarify the legends for beginning students, the terminal (respiratory) bronchioles may be defined as having no cartilages but a firm fibrous support and a non-ciliated columnar or cuboidal epithelium; the alveolar ducts have irregular septate walls with thin respiratory epithelium through part of their course.

The alveoli are saccular structures. In section, they appear in three positions—subpleural, peribronchial and periductal, but all open widely into ducts. They are approximately 0.1 mm. in diameter when collapsed and 0.3 mm. when dilated. It is thought that they change little in form during inspiration and expiration in order not to occlude the capillaries within their walls. The wall is extremely thin. It is composed primarily of a close meshwork of capillaries supported by a very fine

membrane of reticular and elastic fibers. The latter are supposed to form the "recoil" tissue by which deflation is produced. No muscle fibers are present beyond the ducts. Spasm of these is supposed to produce the difficulty in expiration in true asthma (Fig. 60).

Whether or not a respiratory epithelium exists as the lining membrane of the alveolus is still subject to dispute. Kolliker (1880) described such a membrane composed of large, flat, enucleated plates, interspersed with a few small typical "fetal" cells, considered to be replacement cells. Many authorities deny the existence of such a membrane, since it is not easily identified in section. The following observations favor its presence: (1) complete cuboidal epithelium line the alveoli throughout in the fetus; (2) fatty vacuolization and tension convert these cells into squamous plates during the last two months of uterine life (Stewart); (3) the membrane is sometimes lifted off intact by serous exudate in pneumonia (Miller).

According to Miller, this membrane is also the source of the "dust cells" "heart-failure cells," frequently seen within the alveoli and bronchioles in disease. He believes they slough off and round up. These "septal cells" will phagocytize carmine blown into the trachea (Sewall). Fried believes that they are members of the reticulo-endothelial system and mesenchymatous in origin.

The blood supply to the lung is two-fold. Venous blood passes by the pulmonary arteries to the capillaries of the alveoli for aeration. The vessels lie within the fibrous coats of the bronchi and bronchioles. The capillaries drain by the pulmonary veins which, in the respiratory region, lie in the septa between the lobules (Fig. 60). They soon return to a position in the bronchial wall, on the side opposite the artery. The bronchial arteries arise from the thoracic aorta or right intercostals and course in the submucous coat of the bronchus (i.e., within the cartilages). They do not extend into the respira-

tory bronchioles. They drain by way of the pulmonary veins, except at the hilus of the lung where true bronchial veins are tributary to the azygous system. It is generally stated that the bronchial arteries do not supply the respiratory epithelium, but this point may be disputed on the basis of the anomalous condition of cor-biloculare (two chambered heart) where the pulmonary circuit is negligible and aeration is accomplished in the bronchial circuit.

The pressure in the pulmonary circuit is 40/20 mm. Hg, low as compared to the systemic blood pressure of 120/80.

The lymphatics of the lungs and pleura are important since they may be the routes of tuberculous invasion and spread. There is a superficial set in the pleura and a deep set in the lung. On the whole they follow the vascular bed, but there are no vessels distal to the alveolar ducts. Both systems drain by way of the bronchial lymph nodes. Miller maintains that there are no nodules in the normal lung.

The nerves are medullated and non-medullated, with small sympathetic ganglia in the fibrous layers of the bronchi. Sensory endings have been described from the epithelia of the bronchi of various orders and from the atria (Larsell). Sensory endings on the muscles have also been found. Motor fibers pass to muscle and glands. Broncho-constrictor fibers are from the vagus; broncho-dilator fibers from the sympathetics. Vasomotor fibers are both sympathetic and parasympathetic.

THE PLEURAE

The pleura consists of a mesothelium resting on a fibro-elastic coat which enmeshes some smooth muscle. A subserous coat is normally scanty. Blood vessels are from the pulmonary trunks. The visceral pleurae are poorly innervated and generally considered insensible. Pain fibers terminate in the parietal pleurae.

Fibrous exudate into the pleural space may lead to "friction

rub" in pleurisy which is very painful. Adhesions between the two layers occur frequently in inflammation of the pleura (Fig. 60).

Both lungs are not essential to life. Only about one-twentieth of the pulmonary aerating surface is normally used. (It is estimated that the total area is 70 square meters.) Hence phrenectomy, collapse and resection are commonly practiced.

In passing it is of interest to note that artificial respiration was first introduced by Hooke in the seventeenth century.

Chapter XXIV

THE KIDNEYS

The urogenital system includes the urinary organs and the reproductive organs. Embryologically they are very closely related, while in the adult a portion of the duct system is common to both. The urinary system comprises the two kidneys, their ducts, the ureters, a urinary bladder and the terminal duct or urethra.

The kidneys are paired, bean-shaped, compound, tubular glands. They measure 3 x 5.5 x 10 cm., and have a weight of 115 grams each. They are situated in the posterior part of the abdominal cavity, laterad to the vertebral column in the lumbar zone. They are retroperitoneal. The right kidney is slightly lower than the left.

The medial border of the kidney is concave, presenting a slit-like aperture or hilus which opens into a cavity, the sinus, 2.5 cm. deep. This is occupied by the dilated end of the ureter or pelvis, and the blood vessels, nerves, lymphatics embedded in a loose areolar tissue which is frequently invaded by fat. The outer surface of the kidney is covered by a thick, fibrous capsule, which "strips" off readily except at the hilum. A layer of perirenal fat supervenes between the capsule and the subperitoneal renal fascia. Peritoneum covers the anterior surface. The fascia lend support to the organs.

Sections of kidney show two zones, a pale inner medulla and a reddish outer cortex. The medulla presents 8 to 18 conical segments or Malpighian pyramids, the apices of which project into the sinus and subdivide the pelvis into renal calyces. Their bases are turned toward the cortex. Small areas of cortical substance extend between the pyramids to reach the

sinus. These are the columns of Bertini. They represent the "back to back" fusions of the primitive fetal lobes (Fig. 61).

The pyramids are smooth, pale and glistening. They show a series of delicate longitudinal striations, straight and parallel, increasing in size as they converge at the apex. These markings are due to the presence of the fine collecting tubules tributary to the larger excretory ducts of Bellini which open on the

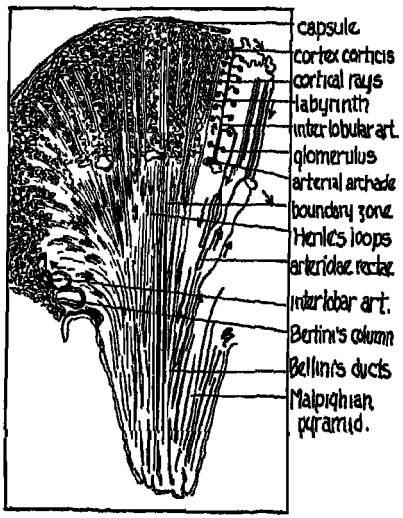

FIG. 61. Semidiagrammatic sketch of a renal pyramid and its associated cortex. (Human.) To the right of the figure, the circulation is indicated by a series of arrows.

papilla in the area cribrosa, as 20 to 80 pores. Through these the urine reaches the pelvis.

The cortex also shows a series of striae, radial subdivisions into light and dark tracts. The former constitute the processes or pyramids of Ferrein and represent the finer radicals of the straight tubules, continuous with those in the medulla. The dark portions present a granular appearance due to the irregular course of the tubules in this, the labyrinth or pars convoluta. Minute little spheroids 0.2 mm. in diameter, are visible under

the hand lens. These are the Malpighian or renal corpuscles. The anatomic lobule of the kidney is generally taken as a pyramid of Ferrein with its surrounding and associated tubules in the pars convoluta. The borders are not discrete nor set off by septa (Fig. 61).

Each kidney is made up of some 100,000 renal tubules or nephrons. The nephron presents the following subdivisions in sequence of urine flow: (1) Bowman's capsule, (2) neck, (3) proximal convoluted tubule, (4) descending arm of Henle's loop, (5) ascending arm, (6) distal convoluted tubule. With this is associated the excretory (7) arched tubule, (8) straight tubule and (9) Bellini's duct. The structure and position of each subdivision has its histological and physiological significance.

The outer blind end of the nephron or Bowman's capsule has a diameter of 200μ (Fig. 62). It is composed of a visceral and a parietal layer enclosing a lumen or ampulla of Müller. The visceral layer of simple squamous epithelium invests a netknot of capillaries forming a glomerulus. This layer is reflected at the peduncle or stock of the glomerulus, as the parietal layer. A neck, composed of slightly larger cells, leads into the proximal convoluted tubule, with a diameter of 40–70μ. The cells are tall columnar and strongly eosinophilic in staining reaction. Granulation within the cytoplasm presents a radial basal striation. The free surface shows a "brush border" in the mammals and is ciliated in the reptiles. Secretory blebs are frequently seen. This division may be 14 mm. in length. A straight portion has been described by Huber, which may extend into the border zone between cortex and medulla.

The proximal convoluted tubule leads into the descending arm of Henle's loop. This division of the nephron is 10 to 20μ in diameter and composed of low pavement epithelium. Since the nuclei are flat and bulging, transections may be mistaken by the novice for capillaries (Fig. 62).

The ascending arm of Henle's loop has a diameter of 20 to

30μ. It parallels the descending arm and has a length of 4.5 to 10mm. It returns to a position in close approximation to the glomerulus of the nephron of which it is a part. The loops of the majority of nephrons lie in the zone at the base of the pyramids which forms the margin of the cortex and medulla. Hence, in transections, the loops of Henle are to be distin-

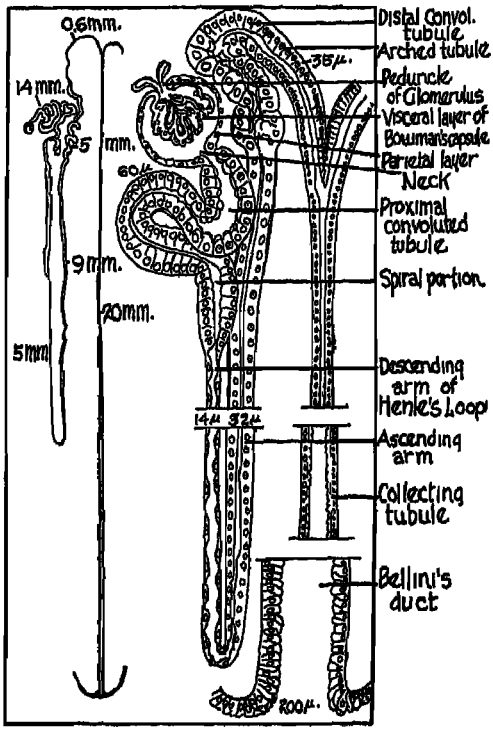

FIG. 62. Semidiagrammatic sketch to show the relative lengths, diameters and cellular construction of the several segments of the uriniferous tubule.

guished from the straight tubules of the medulla. The cytoplasm of the cells of Henle's loop is pale staining and the nuclei are conspicuous, while the diameter of the tubule is about half that of the straight (Fig. 62).

The distal convoluted tubule lies in the pars convoluta. It may be distinguished from the proximal convoluted tubule in

that its cells show no brush border and its diameter is only 40 to 60μ. Its length is 4.5 to 5.2 mm.

It is continuous with the arched tubule, an excretory duct which takes a short course to reach the straight tubule in the pars radiata, or pyramid of Ferrein. The arched and straight tubule and Bellini's ducts have a different embryological origin from the nephron. They constitute the subdivisions of the original ureteric buds, while the secretory nephron is developed from the nephrogenous cap of condensed mesenchyme surrounding the bud. The tubules of the excretory portion are lined by pale staining columnar cells that gradually increase in size. The ducts reach an ultimate diameter of 200μ and may show small areas of transitional epithelium at their continuity with the pelvic lining.

The whole system has such an intimate capillary circulation, that next to the tubes, endothelium is the most conspicuous histological feature. Fibrous connective tissue is inconspicuous except along the vascular bed (Fig. 61). A delicate reticulum, with few fibroblasts, lends support to the parenchyma. It is disposed as basal rings and fibrillar membranes on the tubules. It is more conspicuous in the medulla. The amount increases with "interstitial nephritis."

The vascular supply to the kidney is profuse. The renal artery enters at the hilum and breaks up in the sinus into a series of interlobar branches (Fig. 61) which penetrate the interpapillary substance to reach the cortico-medullary zone without conspicuous branching. Here an interanastomoses is formed again by the arcade arteries. These give off the interlobular branches which course radially in the center of each labyrinth as "end arteries," i.e., without anastomoses except at the capsule. They give off the short stem like afferent arterioles to the glomeruli in racemose fashion. The glomerular arteriole breaks up into ten or twenty discrete capillary loops, which recombine after passing through the corpuscle to form the efferent arteriole. This vessel may take one of two courses.

If associated with one of the more superficial corpuscles, it breaks up into a intralobular plexus within the pars convoluta and pars radiata. If associated with the deeper corpuscle, it passes to the medullary substance as an arteriole recta, to nourish the excretory tubes or break up into a "fasciculate plexus" around the loops of Henle.

In some animals, arteriolae rectae arise directly from the arcades and pass to the medulla, but in man, Huber maintains that this distribution is negligible. The point is of physiological interest, since it is stated that all of the blood that passes through the kidney must go through a glomerulus; and secondly that the same blood comes into capillary relation with the nephron a second time. This provides a mechanism for secretion and filtration at the glomerulus and for selective resorption in other parts of the tubule. It is estimated that 500 liters of blood pass through the glomeruli in a day; 60 liters of fluid are filtered out but only 1.5 liters are excreted as urine. Hence 58.5 liters are resorbed—an effective mechanism in maintaining the "water balance" of the body.

The venous drainage duplicates the path of the arterial supply except for the absence of glomerular veins. Capsular veins enter the substance of the cortex as the stellate veins and become the interlobulars which pass to the arcades. Venulae rectae drain directly into the arcades. The arcades are tributary to the interlobars which in turn form the renal veins of the sinus.

The lymphatics of the kidneys are found in both capsule and substance. The capsular vessels drain to the surrounding lymph chains. Those associated with the tubules pass along the blood vessels to drain by way of the hilus.

The nerves to the kidneys include branches of the vagus to the capsule and sympathetic branches from the coelic which are vasomotor to the glomeruli and tubules. Rich claims complete occlusion in certain glomeruli at times.

General pathology of the kidney results from congestion,

thrombosis, infection, and toxemia, leading to albuminuria, hematuria, casts, glomerular and tubular atrophy. Stones of uric acid, oxylate, cystine or phosphate may be precipitated and block the pelvis or ureters, and lead to hydronephrosis, although both ureters may be clamped for 72 hours without damage (Barney). Chronic nephritis occurs in arteriosclerosis and interstitial nephritis is common in syphilis and tuberculosis. When the renal artery is tied off, atrophy and degeneration of the tubules is complete in ten days unless a collateral circulation is established.

Chapter XXV

THE RENAL DUCTS

The kidney pelvis or dilated end of the ureter has three irregularly organized coats—mucosa, muscularis and fibrosa. The epithelium is transitional and from two to five cell layers deep. The stroma is of the fibro-elastic type and is invaded by lymphocytes. Smooth muscle fibers surround the bases of the papillae on which they exert a milking action. The fibrous coat is continuous with the capsule at the sinus.

The ureters have a length of 25 to 30 cm. and a diameter of 5 mm. The mucosa is thrown into a series of longitudinal folds, giving the lumen a star-shape in transection (Fig. 63). The stroma is nonpapillated. The epithelium is transitional. No glands exist. The muscle coats are an outer circular and an inner longitudinal. In the lower third a second longitudinal coat lies outside the circular. The action is a slow peristalsis.

The fibrosa is a loose, fibro-elastic connective tissue and carries the nerves and bloodvessels, with a few scattered sympathetic ganglia in the lower third. The lymphatics in the muscular coat are of some interest in theories that attempt to account for ascending infections of the ureters.

The intramural part of the ureter courses obliquely in the wall of the bladder. Its fibrous coat continues deeply as the ureteral sheath. The mucosa is produced into valve-like folds that are compressed on distention of the bladder and prevent regurgitation of urine. No distinct sphincter is present, but the longitudinal fibers serve to retract the papilla and facilitate secretion.

The ureteral nerves are from the renal, spermatic, hypogastric and vesicular plexuses. Afferent fibers are associated with

the eleventh and twelfth thoracic and the first lumbar segments. The vagus is involved, but the pain fibers remain undetermined. The point is of interest in the mechanism of renal colic associated with the passage of a stone.

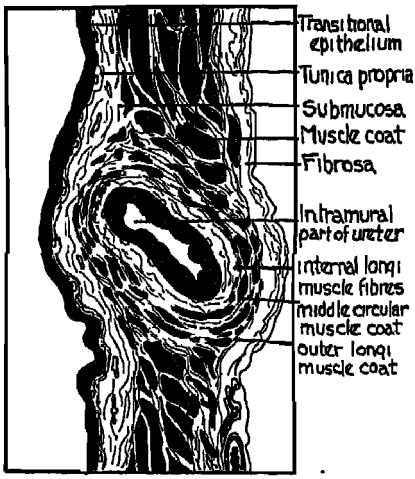

FIG. 63. Section through the intramural portion of the ureter. Its lining epithelium as well as that of the bladder is of the transitional type. (See Fig. 4).

THE BLADDER

The bladder (vesica urinaria) is a musculo-membranous sac which serves as a storage vessel for urine. When moderately filled it contains 500 cc. (Fig. 68). It is ovoid or tetrahedral in shape. It presents a neck, body, fundus and vertex, and an inferior, superior and lateral surfaces. Normally it lies below the symphysis pubis, but when distended may reach the umbilicus. It is connected to the pelvic wall by the fascia endopelvina and is fixed by the middle umbilical ligament, the lateral umbilical folds, and the sacrogenital folds. In the male its posterior surface is in contact with the rectum; in the female, with the cervix and upper portion of the vagina.

When contracted it may have a thickness of 1.5 cm. It consists of four coats (Fig. 63)—mucosa, submucosa, muscularis

and fibrosa. The epithelium is of the transitional type (Fig. 4). Cellular thickness varies with the degree of distention. Embryologically, it is of two origins: the greater part is entodermal; the small area of the trigone (i.e., the triangle between the ureters and urethra) is mesodermal. There is no true basement membrane and as a result the capillaries of the stroma appear to actually lie within the epithelium.

The three muscle coats are irregularly disposed, but are more compact than those of the gall bladder. By continuous overdistention, Carey has converted the smooth musculature into striate in newborn puppies. The outer longitudinal layer is sometimes called the detrusor urinae muscle. The inner layer is thickened at the urethral opening as the internal sphincter.

The fibrosa is of the fibro-elastic variety. In part of its extent it has a peritoneal reflection.

When contracted, the bladder shows a series of internal folds or trabeculae, a significant gross character in the identification of this viscus in operations for hernia.

Glands are absent in the bladder except for (1) the false glands of contraction, (2) blind diverticulae, (3) aberrant prostatic glands at the neck.

The extrinsic nerves to the bladder from the second and third sacral nerves by way of the pelvic nerve (parasympathetic) and from the lumbar and sacral ganglia through the hypogastric nerves (sympathetic) form a vesicular plexus at the neck. Within the wall are found numerous small sympathetic ganglia and nerve fiber bundles, concentrated at the trigone. Stimulation of the pelvic nerves elicits relaxation of the sphincter and contraction of the bladder; stimulation of the hypogastric produces increased tonus of the sphincter. Micturition is a partly voluntary and a partly reflex act.

URETHRA

The female urethra is a short straight tube, 25 to 30 mm. in length, extending from the bladder to the vestibule. The

mucosa is thrown into a series of longitudinal folds, while the lumen is crescentic and practically occluded except during micturition. The epithelium is variable, being either stratified squamous or psuedo-stratified. The stroma is non-papillated. Many complex branched glands of the mucoid type similate the glands of Littré of the male urethra. Their secretions are mucoid. A submucosa of the fibro-elastic variety is invaded by numerous veins which form trabeculate plexuses strikingly like the erectile tissue of the male corpus spongiosum. A rather compact inner longitudinal and outer circular coat of muscle is present forming an internal sphincter at the bladder neck. A voluntary, striate sphincter, derived from the bulbocavernous muscle is present as the constrictor urethrae.

The paraurethral glands of Skene open into the vestibule or urethra. These are the homologues of the prostatic glands in the male.

A definite fibrosa is absent; the adentitial connective tissue is continuous with that of the vagina.

The male urethra is a much longer and more complex structure and will be described in connection with the genitalia (Fig. 70).

The general pathology of the renal ducts includes inflammations of various origin such as tuberculous, gonorrheal; or various blood born infections which have extended from the kidneys downward. Blood in the urine (hematuria) is common with prostatic congestion, stone in the kidney, tumor, acute nephritis or tuberculosis. Pus may occur in the urine in any inflammatory disease. Retention, straining, frequency and painful urination occur in various diseases of the tract. Stone in the bladder is common. It is of interest to note that Cheslenden could perform a lithotomy in 54 seconds in the preanesthetic days of 1700.

Chapter XXVI

THE MALE REPRODUCTIVE TRACT: I. TESTES. EPIDIDYMIS

The male reproductive system includes the paired testes, their ducts, the accessory glands and an intromittent organ, the penis.

The testes are normally lodged in the scrotum, a pouch divided by a septum and derived from the abdominal wall by the fusion of a pair of peritoneal lined outpouchings. The testes are orginally retroperitoneal. During the seventh month they migrate from an abdominal position to their definitive position through the inguinal canals. The peritoneal sacs lose their connection with the abdomen and persist as the parietal tunica vaginalis of the scrotum and the tunica albuginea of the testes. The latter covers the testes on all but the fixed side—the mediastinum or corpus of Highmore (Fig. 64).

The scrotal wall consists of skin, the muscular dartos, the external spermatic fascia, the cremasteric fascia, the infundibuliform fascia and the tunica vaginalis propria. The cremasteric fascia contain the fibers of the voluntary cremasteric muscle. Recent studies show that the scrotum is a mammalian adaptation for the purpose of regulating the internal temperature of the testes. High experimental temperatures tend to produce aspermia—a fact which explains sterility in undescended testes. Descent seems to be under the control of Antuitrin S.

The testis is a compound tubular gland. It is subdivided into a number of lobules by connective tissue septulae continuous with the tunica albuginea and the mediastinum testes. Each lobe is made up of from one to four seminiferous tubules.

They are contorted or convoluted and are peculiar in that they do not end blindly, but are arched and both ends connect with the straight tubules (Fig. 64) in the mediastinum. Their total length is 250 meters, their diameter, 100 to 180μ. Growth waves of spermatogenesis continuously pass along these tubules

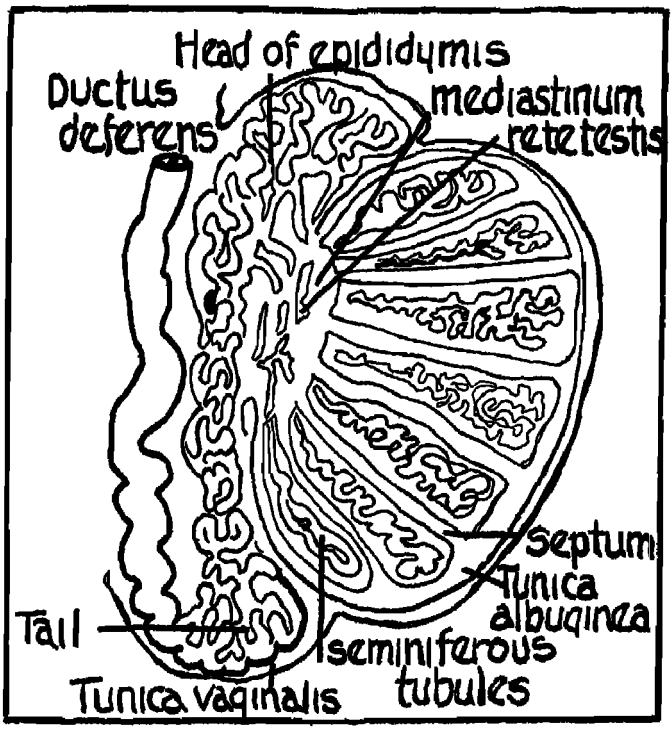

FIG. 64. Diagram to show the duct system of the testis

to produce the vast numbers of sperm—60,000,000 per cubic centimeter of semen.

At a first glance the structure of the tubule appears complicated, but the main steps in spermatogenesis and sperm metamorphosis can be readily made out. The cellular sequence is as follows: spermatogonium, primary spermatocyte, secondary spermatocyte, spermatid, spermatozoan (Fig. 65).

The spermatogonia occupy the basal layer and rest on a basement membrane. These are large cuboidal or polyhedral cells, with conspicuous vesicular nuclei and deeply staining cytoplasm. Mitotic figures are common. The spermatogonia constitute the reserve layer of the testis.

Only one other cell type holds a basal position, namely, the Sertoli sustentacular cell (Fig. 66). These are pyramidal or rod-shaped cells with apices turned toward the lumen. An-

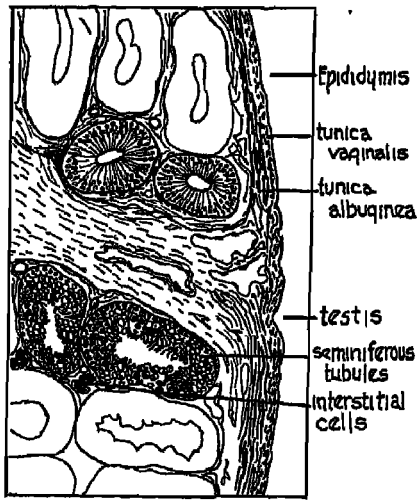

FIG. 65. Section through the junction of the testis and epididymis. The seminiferous tubules are crowded with cells in various stages of spermatogenesis.

chored to them in clusters of ten to twenty are the heads of maturing spermatids. Sertoli cells have a nutritive function only, and while they are considered to be sister cells of the spermatogonia, they never produce sperm. In sterile testes they may increase in number and take on the appearance of a columnar epithelium.

The primary and the secondary spermatocytes lie in clusters on the spermatogonia. The primary spermatocytes are very large, 20 to 24μ, are polyhedral, pale staining and have con-

spicuous chromatic nuclei. The secondary spermatocytes are slightly smaller and generally more peripheral (Fig. 65).

The spermatids may be ordered into a complete developmental series (Fig. 66) representing their metamorphosis into spermatozoa. The older forms have homogeneous nongranular nuclei, flagella, and variable amounts of eosinophilic cytoplasm, while the young forms are typical cells, with small, pale staining "ringed" nuclei, which soon become basal and oval in outline. They are generally superficial but in some areas they may almost reach the basement membrane (Fig. 65).

Spermatogenesis is a special mitotic arrangement for the reduction of chromosomes to the haploid number (single set).

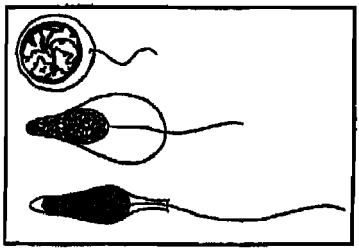

FIG. 66. Three stages in the metamorphosis of the spermatid into a free swimming spermatozoan.

Since similar reduction occurs in the maturation of the egg, the diploid number (double set) is restored when the sperm fertilizes the egg. The haploid number for man is 24; the diploid number, 48. A qualitative difference has been established for one of the pairs of chromosomes. When reduction occurs, two types of spermatids result—one class having 23 + X; the other, 23 + Y. All of the eggs are alike in having 23 + X. Fertilization results in two classes of zygotes: 46 + XX, which develop as females, and 46 + XY, which develop as males (Fig. 67).

The mature sperm, 60μ in length, presents a disk-shaped head, enclosing a uniformly deep staining nucleus; a neck piece, and a tail bearing a partially ensheathed flagellum. Detailed

studies show a galea capitis, which serves as a "perforatorium" by which the initial step of entrance into the egg is effected. The neck bears a distal centrosome controlling flagellate movement; and a proximal centrosome carried into the egg at fertilization where it initiates the formation of the cleavage spindle (Fig. 66).

Clusters of maturing sperm occupy the lumens of the convoluted tubes and also those of the epididymis.

Except for the septa and the basement membranes, the connective tissue of the testis is meager. In the interstices be-

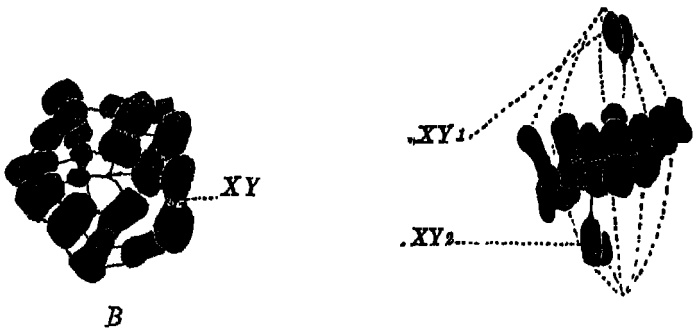

FIG. 67. Two figures representing steps in the maturation of the sperm in man, showing the XY chromosomes. *B*, metaphase in a primary spermatocyte. *C*, later stage showing a precocious division and migration of the XY pair. (After Wieman.)

tween the convoluted tubules are found the capillaries and lymphatics, and a few scattered epithelioid "interstitial cells of Leydig." The latter are of extreme importance, since they constitute the endocrine gland which controls the development of secondary sexual characters (Fig. 65). They are markedly eosinophilic in the fetus.

The nerves to the testes are from the spermatic plexus. Preganglionic and afferent fibers are from the tenth thoracic segment. They are considered vasomotor in function and non-secretory. Gametogenesis is influenced by Antuitrin S, and is normally probably under hormone control.

DUCT AND GLAND SYSTEM

The duct and gland system may be conveniently divided into a genital portion and a urogenital portion, since they have a separate embryology. The epididymis, vas deferens and seminal vesicles are differentiated out of the mesonephros (middle kidney) and its Wolffian duct. The prostate, Cowper's glands and all but the penile portion of the urethra are lined by the endoderm of the primitive cloaca or "hind gut."

The convoluted tubules of the testes continue as the straight tubules of the mediastinum. These are lined by a low cuboidal epithelium. They combine to form a spongy rete testis, and some twenty tubules continue on in a contorted course at the upper pole of the testis as the ductuli efferentes. The epithelium here is variable in height. Secretory blebs are common. The cilia are motile. These join the ductus epididymis (G. *epi*, upon; *didymos*, twin) a coiled tube some twenty feet in length, that serves as a storehouse for ripening sperm. The epididymis is gland-like and caps the testis. It presents a head or globus major, a narrow body and a tail or globus minor. The epithelium is of the tall columnar type, with basal nuclei and non-motile stereo-cilia. The tubules are of the same approximate size as those of the testes, but of a more regular contour and they generally contain clumps of maturing sperm. The connective tissue is more abundant and smooth muscle is in evidence (Figs. 64, 65).

The duct of the epididymis continues as the vas deferens (Figs. 68, 69).

Several accessory vestigial structures are associated with the testes and epididymis. They are the paradidymis, ductus aberrans, and stalked hydatid, all mesonephric remnants, and the hydatid of Morgagni, remnant of the Müllerian duct, homologous to the Fallopian tube in the female.

The vas deferens is a duct of 5 mm. diameter and some 20 inches in length. For part of its course it is one of the constituents of the spermatic cord. It leaves the scrotum to

penetrate the inguinal canal and pass into the abdomen to course behind the bladder and terminate in the prostatic urethra as the narrowed ejaculatory duct. It shows an am-

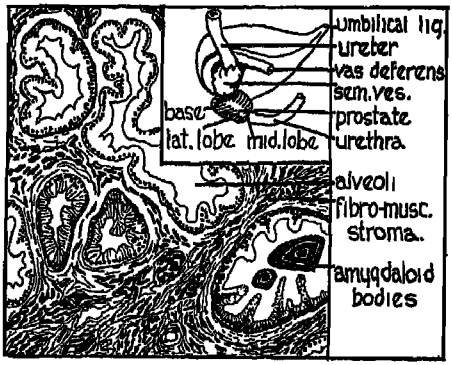

FIG. 68. Sketch to show the relation of the vas deferens to the seminal vesicles, the ureters, the bladder and the prostate. Insert: Section through the alveolar portion of the prostate. Note the characteristic distribution of single smooth muscle fibers. A prostatic concretion is shown in the alveolus at the right.

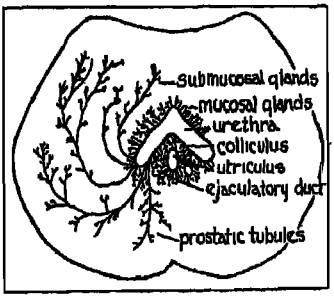

FIG. 69. Transection through the prostate of a new-born human fetus, to show the relation of the urethra to the colliculus and utriculus. Note the spongy character due to the many small blind mucosal glands.

pulla and a lateral seminal vesical. The vasa is lined by a two-layered columnar epithelium. The tunica propria is compact, but thrown into a series of longitudinal folds. The musculature is three-layered and strongly marked and capable

of peristalsis in the sexual orgasm. The fibrosa is very vascular.

The mucosa of the ampulla is thrown into a series of folds, forming crypts. The epithelium is frequently stained a deep yellow. The seminal vesicles, with a length of 10 cm. and a capacity of 2 to 7 cc., have a similar structure. They show secretory blebs and débris within the lumens. They were formerly thought to be storehouses for sperm, but that opinion is now generally discredited. They add a viscid mucoalbumin to the semen. In medicine, chief interest lies in their spongy nature and inaccessibility when subject to ascending infection from foci in the urethra.

Chapter XXVII

THE MALE REPRODUCTIVE TRACT: II. URETHRA AND ITS GLANDS

The male urethra is approximately 20 cm. in length, and a dilated diameter of 5 to 7 mm. It is subdivided into an anterior and a posterior portion, by the triangular ligament or urogenital diaphragm. The anterior portion included a navicular, penile, scrotal and bulboperineal part. The first, outermost, division is lined with stratified squamous epithelium continuous with the skin of the glans; the other three divisions are lined by stratified columnar. The posterior portion includes a short membranous part lined with simple columnar epithelium; a prostatic part with stratified columnar and a trigonal part with transitional (Fig. 68).

An internal smooth sphincter is developed from the musculature of the bladder, while a voluntary sphincter lies embedded between the two layers of the diaphragm formed from the compressor urethrae.

The prostatic and penile portions of the urethra lie at almost right angles to each other, hence the curved shape of the sounds that are passed to relieve urinary obstruction. Infection of the urethra is quite common in medicine. It may extend deeply to produce paraurethral abscess and sinuses, or by healing, form strictures. Except for the penile portion, the urethra and its glands are endodermal lined, being derived from the embryonic cloaca or hind gut. The urethral opening is originally at the base of the penis, a condition which may persist as an anomaly in hypospasia.

Littre's mucous glands are small glands distributed along the entire length of the urethra.

THE PENIS

The penis consists largely of three cylindrical masses of erectile tissue: the paired dorsal corpora cavernosa and the unpaired corpus spongiosum (corpus cavernosum urethrae), bound together by fascia and integument. The corpus spongiosum surrounds the urethra and terminates distally as the blunt conical glans (Fig. 70) and proximally as the bulb. The

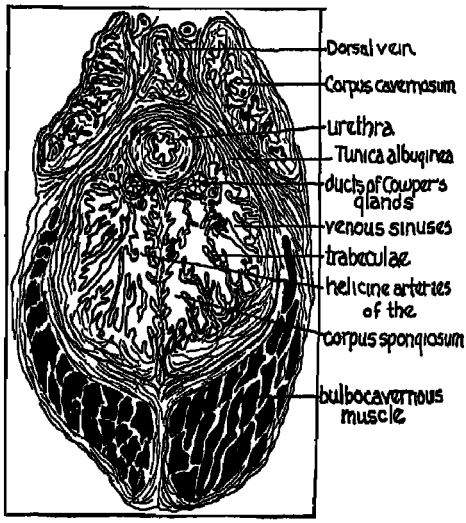

FIG. 70. Section through the penis at the level of the bulb. Note the position of the two corpora cavernosae; the relation of the urethra to the corpus spongiosum and to the bulbo-cavernous muscle. The ducts of Cowper's glands are seen just below the urethra. From a new-born human fetus.

glans is separated from the shaft by a neck or collum glandis and is covered over by the preputial skin.

Some smooth muscle fibers of the dartos layer of the scrotum are present in the skin. Below this layer are the penile fascia which form a suspensory ligament at the symphysis pubis.

The corpora cavernosa flare at the base and become attached to the ischial bones as the crura, in association with the ischio-cavernous muscles (Fig. 70). A pectiniform septum separate them throughout their course to terminate at the base of the glans.

Each corpus is made up of a strong elastic fibrous sheath, the tunica albuginea, from which trabeculae extend into the substance and give it a spongy character. The interstices are occupied by endothelial lined venous sinuses or lacunae. These are empty in the flaccid condition but engorged during erection. The draining veins are provided with valves and they also pass through the tunica at oblique angles, blocking outflow with increased pressure. The arterial supply is from the dorsal penile and the pudics. The branches within the erectile tissue have peculiar thick walls with longitudinal ridges. They take a spiral course hence are called Helicine arteries. Their innervation is peculiar, since it must be assumed that their muscular tone increases during the avascular state of the region which they supply—a condition generally reversed for most organs.

The drainage of the corpus spongiosum and the corpora cavernosa differ to some extent. Pressure is not as marked in the former, and the lumen of the urethra remains patent in erection.

The nerves are spinal, sympathetic and parasympathetic. Many free and encapsulated ending are present. The reflex control centers are located in the lumbo-sacral cord.

Sections through the glans, shaft and bulb show marked anatomical differences but no significant histological variation.

THE PROSTATE

The prostate is a musculo-glandular structure, the shape and size of a chestnut (33 x 35 x 13 mm. (Keyes)). It is generally described as having three lobes—a median and two laterals. Because of the frequency with which hypertrophy begins in it, a posterior lobe is sometimes identified. This portion may be readily felt by rectal palpation and its contents expressed in case of pathological retention (Figs. 68, 69).

A transection through the central portion may show the crescentic outline of the urethra; the median elevation or col-

liculus seminalis; its blind grooved utriculus and the intramural ejaculatory ducts. The glands are all of the compound tubular type, but three distinct forms have been described—the mucosal, the submucosal and the long deep regional. The mucosal glands are so numerous as to convert the urethral zone into a spongy network, and these glands of Albarran are the site of the most frequent hypertrophies.

The ducts of the deeper glands open into the urethra by some 20 to 30 separate orifices. The original invaginations were some 40 to 70. They are all of the compound tubular type with alveoli lined by a single layer of epithelium which is generally cuboidal, but may be high columnar or even squamous. Apparent doubling of the epithelial layer is not uncommon. Secretory blebs are frequent. The most characteristic feature of the adult prostate is the prostatic concretion (corpus amylaceus). These are spherical, ovoid or facetted bodies showing concentric layers of deposition. They may represent the retained secretion products of the prostate. They give certain amyloid staining reactions (brown with iodine). They are significant in that they may block the ducts to the glands and produce cystic enlargement.

The stroma of the gland is peculiar in that it contains an abundance of discrete single muscle fibers arranged in small interlacing bundles of variable thickness (Fig. 68). Various estimates place this muscle as constituting from 25 to 50 per cent of the gland. Its significance in the prostate is unknown, but the development and anatomy of the gland indicate that it is the homologue of the very muscular uterus of the female. It is said to contract during the discharge of semen.

The prostatic secretions are alkaline and are supposed to neutralize the acids of the urethral tract.

The spongy nature of the gland makes it the frequent site of extension of infection from the urethra. Foci may remain dormant for thirty years or more. The prostate is fourth in order of malignancy in the male. Any degree of hypertrophy may

lead to mechanical interference with micturition and call for surgical intervention.

THE BULBO-URETHRAL GLANDS OF COWPER

The bulbo-urethral glands of Cowper are a pair of yellow-brown structures the size of peas, lying in a contractile stroma of striate muscle in the urogenital diaphragm at the base of the bulb. Their ducts open into the urethra just superficial to the external sphincter (Fig. 70).

They are compound tubular glands, homologues of the glands of Bartholin of the female. The epithelium is a single layer, generally of the cuboidal mucous type, but may show tall discrete cylindrical cells with basal nuclei. The alveoli end blindly or may intercommunicate. The stroma is of the fibrous type interspersed with a few muscle cells.

The glands undergo considerable changes following castration or during the administration of male sex hormone.

A prostatic plexus, including both sympathetic fibers from the hypogastric and parasympathetic fibers from the sacral region, is distributed to this portion of the urethra and its glands. It also gives rise to a cavernous plexus in the penis.

Chapter XXVIII

THE FEMALE REPRODUCTIVE SYSTEM: I. OVARY

The female reproductive tract includes the paired ovaries, the Fallopian tubes, the uterus, the vagina and the external genitalia.

The ovaries are paired, pinkish, almond-shaped bodies measuring 1 x 2.5 x 5 cm. and weighing 6 grams. They may be studded by small yellow spots, the corpora lutea, and by dark translucent vesicles, the Graafian follicles, 3 to 5 mm. in diameter. The ovaries lie free in the pelvic portion of the abdominal cavity, supported from the broad ligament of the uterus by a short vascular mesentery, the mesovarium, and by two ligaments, the ovarian ligament and the suspensory ligament (Fig. 71). The mesothelium of the mesentery is replaced at the line of attachment by a simple columnar "germinal epithelium," overlaying a tough, fibrous tunica albuginea which forms a sort of a capsule for the ovary.

The ovary shows two more or less distinct histological zones —the cortex and the medulla. The cortex is occupied by follicles of varying size, corpora lutea, and a reticular stroma; the medulla by loose fibrous connective tissue, a bit of smooth muscle, blood vessels, lymphatics, nerves.

The follicles may be classified as primary, secondary and maturing (Fig. 72). The primary follicles generally lie immediately under the tunica albuginea. They consist of a large single egg cell surrounded by a capsule of flattened epithelial follicle cells. The latter give rise to the stratum granulosum of the mature follicle. Originally both germ cell and follicle cell stood side by side in the germinal epithelium on the surface. By ingrowth into the stroma they became Pflüger's egg tubes,

and by rearrangement lost their contact with the surface and became primary follicles. This process continues through the fifth month of human development and gives rise to some 400,000 primary follicles. In some mammals it may occur throughout the reproductive period.

Before birth some of the primary follicles may pass into the second stage characterized by (1) increase in size, (2) increase in number of follicle cells, (3) assumption of an ovoid form, (4) rift in the layers of follicle cells to form a follicular cavity filled with liquor folliculi. The latter process gives rise to three areas

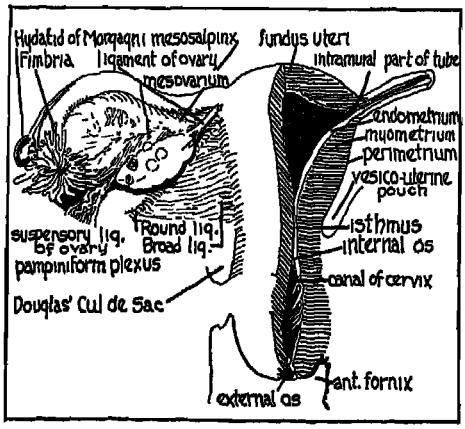

FIG. 71. Sketch showing the general relations of ovary, tube and uterus

among the follicle cells: a stratum granulosum lining the follicle, a basal plate or cumulus oöphorus, and the layer immediately surrounding the ovum, the corona radiata. An egg membrane, the zona pellucida, is secreted between the egg and the corona. In the meanwhile the stroma immediately surrounding the follicle differentiates as an inner vascular, theca interna, and an outer fibrous, theca externa (Fig. 72).

Involution is the ultimate fate of all follicles maturing before puberty. Atresia is a general process of folliclular destruction, since only about 400 eggs are liberated—estimated on the basis

of one per month from puberty (15th year) to menopause (45th year). The steps in the process of atresia are: (1) desquamation and disintegration of the stratum granulosum, (2) leucocytic invasion, (3) cytolysis. The ovum, however, may undergo maturation and pass through several stages of cell division before it eventually disappears. This parthenogenesis

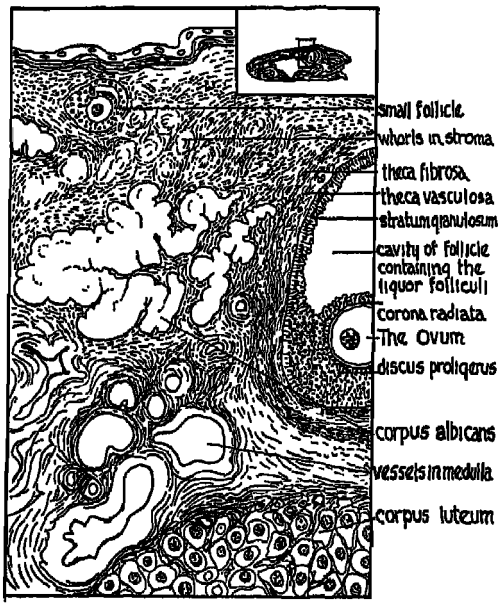

FIG. 72. Section through the cortex of the human ovary. Note the surface epithelium, the intermediate and mature follicles, the corpus luteum and the corpus albicans. The insert shows the section in situ.

(development without sperm) is the basis of Loeb's theory of the origin of a certain class of ovarian tumors (teratoma; included twin).

This process of atresia continues throughout reproductive life, and eventually leaves the senile ovary without follicles, and reduces it to a fibrous stroma.

In some mammals, such as the rabbit and mouse, atresia bears an interesting relation to the origin of the so-called "in-

terstitial glands" of the ovary. These glands consist of closely packed corded epithelioid cells lying in the stroma between the primary follicles. They are supposed to have the same function as the cells of Leydig of the testis, but Kingsbury questions this. In the rabbit they arise from the fibrous cells of the theca externa, but in man the evidence is not so striking. Atretic follicles in man do undergo a fibrosis, however, that gives them a superficial resemblance to old corpora lutea, hence they are called corpora albicantia spuriae.

After puberty the fate of the maturing follicle is different. One large follicle gains ascendancy over the rest, ruptures, and the egg escapes into the abdominal cavity to enter the mouth of the Fallopian tube and to migrate to the uterus. The exact mechanics of rupture of the follicle are still in doubt. Three hypotheses have been advanced: (1) increase in vascular tension in the capillaries of the theca interna; (2) secretory pressure within the follicle; (3) lytic enzyme that softens the follicle. The process is not a "volcanic eruption." The base of the follicle becomes congested; its apex contracts into a projecting cone or teat; and with rupture, the gelatinous contents ooze out and flow down the sides to be wiped off by the fimbria of the tube (Kelly).

The period during which ovulation takes place in the human species is placed at the 14th day after the first day of the last menstruation. This time is subject to some individual variation. Eggs have been recovered by Allen on the 12th to the 19th day.

The cavity of the ruptured follicle is quickly filled in by a corpus luteum (Fig. 72). The cells are large, epithelioid (24 to 40μ). The nuclei are vesicular, nucleolated; cytoplasm pale and acidophilic. Most authorities consider that these cells are derived from the stratum granulosum. There is some evidence that indicates a second source from the theca interna. Capillary twigs are also a conspicuous element in the growth.

The fibrin clot from the original hemorrhage is rapidly absorbed. The lutein cells begin to show fatty vacuolization, a conspicuous character throughout their functional endocrine span during which they secrete both theelin and progestin and control the functional state of the uterus, in preparation for nidation or implantation of the fertilized egg.

Fibrosis converts the retrograde gland into scar tissue of a peculiar hyaline, non-cellular variety. Three stages may thus be recognized: (1) corpus hemorrhagicum, (2) corpus luteum functionalis, (3) corpus albicans. The functional state varies according as to whether or not pregnancy sets in. The corpus luteum menstruationis (spurium) becomes microscopic in size in 6 to 8 weeks; the corpus luteum graviditatis (verum) attains a maximum size of 20 to 30 mm. and begins to undergo involution during the fifth month of pregnancy.

Theelin is the extract of the liquor folliculi. It is also produced for the first two days by the corpus luteum. The production of both theelin and progestin seem to be under the control of Antuitrin S, extract of the pituitary.

The arterial supply to the ovary is double; mainly the ovarian, by way of the suspensory ligament and the ovarian branch of the uterine. The veins form a pampiniform plexus in the mesovarium. The nerve supply is from the ovarian plexus which arise from the aortic and renal plexuses. Many of the fibers arise from the ovarian ganglion at the base of the ovarian artery. Afferent fibers are from T_{10}. Motor fibers are vasomotor or distributed to the smooth muscle of the stroma. None have been demonstrated in the epithelium. Ganglion cells do not occur regularly (Kuntz).

Associated with the hilus or attached border of the ovary are a series of rudimentary epithelial tubules or cords of varying diameters, that represent the remnants of the mesonephros and its duct. They consist of the epoöphoron, paroophoron, canal of Gärtner and ovarian hydatid.

MATURATION, FERTILIZATION AND CLEAVAGE

The ovum undergoes a maturation process, with chromosome elimination, similar to that described for the sperm. The stages recognized are the oögonium, primary oöcyte, secondary oöcyte and ovum. There is however a point of difference between oögenesis and spermatogenesis. When the primary oöcyte divides the two daughter cells are unequal in size. The large one is the secondary oöcyte and the small one is the first polar body. The secondary oöcyte produces a second polar body to become the fertilizable ovum. The first polar body may or may not divide again. Thus one oöcyte produces one mature ovum and three abortive, non-functional polar bodies, whereas a spermatocyte produces four functional sperm.

Maturation generally occurs in mammals as the ovum leaves the ovary. Fertilization takes place in the upper part of the tube. The sperm head enters the egg, swells into a typical nucleus and fuses with the egg nucleus on the first cleavage spindle (Figs. 71–76).

Chapter XXIX

THE FEMALE REPRODUCTIVE SYSTEM: II. FALLOPIAN TUBES. UTERUS

The Fallopian tubes are the site of fertilization. Sperm migrate from the vagina and uterus to the upper quadrant of the tubes and meet the egg on its downward journey after expulsion from the ovary.

The Fallopian tubes are trumpet shaped, approximately 10 cm. in length and from 2 to 8 mm. wide. They course in the superior border of the broad ligament (Fig. 71) in a special mesentery, the mesosalpinx. Each tube presents four parts: (1) an infundibulum, (2) ampulla, (3) isthmus and (4) an intramural portion in the wall of the uterus. The infundibulum opens into the abdominal cavity in close proximity to the ovary by the funnel-shaped ostium abdominale. Its thin walls are ridged by longitudinal fringe-like folds, the fimbria. These folds continue into the ampulla (Fig. 73) in a complicated plication that practically obliterates the lumen. They are reduced to four primary folds in the isthmic and intramural parts. The tubo-uterine junction is angulated and essentially valvelike.

The epithelium is of a low columnar type in which three cell types have been described: (1) ciliated, (2) secretory, (3) (3) "peg" cells. Cilia are relatively fewer at the uterine ends of the tubes. Cyclic changes occur concomitant with the menstrual cycle. The ciliary beat is toward the uterus. No special glands are present.

Three coats are continous throughout the tube, namely, mucosa, muscularis and fibrosa. The musculature is an internal circular and an external longitudinal, which may spread

into the mesosalpinx. Movement of the fimbria and peristalsis of the tube have been commonly observed.

The complex character of the tubes make them ready sites for infection. Stricture and resulting sterility is common. Pus tubes are sources of constant trouble. Tubal pregnancy is frequent. Rupture generally occurs at the sixth week.

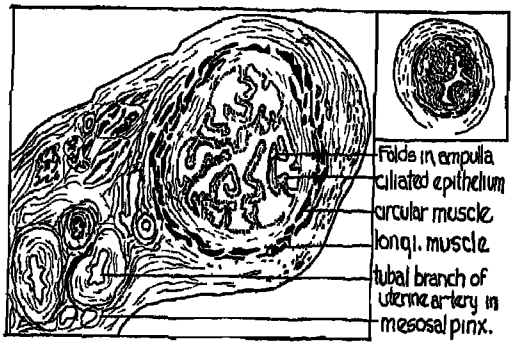

FIG. 73. Two sections through the Fallopian tube; one through the ampulla, the other through the isthmus. The latter shows the four primary longitudinal folds.

THE UTERUS

The uterus is a median, unpaired, hollow, fibro-muscular organ, in the mucosa of which the ovum is normally implanted in pregnancy. It is pyriform in shape and measures 2.5 x 5 x 8 cm. It is divided by an isthmus into a freely movable upper body and a fixed lower cervix. The body is flexed on the cervix at an angle of 80° to 120°. Its anterior surface rests on the bladder, while the posterior surface is in contact with the rectum, the peritoneal cul-de-sac of Douglas intervening. That portion which lies above the level of the tubes is the fundus, greatly hypertrophied during gestation. The cavity of the body is flattened and has a triangular outline, broad above but narrowed at the isthmus into an internal os. The canal of the cervix is fusiform. The mucosa shows oblique folds, the plicae palmatae. The cervix opens into the vagina at the external os (Fig. 71).

The cylindrical cervix presents an imbedded supravaginal portion and a lower part that projects freely into the vault of the vagina. The external os appears on this part as a dimpled or slit-like opening bounded by an anterior and posterior lip. In women who have borne children, it may be star-shaped due to tears. It is the frequent site of infection and cyst formation (Ovuli Nabothi).

The support to the uterus is (1) broad ligaments, (2) round ligaments, (3) uterosacral ligaments, (4) anterior ligament to the bladder, (5) posterior ligament to the rectum.

The uterus presents three coats: a mucosa or endometrium; a muscular myometrium and a serosa or perimetrium. The serosa has a typical organization. On the body it is applied directly to the myometrium, but a subserous areolar layer or parametrium intervenes which provides an extraperitoneal route for the surgical removal of the cervix.

The myometrium may be 15 mm. thick. It is composed of smooth muscle fibers bound firmly together by fibroelastic connective tissue (Fig. 74). Three layers have been described, a fine longitudinal layer or stratum submucosum, a middle circular stratum vasculare, and an outer stratum supravasculare. The coats are not discrete. The fibers are single or clustered in spiral whorls that follow in part the vascular bed. The middle coat bears the large arteries derived from the broad ligaments. The muscle cells are 40 to 90μ in length but in pregnancy may hypertrophy to 500μ. They undergo fatty degeneration in the puerperium. This layer gives rise to the common massive fibro-muscular tumors of the uterus.

The normal mucosa may have a thickness of 0.5 to 1 mm. The surface epithelium is smooth, resting on a non-papillated stroma composed of reticular stellate and spindle cells of the embryonal type. Glands are common throughout, but there is a distinct difference, both structural and functional, between those of the fundus and those of the cervix (Fig. 74).

The fundic glands are simple, straight, tubular glands that lie at right angles to the surface, and extend through the depth

of the mucosa. The epithelium has a uniform height (25 to 30μ) and cytology with that of the surface. Ciliated, secretory and rod cells have been described. The glands do not lie in juxtaposition but the ratio of stroma to gland is about four to one. The secretion is fluid.

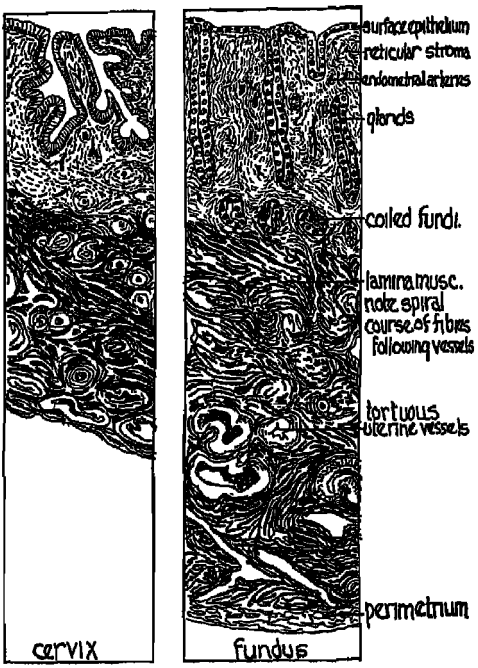

FIG. 74. Longitudinal sections through the fundus and the cervix of the uterus, drawn side by side for comparison.

The cervical glands are either simple tubular or branched sacculated, with a tall cylindrical epithelium (35 to 60μ) basal nuclei and mucoid cytoplasm. The secretion is yellow, viscid, glairy, and may constitute the bulk of the discharge in leucorrhea. The surface epithelium changes abruptly to stratified squamous of the vagina at the external os.

During the child-bearing age, the mucosa of the body and fundus presents a variable picture with (1) the four functional

phases of the menstrual cycle, and (2) with pregnancy (Schroeder, Barthelmez, Williams).

The menstrual cycle has been variously divided into four parts—menstrual, postmenstrual, interval, premenstrual.

The "sign" of the menstrual phase is vaginal hemorrhage. This normally lasts four days. About 35 to 55 cc. of blood are lost. Epithelial shreds are present on the second day. The histology of the uterus at this time shows diapedesis, subepithelial hemorrhage, cytolysis, leucocytic invasion followed by lymphocytic invasion, exfoliation and complete "crumbling" of all but the basal zone of the mucosa (Fig. 75 *f*, *a*).

The postmenstrual period is one of regeneration and growth of the mucosa. The stroma is recruited locally. The surface epithelium is regenerated from the remnants of the glandular epithelium of the stratum basalis, and is complete in two days. Gradual increase in thickness occurs up to the fourteenth day, when ovulation converts the follicle into a corpus luteum (Fig. 75, *b*).

The interval is one of quiescence. The glands gradually assume a secretory phase under the influence of theelin and progestin, of the growing corpus luteum. This period is nine days long, and is concomitant with the time required for the egg to traverse the tube and find lodgement in the uterus (Fig. 75*c*, *d*).

The last five days of the cycle constitute the premenstrual period, characterized by a hyperemia, edema, and congestion. The glands are at the height of their secretory phase and present tortuous compressed, sacculated dilatations that convert the middle zone into a stratum spongiosum. Total depth, 6 mm. (Fig. 75, *e*). Together with the more superficial stratum compactum, it constitutes the functionalis in which the fertilized ovum becomes embedded. In the event that fertilization has not occurred, regression of the corpus luteum begins and the functionalis "crumbles." Turgescence of the mammary glands is a frequent accompaniment of this phase.

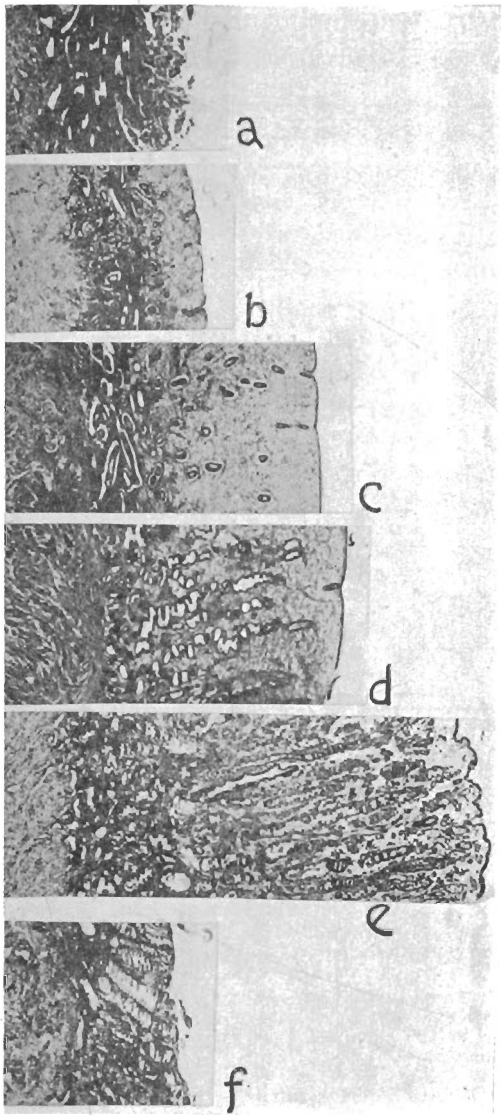

FIG. 75. Sections through the endometrium of the human uterus at different phases of the menstrual cycle. *a*, second day; *b*, sixth day; *c*, tenth day; *d*, twenty-second day; *e*, twenty-eighth day; *f*, first day of menstruation. (Modified from Schroeder.)

While menstruation and ovulation are correlated chronologically, they may occur independently.

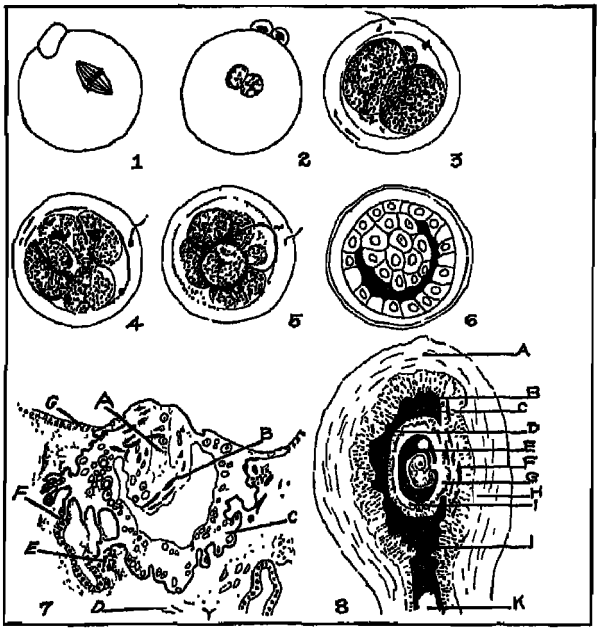

FIG. 76. Steps in the maturation, fertilization, cleavage and implantation of the mammalian ovum. *1*, ovum of rat showing first polar body and second polar spindle. *2*, ovum of rat showing two polar bodies and fusion of egg and sperm nuclei. *3*, *4*, *5*, cleavage of the monkey ovum, cultivated in vitro (photomicrographs by Lewis and Hartman). *6*, diagram of older stage of rabbit's ovum showing inner cell mass and outer trophoblast. *7*, the youngest known human ovum, just after implantation. Probably about nine days old (recovered 21 days after the last menstruation). Redrawn from Müller. *a* reticular magma; *b*, extra-embryonic mesoderm; *c*, cytotrophoblast; *d*, syncitiotrophoblast; *e*, zone of erosion of endometrial glands; *f*, leucocyte reaction; *g*, surface epithelium of the endometrium. *8*, semidiagrammatic sagittal section of a human uterus containing an embryo of five weeks. *A*, uterine wall; *B*, cavity; *C*, decidua vera; *D*, decidua capsularis; *E*, cavity of the chorion; *F*, frondosum; *G*, decidua basalis; *H*, myometrium; *I*, chorion laeve; *J*, internal os; *K*, cervix.

The mucosa, during pregnancy, presents the foregoing premenstrual character on which is superimposed the physiological and mechanical effect of an implanted ovum which, though microscopic at first, grows to include a 3500-gram fetus, 1500

cc. of amnionic fluid and 250 grams of placenta. Three zones are recognized: (1) the decidua basalis, lying between the ovum and the myometrium, (2) the capsularis or portion that covers the ovum, (3) the decidua vera or remaining portion of the mucosa (Fig. 76, *8*).

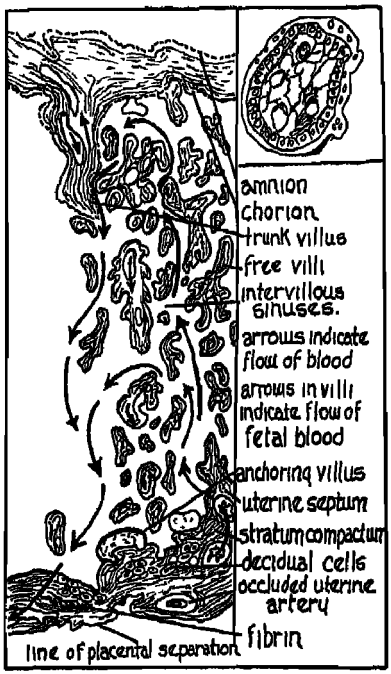

FIG. 77. Section through the human placenta to show the relation of the fetal circulation of the chorionic villi to the maternal circulation in the open intervillous spaces. The arrows indicate the respective blood flows. The insert shows a villus in cross section. Note the mesodermal core enclosing the blood vessels; the two layered epithelium, an inner cellular Langhans' layer and an outer syncitial layer. The rounded cell in the core is significant; it is a Hofbauer cell concerned with the bacteriocidal defense of the fetus.

The ovum at the time of implantation is a hollow vesicle (Fig. 76, *6*) composed of an outer layer of trophoblast and an inner cell mass. The latter literally becomes the embryo; the former persists as the covering membrane. The trophoblast early becomes two layered; an outer plasmoditrophoblast and

an inner cytotrophoblast (Fig. 77). A mesodermal layer extends from the inner cell mass to the cytotrophoblast to complete the membrane, now known as the chorion. Finger-like processes, the villi, extend outward from the surface of the chorion, and the trophoblast cells "erode" the endometrial tissue and open up venous lakes or lacunae which provide nutritive material for the growth of the ovum (Figs. 76, *7*, *e*; 77).

As the ovum increases in size it bulges into the cavity of the uterus and stretches the capsularis before it. The villi on this side atrophy and the remaining ones are gradually confined to the basalis, which assumes the circular disk form of the placenta. The extension of the amnion to enclose the body-stock, yolk sac, and allantois, completes the umbilical cord and becomes the inner surface of the placenta (Fig. 76, *8*; 77).

When the circulation of the embryo is established, the villi become vascularized. The main villous trunks bear "free villi" that are bathed by maternal blood in the lacunae. Here the respiratory exchange of gases and the nutritive exchange is brought about by dialysis and osmosis. The two circulations, however, are entirely separate; maternal blood does not flow in the fetal vessels (Fig. 77).

"Anchoring" villi firmly fix the ovum to the connective tissue septa that form the walls of the endometrial lacunae. The placenta, then, is an organ of double origin—maternal endometrium and fetal chorion (Fig. 77).

One type of cell in the endometrium is considered to counteract or control the degree of extension of the trophoblast cells. These are the decidual cells (Fig. 77, *c*). They are large, 30 to 100μ, epithelioid, generally acidophilic, contain one or two vesicular nuclei. They may store glycogen, fat and pigment. They are concentrated in the stroma of the spongiosum in close approximation to the trophoblast cells.

The decidual reaction is not peculiar to the uterus but may occur at any site where implantation takes place, as in the tube,

abdominal cavity, ovary. A slight decidual reaction occurs in the premenstrual mucosa.

Parturition or "delivery" occurs at the end of ten lunar months (280 days). The musculature of the cervical segment "dilate"; the amnio-chorionic sac ruptures and expels its contents; the fetus "engages" in the pelvic outlet and is delivered, followed later by the placenta or "after-birth." Endometrial separation occurs by rift in the stratum spongiosum. After delivery the uterine musculature contracts forcibly, reduces the uterine cavity, and checks hemorrhage. Regeneration of the epithelium from the stratum basalis is rapid. The extreme hypertrophy of the uterine arteries leave them tortuous and thicker walled after each pregnancy.

The extrinsic nerves of the uterus are from the utero-vaginal plexus, derived from the hypogastric and pelvic nerves. A cervical ganglion of compact or disseminated type is present. There are no intrinsic ganglion cells. Fibers to the endometrium are questionable. The nerves are regulatory only.

Chapter XXX

THE FEMALE REPRODUCTIVE SYSTEM: III VAGINA. EXTERNAL GENITALIA. BREASTS

The vagina is a fibro-muscular distensible tube, composed of three coats, a mucosa, muscularis and a fibrosa. It is approximately 6 to 8.5 cm. long. The lumen presents an H-shaped fissure produced by an anterior and a posterior columna rugarum. It extends from the uterus to the external genitalia where it opens on the exterior after penetrating the urogenital diaphragm. The urethra lies anterior, and the rectum, posterior, while the levator ani muscles strengthen the lateral walls. The external orifice is surrounded by fibers from the bulbocavernous muscle, forming a sphincter vaginae.

The mucous membrane of the vagina is lined by a stratified squamous epithelium. There are no glands. The contained secretions are mainly from the cervix, although epithelial glycogen undergoes fermentation to lactic acid under the influence of the vaginal bacteria. The stroma is dense and papillated on the posterior wall. It is heavily invaded by lymphocytes. The deeper portion is plexiform and has been described as a submucosa.

The muscle layers are an inner circular and an outer longitudinal, neither of which are as thick nor as compact as those of the uterus.

The adventitial layer is of the fibro-elastic type, containing venous plexuses. The arteries are from the vaginal branches of the uterines. The nerves are from the utero-vaginal plexus. Numerous small intrinsic ganglia lie within the fibrosa. No sensory fibers have been demonstrated with certainty in the epithelium.

The vagina undergoes cyclic changes of a lesser degree than the uterus. The changes in the cellular content of the vaginal fluid as established by Stockard and Papanicolaou follow closely the ovarian cycle. The exact stage of "heat" of an animal may be determined.

EXTERNAL GENITALIA

The female external genitalia present an elongated depression occupying the perineal region and bounded laterally by the labia majora, a pair of skin folds. Their outer surfaces are hirsute; the inner bear abundant sweat glands. Subcutaneous fat and smooth muscle characterize the supporting core. These two folds are continued anteriorly into the mons pubis. Their medial borders are normally in contact. Within the depression between them is a second pair of integumentary folds, the labia minora. The epithelium is of the moist, cornifying, stratified type;—sebaceous glands are numerous, but no hair is present. The stroma is of the venous erectile tissue type. No fat. The space between them is the vestibule. At the angle of their anterior convergence, is a small erectile organ, the clitoris, composed of two corpora cavernosa. At the base of the clitoris lies the urethral orifice. The vulvo-vaginal glands of Bartholin, corresponding to the bulbo-urethral glands of Cowper, open into the vestibule between the hymen and the labia minora. They are tubulo-acinar glands about the size of peas. They are frequent sites of gonorrheal infection.

Sensory nerve endings of the encapsulated type are numerous throughout the clitoris and labia minora. The reflex centers for the control of the female sex organs are in the sacral and lumbar segments of the cord.

THE MAMMAE

While the mammary glands are not to be considered an integral part of the female reproductive system, their functional

development and involution is intimately correlated with and dependent upon the ovary.

The two mammary glands are situated on the thorax—one on each side of the sternum. Supernumerary nipples, common in both sexes, may be distributed along the line of the embryonic milk ridge, extending from the border of the axilla to the symphysis pubis.

In the female the glands are conical or hemispherical; somewhat firm and elastic. The bases are supported on the fascia of the pectoralis major, the serratus anterior and the external oblique muscles. Each measures about 12 cm. in diameter, 50 to 60 mm. thick, and weighs 140 to 200 grams. The superficial surface is covered by thin smooth skin. The raised central nipple is surrounded by a pigmented areola, stippled by the pores of Montgomery's glands.

Each gland is composed of the epithelial parenchyma and the interstitial stroma. The parenchyma is made up of some twenty separate pyramidal lobes, whose apices terminate on the nipple as the single excretory lactiferous ducts. The latter are lined with stratified squamous epithelium continuous with that of the epidermis. They are about 4 mm. wide, but in the areolar zone they dilate as the ampullae or lactiferous sinuses. Beyond this point continued branching reduces the ducts to microscopic size (Fig. 78).

The lobes are separated by vertical septae, the retinaculae mammae, known on the upper border as the suspensory ligaments of Cooper. The whole gland is covered above and below by a fatty capsule derived from the tela subcutanei.

The nipple has a height of 11 mm. The skin is thin, pigmented and marked by 15 to 20 depressions, the ducts of the gland. The corium is marked by tall vascular and nervous papillae. Sebaceous glands without hairs are numerous. Smooth muscle is both vertical and circular and is considered to give the nipple a turgor on contraction.

Both parenchyma and interstitial tissue are subject to

marked functional change at the critical periods of puberty, pregnancy, parturition, weaning and menopause. In section, the resting gland consists mainly of connective tissue and small discrete "islands" of branching, slightly dilated, excretory ducts which terminate in collapsed alveoli, "end pieces" or "embryonic cell cords." These rounded islands are immediately surrounded by a loose, pale staining, reticular, connective tissue. This cellular "intralobular," "intercanalicular" tissue is whorled about each duct. It is supposed to provide an immediate expansile zone for the hypertrophy of the gland (Fig. 78).

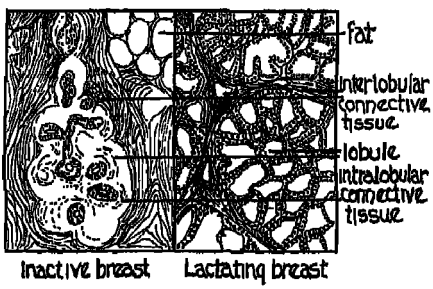

FIG. 78. Sections through the breast at different phases of activity. To the left is a lobule of inactive breast; to the right, a breast near the end of the lactating period. Compare the relative amounts of intralobular connective tissue and the size and appearance of the acini.

It is quite distinct from the course, fibrous, interlobular tissue in which various amounts of fat develop.

The epithelium of both the resting alveoli and the ducts is two-layered. The inner layer is cuboidal, but there is still some dispute as to whether or not the outer layer is true epithelium or "basket cell" (Loeb).

The active gland develops under the influence of the sex-hormone system during pregnancy. The "endpieces" or collapsed alveoli become greatly distended, reaching a diameter of 300μ. They lie in juxtaposition and exert mutual lateral pressures so that the intralobular connective tissue becomes reduced to inconspicuous strands supporting the capillaries

and lymphatics. The interlobular connective tissue becomes thin and septate as the lobules come to lie adjacent to one another (Fig. 78).

The epithelial cell first shows granular cytoplasm. Then droplets appear which coalesce to form a large fatty vacuole at the free surface. This fat is discharged into the lumen of the alveolus by detachment from the basal nucleated portion of the cell. Regeneration is prompt and the secretory process is repeated.

Milk consists of a fluid or plasma in which these milk globules are suspended. They are 2 to 5μ in diameter and average about 1,000,000 to the cubic millimeter. Casein, milk sugar and various salts are dissolved in the plasma. Leucocytes are present in varying numbers, wandrants from the blood stream through the epithelium.

The secretion at the end of pregnancy and the first few days of lactation differs from that which appears later. It is poor in fat and milk corpuscles, but contains large ameboid cells that show evidence of phagocytosis of some fat. The latter are considered either cast-off epithelial cells or macrophages. A similar substance, "witch's milk" frequently oozes from the breasts of newborn infants. The true secretion of milk begins on the second or third day under the stimulus of nursing; otherwise the gland regresses to the inactive stage.

The nerves to the breasts are from the lateral cutaneous branches of the second to the sixth intercostals. No ganglion cells are present within the gland nor have secretory fibers been demonstrated in the epithelium.

Chapter XXXI

THE ENDOCRINE GLANDS: I. THYROID. PARATHYROID. THYMUS

The thyroid (G. *thyreos*, shield) was named by Wharton in 1659. It is a ductless gland weighing 25 grams, and covering the 2nd and 3rd tracheal cartilages anteriorly. It is composed of a pair of lateral lobes and an isthmus. It is subject to growth changes and varies with menses, food, puberty, pregnancy, climate and geography. Aristotle noted its general dysfunction and called it the globus hystericus (Figs. 79, 80).

The thyroid is made up of a close aggregate of small follicles, varying in diameter from 40 to 150 μ. Some are spherical and discrete while others are irregular, constricted and budded with connecting trabeculae or "cell rests" (Fig. 79). The alveoli contain colloid which gives the whole gland an amber color, a pale translucency and a firm elastic consistency. The outer areolar capsule strips readily, but the inner true capsule is adherent. Lobulation is incomplete. The septa bear the larger blood vessels, a network of sinusoidal lymphatics and the extrinsic nerves. The latter are the postganglionic nonmedullated fibers from the middle cervical ganglion, and vagal fibers from the superior and inferior laryngeal nerves. No sympathetic ganglion cells have been found within the thyroid except in the dog (Nonidez). The regulatory nerves are vasomotor; no secretory fibers have been definitely shown.

The connective tissue between the follicles is sparse. No true basement membrane exists. The capillary bed is profuse, being second only to that of the lung.

The follicles are lined by one cell layer of cuboidal epithelium. Flattened epithelium is indicative of hypofunction; tall colum-

nar cells are considered to be due to hyperfunction. Four cell types have been described: chief, colloid, ovoid and para-

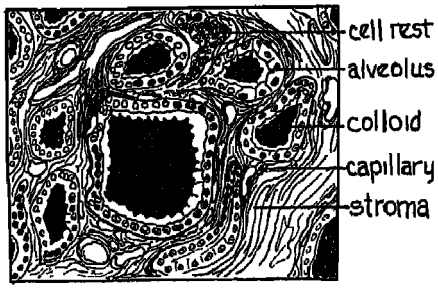

FIG. 79. Section through the lobule of the thyroid gland. Note particularly the so-called "rest cells."

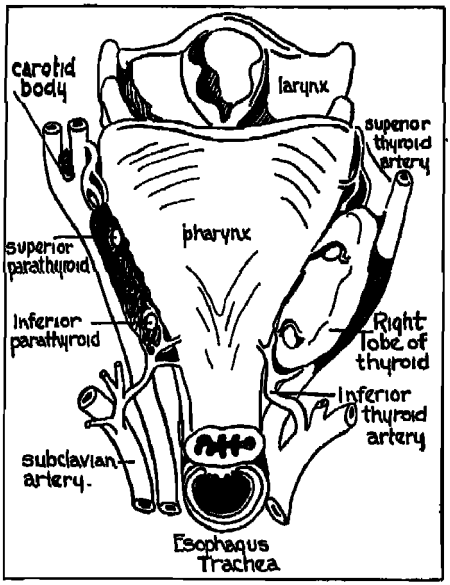

FIG. 80. Sketch of a dissection showing the position of the thyroid and the parathyroid glands and associated structures.

follicular. The majority of cells is of the "chief" type. The significance of the others is unknown.

The colloid is a homogeneous, hyaline susbstance which

stains deeply with eosin. It completely fills the follicle, but in fixed preparations it retracts from the epithelium with a scalloped margin that suggests a greater fluidity for the most recently secreted colloid. Occasionally it may show vacuolization, basic staining and numerous cell inclusions.

Baumann discovered iodine in the colloid in 1895. Kendal isolated crystalline thyroxin in 1915 and analyzed it as $C_{15}H_{11}O_4NI_4$. The action of the hormone is the control of the metabolic rate of the body. One milligram increases the rate 3 per cent. The colloid has a special affinity for ingested iodine. In geographical regions where the iodine content of the soil is low, goitre is common.

Since thyroxin is stored in the follicles, and has its action mediated through the blood stream, a "reversal of polarity" of secretion is generally assumed, that is, the secretion may pass either to the free surface of the cell or to the basal surface. This hypothesis has some cytological support in the shift of position of the Golgi apparatus and the mitochondria (Cowdry). The lymphatics do not seem to be concerned in resorption and distribution of the hormone (Rienhoff).

Thyroid deficiency in infancy produces cretinism, characterized by stupidity, dwarfism, low basal metabolism. Hypofunction after maturity results in myxedema (Gull's disease (1874)) marked by dry swollen face and hands, loss of hair, sexual incompetence, mental and physical sluggishness and metabolic rate of -15 per cent.

Hyperfunction produces exophthalmos (Graves disease) with bulging eyes, mental restlessness, high blood pressure, glycosuria, and a basal rate of $+50$ to 75 per cent. It seems to be a visceral nervous affection, possibly associated with disturbance in the thyrotropic hormone of the anterior pituitary.

Growth and regeneration of the gland is supposed to be carried out by the so-called "cell rests" or cords of cells without lumens (Marine), but Zeckel considers these to be disorganized follicles. No budding occurs after puberty, but tumor forma-

tion is frequent and about 0.5 per cent of these become malignant.

PARATHYROIDS

The parathyroids were discovered by Sandström (1880). Gley showed their relation to tetany by extirpation in 1891. MacCallum and Voegtlin found that the cause of this tetany was a low blood calcium (normal 9 to 11 mgm. per 100 cc. blood). Collip prepared an extract of the gland in 1924 but the hormone itself has not as yet been isolated.

The parathyroids are four in number. They are intimately associated with the internal surface of the lateral lobes of the thyroid. Each is about 6 x 3 x 2 mm. and collectively they

FIG. 81. Section of a lobule of the parathyroid showing the corded arrangement of the "chief" cells.

weigh 0.05 gram. Each is surrounded by a connective tissue capsule, or may lie embedded in the thyroid tissue. Delicate septa subdivide the glands into lobules (Figs. 80–81).

The parenchyma is composed of anastomosing cords of epithelial cells between which are capillaries. Occasional cords may show acinar arrangement and enclose a basophilic colloid. Three cell types are recognized: (1) pale chief cells,—nongranular, poorly staining and with vesicular nuclei; (2) dark chief cells with fine granulations and pycnotic nuclei; (3) oxyphil cells, with small nuclei and eosinophilic cytoplasm. The first type are present at birth; the second occur later but the third do not occur until the seventh to the tenth year in

man. They are considered to belong to the "colloid" series by some investigators. Their significance is unknown.

The nerves, derived from same source as the thyroid, are vasomotor only.

Small islands of adipose tissue are common in the adult parathyroid.

THYMUS

On the basis of its embryology, the thymus may be considered along with the thyroid and the parathyroids: its histology warrants a discussion under the lymphatic system.

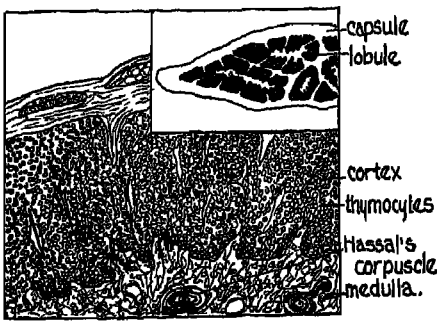

FIG. 82. Section of the thymus of a new-born child. Note the cortex, the medulla and the thymic corpuscles. Insert represents a topographical sketch of a lobule.

Since its function is obscure, it still merits the name of "enigmatic organ." It consists of two (three or four) lobes, loosely joined in the median line. It is roughly pyramidal in shape with the base resting on the pericardium and the "horns" of each lobe extending into the neck on either side of the trachea. It is subject to a considerable variation in weight (6 to 25 grams in the new born). It increases in actual weight until the fourteenth year when involution begins, that converts it into fatty or fibrous cords (Fig. 82).

Each lobe is subdivided into lobules of 1 to 2 mm. diameter by septa. Each lobule shows a cortex and a medulla. The

cortex has a superficial resemblance to a lymph node, although the germinal centers are lacking. A reticulum is closely packed with small thymic cells having a resemblance to lymphocytes. It is generally held that the reticular cells represent the original endodermal epithelium, and since the thymic cells arise from the reticular cells, they, too, are endodermal in origin. General opinion holds, however, that these cells arise from mesodermal cells that have migrated into the reticulum. Eosinophilic mononuclears (myelocytes?) are also conspicuous in the medulla. Their source is undetermined.

The characteristic structure of the thymus is the peculiar thymic corpuscle of Hassal (1846). These are large single cells; lamellated concentric cellular bodies or irregular knobbed structures of varying size. Their source is much disputed but it is now held that they arise from the reticular cells (Hammar). They are more common in the newborn but may be found as remnants in the fatty atrophic thymus of old age. Marine characterizes them as spent, redundant, hyalinized degenerating cells. Their function is unknown (Fig. 82).

The blood supply to the thymus is from the internal mammary, inferior thyroid and pericardial arteries. The nerves are from the inferior cervicals and the vagus.

Since the thymus begins involution at the time of maturity and is delayed by gonadectomy and in status thymolymphaticus, an endocrine function has long been suspected, but extirpation and feeding experiments are negative, although Riddle has shown a relation to shell formation in birds. "Accidental" involution occurs with infections, inanition, x-ray and pregnancy. But Friedleben's aphorism (1858) is still significant —"Es gibt keine Thymus Tod."

Chapter XXXII

THE ENDOCRINE GLANDS: II. ADRENALS. PITUITARY. PINEALIS

The adrenals are a pair of small glands that cap the kidneys. Their combined weight is 14.1 grams. They were first described by Eustachius in 1563, but no indication of their function was suggested until the study of Addison (1855) on tuberculosis of the cortex. Brown Sequard next showed that removal of both adrenals was invariably fatal (1856). Balfour called attention to the double nature of the gland as medulla and cortex (1876). These two portions have separate embryologic origins. The cortex is derived from peritoneum (mesodermal) and the medulla is made up of migrant sympathetic cells (ectodermal). Their functions seem to be entirely independent.

The cortex extract, cortin (Hartmann); synonym, interrenalin (Stewart and Rogoff); eschatin (Swingle, 1930) protects against death after adrenalectomy and is of service in Addison's disease. Its normal function seems to be a general cell stimulant; a blood volume regulator, or a carbohydrate regulator.

Epinephrin (syn., adrenalin, adrenin) is a general arteriole constrictor of wide application in medicine. It is a bronchodilator in asthma. It is effective in doses of $1:10^{12}$. It was first extracted from the medulla by Oliver and Schaeffer (1894); concentrated by Abel (1897); crystallized and analyzed by Aldrich (1901); and synthesized by Stolz (1906). It has an empirical formula of $C_9H_{13}O_3N$. According to Cannon's emergence theory, adrenin is delivered to the blood stream on reflex demand. It improves the vascular and muscular tone

so that unusual feats of strength and endurance may be performed under emotional stress. Stewart and Rogoff question such a rôle for this hormone since animals in which the medulla is destroyed stay in good health and normal behavior.

The gland has a fibro-elastic capsule. The major vessels are the superior, middle and inferior adrenal arteries. These are distributed to the capsule. They break up into cortical sinusoids that drain toward the medulla and furnish it with its

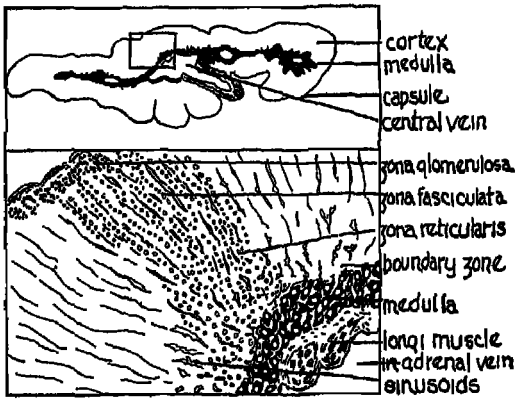

FIG. 83. The suprarenal gland. Insert shows topography of a section. Below, the four zones of the cortex and the medulla are represented. A portion of the wall of the central vein shows its peculiar longitudinal musculature.

blood supply. The medulla drains into the central adrenal veins, peculiar for their thin walls and for the unusual distribution of cords of longitudinal muscle within the media (Fig. 83).

Three zones were described for the cortex by Arnold (1866) —zona glomerulosa, zona fasciculata, zona reticularis. The glomerular zone, immediately under the capsule, is narrow. It is made up of small solid spheroids of cell cords. The cells are small and stain deeply. They are considered to be the germinal cells of the cortex, although mitotic counts fail to establish this fact.

The fascicular zone is made up of straight double rows of cell cords, separated from each other by wide sinusoids. These cells are sometimes called spongiocytes because of the nature of their cytoplasm which is practically filled with numerous fatty vacuoles. This lipoid is mainly cholesterol and lecithin, which has led to the hypothesis that the adrenals are the site of storage of these metabolites. Lipoids increase remarkably during pregnancy.

The reticular zone is made up of irregular rows of monocellular cords, in which the cells are smaller, contain little fat and stain with a deep neutral cast. Granules are present which blacken with osmic acid.

An inner fourth zone is sometimes recognized as the juxtamedullary part of the reticularis. The cells show a natural brown granular or general pigmentation. This pigment is of some interest since "bronzing" of the skin occurs in Addison's disease, but the relationship is obscure. Aschoff calls this lipochrome a "wear and tear" pigment. It develops after puberty.

The medulla is made up of a series of irregular anastomosing cell cords, interrupted by sinusoids, and the branches of the veins. The staining reaction and the shapes of the cells depend upon fixation time, since changes occur rapidly after death. In the gross, the medulla becomes green with ferric chloride (Vulpian's reaction, 1856) or brown with chromic acid (Henle's reaction, 1865). These colors are due to the presence of adrenalin. It is one hormone, the secretion of which is under the control of the nervous system, since stimulation of the splanchnics increases the amount in the blood. Ganglion cells are frequently described in the medulla, but they are rare.

Connective tissue is sparse. Corner claims that there is no fibroblast, that the reticulum is a product of the endothelium.

The adrenals are subject to marked changes at birth, puberty, menses, and pregnancy, but the significance of these changes is unknown.

Other glands which give Henle's chromafin reaction are the paraganglia of Zuckerkandl and the carotid body. The latter is of some significance since it is supposed to assist in the regulation of the respiratory and heart rate (Fig. 80).

THE HYPOPHYSIS

The hypophysis is a small compound endocrine gland attached to the floor of the third ventricle by the infundibulum. It is a flattened ovoid—10 x 6 x 13 mm. Its weight is 0.56 gram. It is securely anchored within the dural capsule of the sella turcica and covered over by the diaphragma sellae. It was called the pituitary by Vesalius because it was supposed to secrete phlegm; an error corrected by Schneider when he described the membrane of the nose.

The hypophysis is composed of two parts—an anterior buccal portion and a posterior neural portion. The first part is derived from an invagination of the roof of the stomodeum as Rathke's pouch. The second portion is a hollow downgrowth from the floor of the twixt-brain. Both are ectodermal (Figs. 84, 92).

The neural portion early becomes converted into a solid stock in man, but in many animals it retains its lumen. It is a typical glial fiber structure, but contains three cell types: (1) glial cells, (2) ependymal cell, (3) nerve cells. The last point has been questioned. The original extract, pituitrin, widely used in obstetrics and surgery, contains two principles, pitressin, an antidiuretic used in diabetes insipidus, and pitocin, a smooth muscle contractant, used in obstetrics.

The pars buccalis has been subdivided into two portions: (1) the pars distalis and (2) the pars juxtaneuralis. These were originally separated from each other by the residual lumen of Rathke's pouch, but this becomes obliterated by overgrowth of the pars distalis, which eventually makes up 75 per cent of the gland. The pars juxtaneuralis is further subdivided into (1) pars infundibularis which surrounds the infundibulum, and

(2) a pars tuberalis which covers the tuber cinereum or base of the infundibulum (Fig. 84).

The cellular arrangement in the pars juxtaneuralis (intermediate lobe) is that of cords with an occasional lumen filled with colloid. The cells are mostly of the deep staining basophile type or chromophobes. Rasmussen has shown a migration from this layer into the pars nervosa. Herring has given evi-

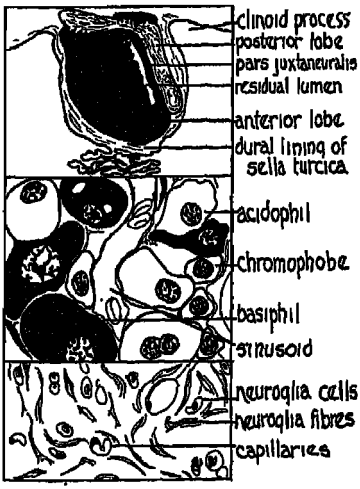

FIG. 84. The upper figure is drawn from a sagittal section through the hypophysis of a six-months human fetus. Note the anterior lobe, the residual lumen, the intermediate lobe and the posterior lobe. The middle and lower figures represent the cell types as seen in the hypophysis of a middle aged man.

dence for direct absorption from this zone into the third ventricle of the cat.

The anterior lobe shows four cell types: (1) acidophiles, (2) basophiles (collectively known as chromophiles), (3) large and (4) small chromophobes (Fig. 84). The acidophiles are the most conspicuous. They are large ovoid cells with prominent vesicular, excentric nuclei. They occur in small groups or clusters, but no definite polarity has been shown. They constitute 37 per cent of the cells by count. They increase in pregnancy. Acidophilic tumors produce gigantism or acromegaly. Hence it is inferred that they are the source of the growth hormone of Evans and Long (1922) (Antuitrin G).

The basophiles are very similar to the acidophiles except for their tinctorial reaction. They constitute 11 per cent of the cells. Basophilic tumors are accompanied by precocious development or overdevelopment of the sexual organs. These cells increase in number in period of sexual activity following hibernation. They are the typical "castrate" cells. Hence it is supposed that they produce the anterior pituitary sex hormone (Antuitrin S).

The chromophobes (G. *chroma*, color; *phobos*, fear) are cells that stain poorly. They have been described as "nuclear heaps." They are considered to be the reserve stock from which the others are recruited.

The vascular bed is profuse in both the anterior and posterior lobes. The blood supply is from the Circle of Willis. Nerves pass to the anterior lobe by the carotid plexus and to the posterior lobe from the nucleus supraopticus.

The detail of the hormone properties of the hypophysis are still to be worked out. The gland has been referred to as the "motor of the endocrine system." There is experimental evidence for a thyrotrophic, adrenotrophic and pancreatrophic endocrine. Riddle (1932) has isolated a lactogenic hormone, prolactin. Most investigators postulate two sex regulatory hormones: an acid extract, Prolan A (Rho 1) which promotes growth of the ovarian follicles, and an alkaline extract, Prolan B (Rho 2) that stimulates growth of the corpus luteum. There is still an open discussion as to an extrahypophyseal source of Antuitrin S which is obtained from pregnancy urine.

PINEALIS

The pineal gland is regularly considered in the endocrine system although there is no positive proof of its function. It is a small cone-shaped solid organ 5 x 8 mm. It is pedunculated and attached to the roof of the third ventricle. It is made up of neuroglia and modified epithelioid cells. Calcareous granules (brain-sand, acervuli) are frequently seen in older glands. The Ancients considered the pinealis the "seat of the soul."

Chapter XXXIII

THE EYE

The eyeball (bulbus oculi) is a hollow spherical, slightly compressible body (23 x 25 mm). Its firmness or turgor is maintained by an internal hydrostatic pressure of 25 mm. mercury. The posterior hemisphere is lodged in the anterior half of the bony orbit and is partially supported by a thick adipose body from which it is separated by the capsule of Tenon. The latter permits the rotatory movements produced by the six voluntary extrinsic muscles: superior, inferior, lateral and medial recti; superior and inferior oblique. These are all inserted in the eyeball and except for the last-named, arise from the annular ligament of Zinn which surrounds the optic nerve near its exit from the orbit (Fig. 85).

The anterior hemisphere is partially exposed and may be completely covered by the lids. It is continuous with their inner surfaces as the membranous conjunctiva. The exposed portion presents the "white" sclera, continuous with the transparent cornea which overlays the "colored" iris and its central aperture, the pupil. Between the iris and the cornea is an anterior chamber filled with an aqueous humour. Projecting slightly through the pupil into the anterior chamber is the transparent "invisible" lens. It is supported from the wall of the bulb by a circular suspensory ligament attached to the ciliary body just posterior to the base of the iris. The narrow slit-like space between the iris and the lens is the posterior chamber. The transparent jelly-like vitreous body occupies the major cavity of the bulb between the lens and the inner lining, the retina.

The eye is essentially a camera obscura, equipped with a

photosensitive retina and a dioptric apparatus designed for rapid, universal reflex focusing. The optical and anatomical axes are slightly divergent. The "blind spot" which marks the exit of the optic nerve, is removed 20° from the posterior pole. The latter is occupied by the "yellow spot" (Macula lutea) and its pit, the fovea, most sensitive spot in the eye.

The eye is composed of three membranous coats—an outer fibrous, a middle vascular and an inner retinal. The outer one

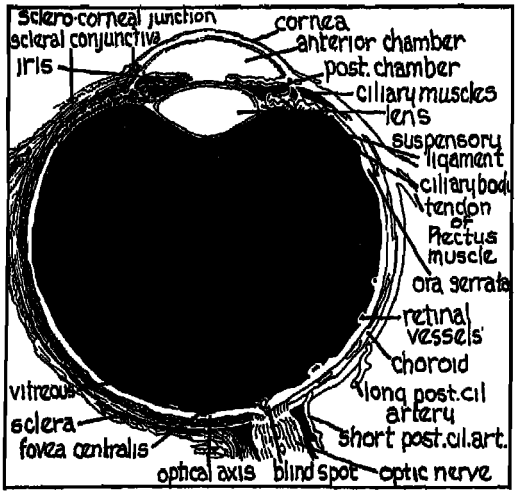

FIG. 85. Diagram of a horizontal section through the left bulbus oculi

consists of the sclera and cornea; the middle one of the choroid, ciliary body and body of the iris; the inner one as the visual, ciliary and iridical portions of the retina (Fig. 85).

The sclera (G. *skleros*, hard) is a firm, thick, fibrous coat composed of interlacing bundles of connective tissue poorly supplied with vessels. It is continuous with the dural sheath of the optic nerve and with the tunica propria of the cornea. It contains the canal of Schlemm, a venous channel draining the anterior chamber through the lymph spaces of Fontana at the sclero-corneal junction—a mechanism for the maintenance of

normal pressure since permanent increased pressure leads to atrophy of the retina (Glaucoma). The inner layer of the sclera is the loose pigmented lamina fusca.

The cornea is transparent and avascular. Its transverse diameter is 11 mm. Its anterior surface is a stratified squamous epithelium of several layers, continuous with the epithelium of the conjunctiva. The stroma consists of an outer nonpapillated elastic membrane of Bowman; a middle lamina propria and an inner elastic membrane of Descemet. The inner surface is completed as an endothelium lining the anterior chamber (Fig. 85).

The choroid coat is very vascular, particularly near its outer surface or lamina vasculosa. A special thin layer, the suprachoroidale, lies adjacent to the lamina fusca. An inner choriocapillaris and a Bruch's basal lamina completes the coat. The cells are stellate or fusiform and contain densely packed black to brown pigment.

The ciliary body is a circular shelf-like thickening just behind the base of the iris. Two particular sets of structures are developed in it: (1) the ciliary muscles, and (2) the ciliary corona. The former constitute the "muscles of accommodation" and consist of an outer meridional and an inner circular bundle. The corona is composed of 70 radiating folds which lend attachment to the fibrils of the suspensory ligament (zonule of Zinn) of the lens. A thin basal, non-pigmented zone, the orbicularis ciliaris, lies between the corona and the choroid proper (Fig. 85).

The iris has a double origin. Its anterior surface is a continuation of the vascular choroid coat. Its posterior surface is composed of a double layer of pigmented cuboidal retinal epithelium (Fig. 85). Various amounts of pigment are present in this fibrous layer. If poor, the retinal pigment shines through and the iris has a blue-gray color; if profuse, the brown black predominates. The anterior surface of the iris is endothelial, continuous with the lining of the anterior chamber.

The muscles of the iris are smooth, and constitute a circular sphincter pupillae and a radial dilator pupillae. These muscles are peculiar in that they originate from retinal cells and hence are ectodermal in origin.

The retina, developmentally, comprises two layers (Fig. 86): an outer and an inner layer continuous at the pupillary margin of the iris. In the pars cecum, that portion covering the backside of the iris and the ciliary body, each layer is a single layer of pigmented cuboidal cells, but at a line just behind the at-

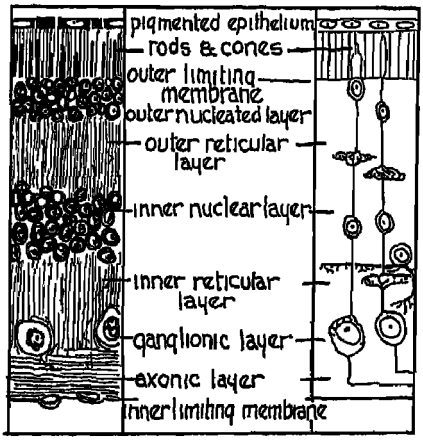

FIG. 86. Drawing of a section of the retina as it appears with a hematoxylin-eosin stain. To the right is a diagram of a reconstruction of the nervous connections in the retina as made out by the Golgi method. The more complex relations are omitted.

tachment of the lens (the ora serrata), the inner layer thickens into nine strata that mediate the visual function. The outer layer persists as (*10*) "pigmented epithelium of the retina" and its cells are supposed to have a light absorptive function. The adjacent inner layer (*9*) contains the rods and cones. These are special end processes of bipolar cells that lie in (*8*) outer nuclear layer. The axones of these cells pass toward the vitreous and synapse with the dendrites of cells in (*6*) inner nuclear layer in (*7*) an outer molecular or plexiform layer. A

second plexiform layer (*5*) is formed by the synapses of the axones of the inner nuclear layer and the dendrites of the giant cells in (*4*) the ganglionic layer, and inner fibrous layer (*3*) includes the axonic process of the giant cells as they bend abruptly to take a radial path and converge in the blind spot to exit at the cribriform plate as the fibers of the optic nerve. An inner limiting membrane (*2*) and an outer limiting membrane (*1*) complete the ten coats of the retina. The last two represent a part of the glial fibrous framework formed by the sustentacular cells of Müller.

The rods measure 60 x 2μ; the cones 30 x 7μ. The rods contain rhodopsin or visual purple which undergoes bleaching under light. Brightness is mediated by the rods; color by the cones. The rods are twenty times as numerous as the cones, numbering 130,000,000. Cones, only, occur in the fovea, point of visual acuity.

The lens is an elastic biconvex body with a transverse diameter of 9 mm. and a polar axis which may be varied from 3.7 to 4.4 mm., by the state of tension of the ciliary muscles. It is both avascular and without nerves. Its index of refraction is 1.36. It is purely epithelial in structure, being derived from a hollow ectodermal vesicle whose anterior surface persists as a single layer of cuboidal epithelium, continuous at the equator with a complex thickened posterior body composed of elongated ribbon-shaped lens fibers arranged in concentric lamellae. It is encapsulated in a fibrous non-cellular sheath, continuous with the suspensory ligament (Fig. 85).

The vitreous is a gelatinous, non-cellular, transparent body. It is considered to be a secretion from the surrounding epithelium. It is traversed by the hyaloid canal, a rudiment of the embryonic artery which passed from the central artery of the retina to the posterior pole of the lens to become the transient lenticular artery. The refractive index of the vitreous is 1.33 (Fig. 85).

The nutrient arteries of the eye consist primarily of two sets,

the central artery of the retina and the ciliaries. Both are branches of the ophthalmic, but they form no anastomoses within the bulb. The retinal enters the optic nerve, and at the blind spot divides into four branches which spread out radially over the retina in the layer of nerve fibers. Capillaries penetrate as deeply as the inner molecular layer. This artery may be seen with the ophthalmoscope, and significant data as to the condition of the general vascular bed may be had in various diseases.

Fifteen short ciliary arteries enter the posterior pole and course in the choroid. The two long posterior ciliaries anastomose with the anterior ciliaries which have entered the bulb through the sheaths of the recti muscles. They go to the ciliary body and the iris, and form the circulus arteriosus major and minor, at the peripheral and pupillary borders of the iris, respectively. The venous system parallels the arterial. Four to six cortical veins drain the choroid from a "fountain-like" tributary system, and leave the sclera below the equator.

The extrinsic nerves of the eye include sympathetic, parasympathetic and sensory fibers which reach it through the ciliary nerves. The fifteen short ciliary nerves arise from the parasympathetic ciliary ganglion in the orbit. The long sensory ciliary nerves from the ophthalmic branch of the trigeminal form an annular plexus around the cornea. The sympathetic fibers that control dilation of the pupil include preganglionic fibers from thoracic segments *I*, *II*, *III*, and the postganglionic fibers from the superior cervical ganglion by way of the carotid plexus. The parasympathetic fibers that are motor to the sphincter pupillae and the muscles of accomodation comprise the preganglionic fibers from the Edinger Westphal nuclei (parts of III) and the postganglionic fibers from the ciliary ganglion. The light reflex is mediated through sensory fibers from the retina that pass to the superior colliculus. The latter sends fibers to the Edinger Westphal nucleus.

The neural mechanism for sight includes (1) rod and cone

cells; (2) cells of inner nuclear layer; (3) ganglion cells with axones in the optic nerve which terminate in (*a*) the lateral geniculate body, or (*b*) pulvinar; (4) axones from cells in these nuclei course in the optic radiation, through the internal capsule to the visual receptive centers of the cortex along the calcarine fissure. The fibers from the medial side of the retina decussate in the optic chiasma, hence lesions in the tract beyond this point produce a queer "half blindness" or hemianopsia in both eyes.

The accessory organs of the eye include the lids, conjunctiva, lacrymal glands and lacrymal ducts. The lids are two moveable folds of skin born on the fibrous tarsal plates and enclosing the striate fibers of the orbicularis oculi muscles. At the base of the upper lid is the tendon of the levator palpebral muscle. The palpebral margins are beset by eyelashes, the ciliary glands of Moll and the ducts of the racemose Meibomian glands.

The lacrymal gland is a branched compound tubulo-alveolar gland in the upper and outer part of the orbit. Histologically it has the structure of a typical serous gland. The 10 to 15 ducts are lined with stratified squamous epithelium and open independently into the upper conjunctival sacs. The lacrymal canal begins as two minute pores on the apices of the lacrymal papillae situated near the inner canthus. They open into the lacrymal sac, an expanded portion of the nasolacrymal duct which drains into the inferior meatus of the nose.

Chapter XXXIV

THE EAR

The inner ear is in reality two special sense organs: the cochlea subserves the auditory function; the vestibular portion, including the saccule, utricle and semicircular canals, are concerned with equilibration. The endolymph canal and its sub-dural sac are thought to control the internal pressure of the endolymph (Fig. 87).

Both external and middle ear are accessory to the inner ear. The external ear consists of a pinna, 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. It contains a few obsolete intrinsic striate muscles and three extrinsic muscles. The first part of the auditory canal is lined with skin continuous with that of the pinna, and in which are differentiated large coiled ceruminous (wax) glands. The supporting structure is a tube of cartilage. In the deeper part the skin is thin, free from accessories, and firmly attached to the periosteum of the bony canal (Fig. 87).

The tympanic membrane, 1.1 mm. thick, is almost circular in outline. It has a diameter of 9 mm. It separates the outer from the middle ear. It has an outer layer of stratified squamous epithelium, a middle layer of mesenchymatous substantia propria, and an inner single layer of endodermal epithelium. The latter is continuous with the lining of the tympanic cavity and the Eustachian tube. The base of the membrane is supported by a fibrocartilaginous ring. The manubrial process of the malleus is embedded in the substantia propria from the marginal flaccid area to the central umbo, and

tenses the membrane like a funnel, through the tonus of the tensor muscle. The innervation to the tympanic membrane is by the tympanic nerve. The chorda tympani, while traversing the flaccid area, gives off no branches. The blood vessels are from many neighboring sources.

The tympanic cavity is lined with a delicate mucous membrane throughout. It is a six-sided air containing cavity within the temporal bone. The tympanic membrane forms its lateral wall; the mastoid antrum, the posterior; the Eustachian tube, the anterior; the medial wall is the labyrinthian; the roof is from the temporal bone and the floor is the jugular wall.

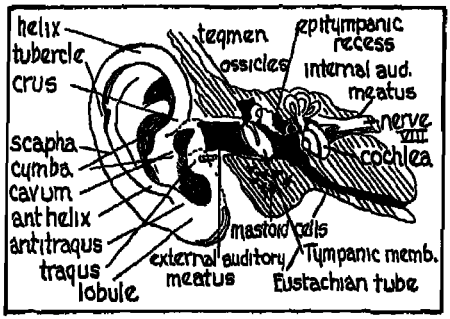

FIG. 87. Semidiagrammatic sketch of the outer, middle and internal ear

The labyrinthian wall is pierced by two openings; the foramen vestibuli (fenestra ovale, oval window) and the foramen rotundum (round or cochlear window). The three auditory ossicles, malleus, incus and stapes (hammer, anvil, stirrup) are suspended by ligaments in such a way as to span the tympanic cavity from the tympanic membrane to the fenestra ovale. Here the foot of the stapes comes in contact with the perilymph space of the vestibule. Since the middle ear is in contact with the pharynx through the Eustachian tube, infections frequently extend into this zone and produce a "bulging" ear drum that may require lancing in order to drain.

The inner ear is composed of a membranous and a bony

labyrinth (Fig. 88). The membranous labyrinth is a system of thin-walled, epithelial lined, intercommunicating canals, ducts and vesicles. The bony labyrinth is the bony cast or wall which immediately surrounds the membranous labyrinth. Its form is similar to, but not identical with the latter, since the vestibule is a comparatively large space which surrounds the membranous utriculus, sacculus and the cecal portion of the cochlear duct.

Three semicircular canals occur in each inner ear. Two are vertical; one is horizontal. Each forms approximately two-thirds of a circle. The longitudinal plane of any one is at right angles to that of either of the other two. The superior vertical one crosses the transverse diameter of the temporal bone; the posterior one lies in the longitudinal axis. Each duct opens into the bulbous utricle by an outer spherical enlargement, the ampulla, and by an inner tubular junction. The ampullar portion bears an internal semicircular fold, the crista, in which the lining epithelium takes on a special sensory character. The hair cells, supported by the sustentacular cells, bear tufts of cilia that are embedded in a gelatinous cap, or cupula.

The saccule is a second bulbous enlargement. The delicate utriculo-saccular duct gives rise to the endolymph duct which passes through the temporal bone to end blindly in the sac, lying within the dura. Both utricle and saccule are loosely attached to the vestibular wall by connective tissue derived from the endosteum, but the bulk of the cavity is filled with perilymph. A special sensory spot, the macula acustica, is found within both of these vesicles.

The macula utriculi is 3 x 2 mm.; that of the saccule the same. The epithelium is composed of sustentacular cells and neural cells. The sustentacular cells are cuticulate. The hair cells are lodged in the interstices at the free ends of the sustentaculars. They bear tufts of fine non-motile cilia held together by cement substance. Each cell also bears a flagellum. The

whole surface is covered by an otolithic membrane 22μ thick composed of a gelatinous substance into which the hair cells penetrate. The outer layer is filled with small crystals of calcium carbonate 0.3 to 5μ in length.

The cochlear duct is practically isolated from the remainder of the membranous labyrinth, being connected only through a narrow ductus reuniens. It is a narrow spiral canal, triangular in cross section, making two and one-half turns. It begins with a blind vestibular cecum and ends in a small blind cupular cecum. It bears a special relation to the perilymph space. The latter is divided into two ducts—the scala vestibuli above and the scala tympani below. These two are separated by a septum composed of (1) osseous spiral lamina, (2) the membranous spiral lamina, (3) the lateral spiral ligament, and bearing on the outer half of its upper surface the cochlear duct. Unlike the cochlear duct, the scala tympani and scala vestibuli do not end blindly at the top of the spiral, but communicate through the helicotrema. At the lower end the scala vestibuli communicates with the vestibule while the scala tympani ends blindly at the foramen rotundum. Both scala are fibrous and lined with simple squamous epithelium (Fig. 88).

The cochlear duct is called the scala media because of its position relative to the perilymph ducts. It presents a lateral, basal and upper wall. The upper or vestibular wall is the extremely thin Reisnner's membrane, composed of the vestibular connective tissue and the simple cochlear epithelium. It extends from the middle of the upper half of the spiral ligament to the limbus. The lateral wall is backed by the spiral ligament, a thickened periosteum. The epithelium is of several layers and shows irregular prominences due to the underlying blood vessels. Hence it is called the stria vascularis and its supposed function is to secrete endolymph. The basal wall is very complex, including the limbus, basilar membrane, tectorial membrane and the Organ of Corti.

The limbus is a special thickening of the periosteum of the

outer margin of the bony lamina. It falls away sharply at the margin of the basilar membrane to form the internal spiral sulcus. Its fibers are radially arranged and as seen from above

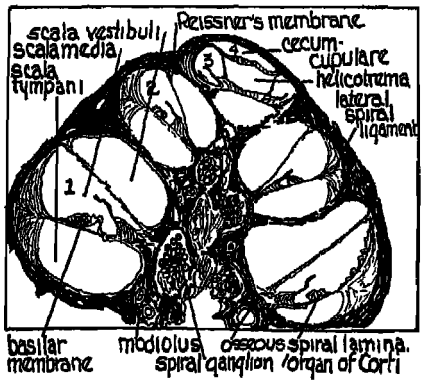

FIG. 88. Polar section through the cochlea of a guinea pig

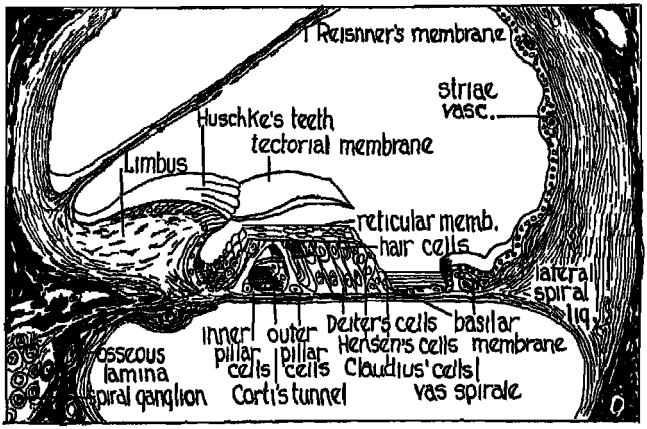

FIG. 89. Stereogram of the cochlear duct to show the relation of the reticular membrane to the sustentacular cells and the "hair" cells, and of the tectorial membrane to the limbus.

present a series of fine ridges, the auditory teeth of Huschke. The overlying epithelium is columnar and the cuticle is continuous with a special cuticulate membrane, the tectorial

membrane, which bridges over the internal sulcus to rest lightly upon the hair cells of the Organ of Corti.

The basilar membrane is continuous from the tympanic lip of the limbus to the crest of the spiral ligament. It shows a series of fine radial fibers, the auditory strings, which vary in length from the base to the cupolo from 64 to 480μ. The epithelium resting upon the basilar membrane has been divided into two zones—the zona pectinata covered by the simple cells of Claudius, and the zona tecta, forming the Organ of Corti (Fig. 89).

The Organ of Corti presents four cell types—three sustentacular and one of sensory epithelium. The sustentacular cells are the pillar cells, Deiter's cells and Hensen's cells. The outer and inner pillar cells form Corti's arches and enclose Corti's tunnel. Four rows of Deiter's cells bear long flanged cuticular processes which fuse at their outer ends into a reticular plate. The outer sensory hair cells are short cylinders which lie "nested" between the fusiform ends of Deiter's cells. The terminal hairs project through the openings in the reticular membrane and are "played upon" by the vibratory tectorial membrane. The inner row of hair cells is pressed between the inner pillar cells and the border cells. Hensen's cells are the outer border crest cells and are continuous with the low epithelium composed of Claudius's cells.

Bipolar nerve cells form a spiral ganglion which rests within the bases of the bony spiral lamina. Their dendritic processes pass through the foramina nervosa of the basilar membrane and arborize around the sensory hair cells. Their axones pass by way of the modiolus to form the cochlear division of the auditory nerve which passes through the internal auditory meatus to reach the cochlear nuclei in the medulla.

A rather complex blood supply is derived from the labyrinthian branch of the inferior cerebellar artery.

Chapter XXXV

THE SPINAL CORD

The spinal cord is a solid, firm, pliable, white cylinder, approximately 18 inches in length and ½ inch in diameter. It shows two enlargements—a cervical and a lumbar, associated with the entrance of the large plexuses from the arms and legs. It is continuous with the medulla at the base of the skull. It does not extend the full length of the vertebral canal but at the level of the second lumbar vertebra tapers into the thread-like filum terminale which together with the numerous spinal nerves constitute the cauda equina (horse's tail). Thirty-one pairs of spinal nerves arise from the spinal cord in segmental fashion and pass by way of the vertebral foramina to the somatic musculature and the overlying segmental skin areas. Each nerve is composed of a dorsal ganglionated sensory root and a ventral motor root (Fig. 90).

The cord is encased in a dural sheath, separate and distinct from the periosteal lining of the vertebrae by a layer of extradural fat and a venous plexus. The subarachnoid space is rather extensive. It is filled with cerebrospinal fluid maintained at a pressure of 30 mm. The cord is supported within this space by the lateral denticulate ligaments.

The cord is bilaterally symmetrical. It shows an anterior median fissure and a posterior median sulcus occupied by a pial septum. A distinct posterior lateral sulcus marks the line of entrance of the dorsal roots and an indistinct anterior lateral sulcus accompanies the exit of the ventral roots. Transections show a central gray H surrounding a canal of microscopic size, closed at the caudal end but continuous with the fourth ventricle at the cephalic end. The arms of the H

are designated as the anterior or posterior horns (cornuae) while the parts of the connecting bar are the anterior and

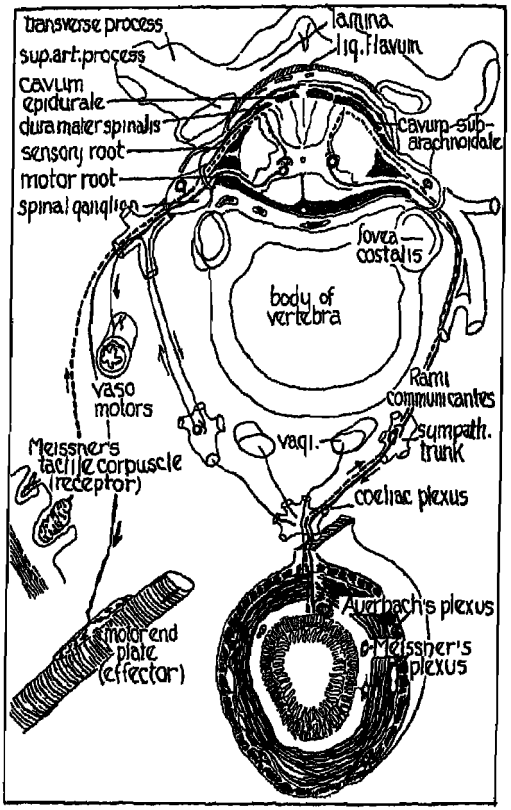

FIG. 90. Diagram showing the relation of the spinal cord to the vertebral canal, the manner of exit of the spinal nerves, the position of the ganglia and their relation to the mixed nerves. On the left the cells concerned with effecting a simple reflex are represented; on the right the mechanism of a visceral reflex is indicated.

posterior gray commissures according to their relation to the central canal (Fig. 91).

The gray substance of the cord is composed of a neuropile made up of scattered nerve cells and nerve processes, a few

glial cells and an unmyelinated glial substance. Of the nerve cells three principal types are recognized: (1) the large multipolar motor cells in the anterior columns that give rise to the anterior root of the spinal nerves; (2) smaller motor cells in the intermedio-lateral columns that belong to the autonomic system and mediate the visceral reflexes; (3) the small rounded sensory association cells (Neurone II in the sensory chain) in

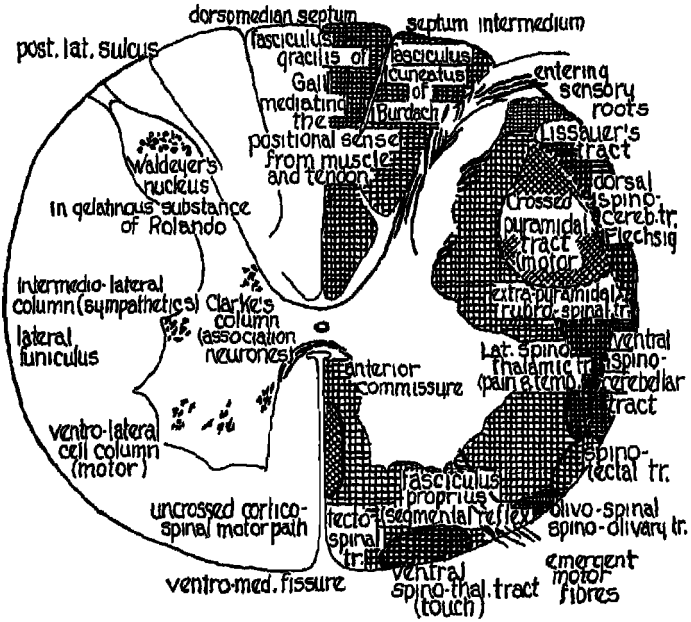

FIG. 91. Diagram presenting the more significant cell columns and fiber tracts in the spinal cord.

the nucleus dorsalis (Clarke's column), that transmit stimuli to higher levels (Fig. 91).

It is in the gray substance that the axones of the ganglion cells of the dorsal roots synapse about the dendrites of the motor cells and provide a mechanism for a simple reflex (Fig. 90). Synaptic associations are also formed with association cells that conduct stimuli to the brain. Secondary associations

are also effected between the pyramidal cells of the cortex and the motor cells of the cord by which volitional movements are carried out, or reflexes modified or suppressed.

The gray matter of the cord is surrounded by white matter, divided into anterior, posterior and lateral columns. These columns are made up of ascending and descending nerve fibers with their sheaths of myelin. Some few fibers are naked. The gray and white substances are discrete except at the neck of the posterior horns where a reticular formation is produced by an admixture of white and gray. The apical portion of the posterior gray horn is made up of a special variety of matter known as the gelatinous substance of Rolando (Fig. 91).

Pathological lesions within specific parts of the white columns early led to the hypothesis that they were composed of specific fiber tracts mediating specific functions. Thus the observed lesion in the dorsal columns in locomotor ataxia was accompanied by loss of positional sense. Experimental hemisection of the cord showed loss of pain and temperature sense on the opposite side; loss of positional sense, exaggerated reflex and loss of volitional control on the same side. Neurologists, by following the course of degeneration of cut fibers, have been able to determine whether the tracts are ascending or descending.

The detail is rather complex and belongs to the subject of neuro-anatomy, but the essential topography involves only ten tracts; two volitional and two reflex descending motor paths and six ascending sensory tracts (Fig. 91, right).

(1) A principal motor tract is the "pyramidal" tract, so-called because in the brain stem it makes up the bulk of the pyramids. The fibers of this tract are the axones of the Betz cells lying in the deeper layers of the cerebral cortex in the "motor" area along the precentral gyrus bordering the fissure of Rolando. These fibers course through the internal capsule, cerebral peduncles, pyramids and decussate or cross to the opposite side in the medulla, to descend in the deeper portion

of the lateral columns of the cord. They establish synaptic relations with the dendrites of the "motor cells" in the anterior horn and control volitional movements (Figs. 91–93).

(2) An "uncrossed" pyramidal tract is composed of a small bundle of fibers that fail to decussate in the medulla and pass caudally in the anterior columns until they approximate their destination, when they suddenly cross to the opposite side in the anterior white commissure (Fig. 91).

(3) An "extra-pyramidal" motor reflex complex has a primary neurone in the cortex, a secondary neurone in the corpus striatum with fibers in the anterior columns.

(4) The cerebello-rubro-spinal path is a reflex tract of three neurones: I, from the Purkinje cells of the cerebellum to the dentate nucleus; II, from the dentate to the Nucleus Rubra in the mid brain; III, rubro-spinal fibers decussate and descend in the lateral columns just ventral to the pyramidal tract. They control muscular coördination, muscle tone and equilibration. Accessories are the bulbo-spinal, the tecto-spinal and the vestibulo-spinal tracts.

The ascending sensory paths are: (1) the ventral spinothalamic tract (touch); (2) lateral spinothalamic tract (pain and temperature); (3) dorsal spinocerebellar, and (4) ventral spinocerebellar (musculo-skeletal reflexes); (5) fasciculus gracilis, and (6) fasciculus cuneatus (positional sense). The last two differ from the remaining in that they represent the axones of some of the cells in the dorsal ganglia that enter the spinal cord in the dorsal roots and ascend in the posterior columns to reach the nucleus gracilis or nucleus cuneatus at the base of the brain (Fig. 91–93). They mediate the muscle, joint and positional sense. Two additional neurones complete the tract; nucleus cuneatus to thalamus,—thalamus to sensory post central gyrus of the cortex (Fig. 93).

The "touch fibers" arise from cells in Clarke's column, cross the median plane in the anterior commissure and ascend in the ventral funiculus to end in the thalamus. A third neurone

passes to the sensorium from the thalamus by way of the internal capsule. The primary neurone in the system is a dorsal ganglion cell. Its axone enters the cord by the dorsal root and synapses about cells at its own level or passes to a higher level and "filters" through gradually (Fig. 91).

The "pain and temperature" fibers arise from cells in Clarke's column, cross in the anterior commissure to the opposite side at the same level at which the primary neurone enters the cord, course up the cord in the lateral columns to eventually reach the thalamus. Neurone III is from the thalamus to the sensorium. Neurone I is again a dorsal ganglion cell. Touch, pain and temperature rise to a functional conscious level; the positional sense is ordinarily not recognized unless it is interfered with. The two spinocerebellar tracts function at an unconscious reflex level.

The dorsal spinocerebellar tract (direct tract of Flechsig) is made up of fibers that have their origin in cells in the nucleus dorsalis of the same side. They pass to the cerebellum by way of the restiform body, and end in the cortex of the vermis (Fig. 91).

The ventral spinocerebellar tract (Gower's tract) is made up of fibers that originate in cells of the dorsal nucleus of the same and opposite side. They pass to the cerebellum in the lateral columns, through the medulla and pons to join the brachium conjunctivum (anterior cerebellar peduncles) to terminate in the vermis and nucleus fastigii (Fig. 91).

Chapter XXXVI

THE BRAIN

The brain is a massive, soft, friable organ weighing 1375 grams. It rests upon the floor of the cranium in three fossae. It practically fills the cavity of the skull, being bathed by a thin layer of cerebrospinal fluid contained in the subdural space. The dural septa lend support to the flaccid substance, as the falx cerebri, lying in the longitudinal cerebral fissure between the two hemispheres, and the tentorium, a transverse shelf between the cerebrum and the cerebellum.

Developmentally the brain consists of three portions: a fore, mid and hind brain; represented by three vesicles which form from the simple primitive neural tube. The latter arises by the invagination of the neural plate from the surface epithelium and hence is ectodermal in origin. The three vesicles differentiate into five major parts: (1) telencephalon, (2) diencephalon, (3) mesencephalon, (4) metencephalon, (5) myelencephalon. The telencephalon develops further into the cerebral hemispheres above; the corpora striata laterally, and the olfactory rhinencephalon below. The cerebral hemispheres enclose the lateral ventricles.

The diencephalon (twixt-brain) bears the pinealis above; its lateral walls are the thalami, and its floor the hypophysis, tuber cinereum and mammilary bodies. Its enclosed slit-like cavity is the third ventricle which communicates with the lateral ventricles by the foramina of Munro.

The mesencephalon (midbrain) encloses the narrow aqueduct of Sylvius. Above, it bears the two pairs of quadrigeminal bodies; below, the cerebral peduncles.

The metencephalon is formed of the cerebellum above and

the pons below. Together with the medulla oblongata, it encloses the fourth ventricle. The medulla is continuous with the cord (Fig. 92).

The brain, like the cord, is composed of white and gray matter, but the arrangement in the former is much more highly

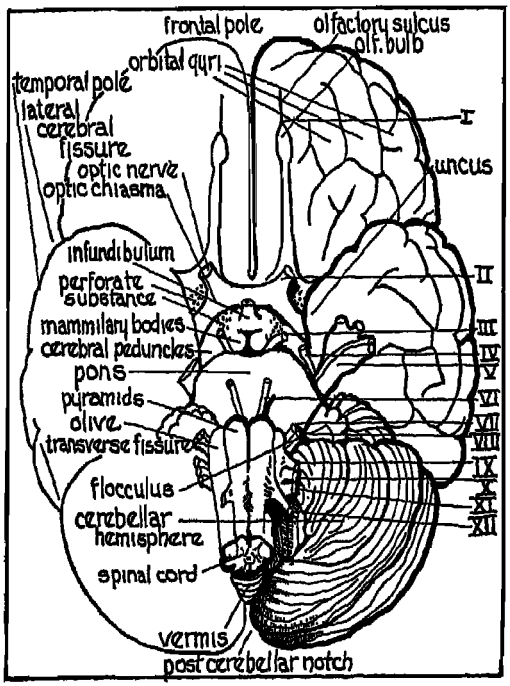

FIG. 92. Sketch of the base of the brain with the cerebral nerves attached. Note particularly the positions of the infundibular stalk of the hypophysis, the cerebral peduncles (basis pedunculi), the pons, the pyramids and the olives.

specialized, associated as it is with the conscious centers, reflex centers and centers for the twelve pairs of cranial nerves. The latter are: (1) olfactory, (2) optic, (3) oculomotor, (4) trochlear, (5) trigeminal, (6) abducens, (7) facial, (8) auditory, (9) glossopharyngeal, (10) vagus, (11) accessory, (12) hypoglossal (Fig. 92).

The most conspicuous feature of a transection of the lower medulla is the decussation of the pyramids, which pass from

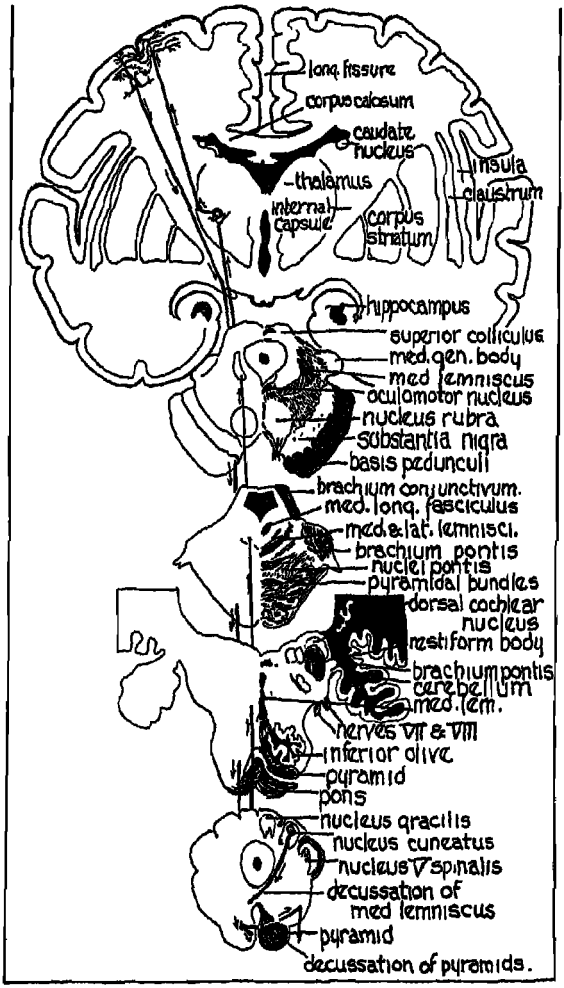

FIG. 93. Semidiagrammatic sketches of five levels through the brain, showing the more important nuclear centers and the fiber tracts. The pyramidal (motor) and a sensory tract are indicated on the left.

their lateral position in the cord to the anterior column of the opposite side (Figs. 92–93). At slightly higher levels occur the

nucleus gracilis, nucleus cuneatus, and spinal nucleus of the trigeminal nerve. Fibers from the nucleus gracilis and cuneatus sweep down and around the central gray matter as the internal arcuate fibers and decussate as part of the medial lemniscus (Fig. 93). At its upper ridge, the latter bears the medial longitudinal fasciculus (reflex path for movements of head and eyes). Lateral to the pyramids are the inferior olives. Nucleus XII is in the central gray susbstance surrounding the canal. Its fibers course downward to exit at the lateral border of the pyramids. Above and lateral to the Nucleus XII is the tractus solitarius (VII, IX, X, taste and respiratory control) and its nucleus. At the level where the central canal opens into the fourth ventricle, occur the motor nuclei of X; the nucleus ambiguous (motor IX, X, XI); intercalatus and the restiform body (inferior cerebellar peduncle) formed mainly by the olivocerebellar and the dorsal spinocerebellar tracts (Fig. 93).

At the level of the posterior border of the pons, the dorsal cochlear, medial and spinal vestibular nuclei lie above the restiform body, while the accessory nerve makes its exist below. In sections immediately above this, the auditory (VIII) and facial (VII) nerves leave at the angle between the pons and the brachium pontis while the ventral cochlear and lateral vestibular nuclei border the restiform body. Laterad to the medial lemniscus is the thalamo-olivary tract and the olivocerebellar tract, and the facial nucleus. The longitudinal fibers of the pyramidal tract (corticospinal and corticobulbar) are embedded in the upper part of the transverse fibers of the pons (Fig. 93).

At the level of the brachium pontis (middle cerebellar peduncles) the pons shows a superficial part made up of its transverse fibers and flattened nuclei, and a dorsal or tegmental part which includes the trapezoid body (Neurone II in auditory pathway from inferior cochlear nucleus to inferior colliculus and medial geniculate body), medial lemniscus, thalamo-oli-

vary tract, nucleus of the abducens nerve, superior olivary nucleus, motor and sensory nuclei of the trigeminal. Here the ventral spino-cerebellar tract joins the brachium conjunctivum (fibers from dentate to nucleus ruber and thalamus). In the rostral portion of the pons, the trapezoid body and the striae medullares from the dorsal cochlear nucleus join to form the lateral lemniscus (Fig. 93).

The cerebellum is composed of a median central vermis and two large lateral hemispheres. These are further subdivided into lobes and are folded as long slender convolutions or folia, composed of thin plates of gray matter spread over irregular white centers. They produce secondary and tertiary lamina, which in section give an arborescent appearance. The dentate nuclei lie in the main white mass of each hemisphere. Small accessory nuclei are also present.

All lobules present practically a uniform histological picture (Figs. 93–94). A folium shows a central white and a superficial gray stratum. Fibers are grouped in parallel bundles in the white substance. The cortex presents three zones; a superficial molecular layer; a layer of Purkinje cells; and a subjacent granular layer. The Purkinje cells are conspicuous flask-shaped bodies arranged in single rows spaced at intervals. Profuse dendritic branchings arise from one or more processes and extend to the surface in a single flat plane at right angles to the long axis of the folium. A basal axone passes centrally to terminate in the dentate nucleus. Collaterals may pass backward to synapse about neighboring Purkinje cells, supposedly to provide a mechanism of simultaneous discharge.

The molecular layer is composed largely of the dendritic processes of the Purkinje cells, plus a few scattered basket cells which form pericellular networks about them. The granular layer is made up of many small granule cells, whose axones pass through the Purkinje arbors. They synapse with the terminals of the "mossy" fibers, afferent processes from the spino-cerebellar tract. A second type of afferent fiber is the

"climbing" fiber from the pons, which climb the trellis of Purkinje fibers like a vine.

The mesencephalon shows a central canal surrounded by a central gray stratum. At the level of the inferior colliculus may be seen the entering fibers of the lateral lemniscus (audi-

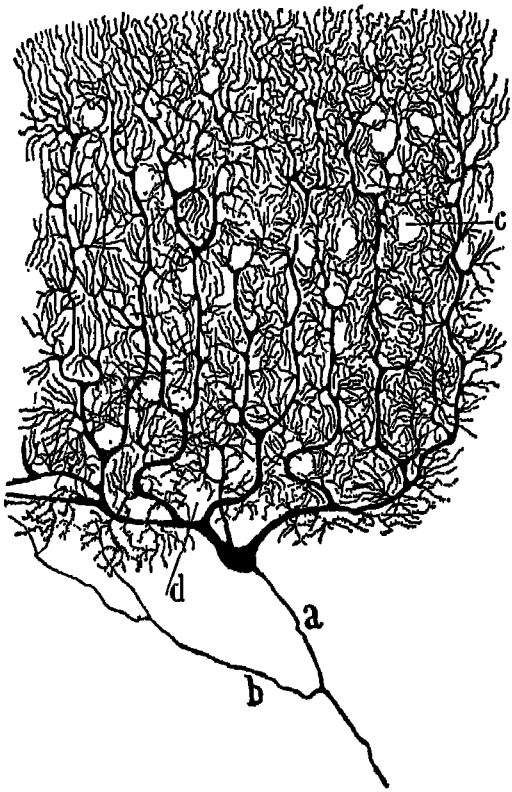

FIG. 94. Purkinje cell from the human cerebellum. *a*, axis cylinder; *b*, collateral; *d*, dendrite. (Method of Golgi.) (After Cajal.)

tory tract from cochlear nucleus to inf. colliculus); the nucleus and fibers of the trochlear nerve; the thalamo-olivary tract and medial longitudinal fasciculus. The great part of the base is occupied by the cerebral peduncles, separated by the interpeduncular fossa. A substantia nigra separates the peduncles from the medial lemnisci. Above the latter is the decussation

of the brachium conjunctivum. At the level of the superior colliculus, the nucleus of the oculomotor nerve lies in the floor of the central gray matter. Its fibers pass around the large spherical nucleus ruber and emerge in the interpeduncular fossa, at the anterior border of the pons. The medial lemniscus is joined by the dorsal spino-thalamic and the ventral spino-thalamic tract in the mesencephalon, bringing all of the main "conscious" sensory paths in close approximation. A central sensory path of the trigeminal nerve also joins it (Fig. 93).

The diencephalon encloses the third ventricle. Its lateral walls are made up largely of the four nuclear masses of the thalami—main sensory relays in the "conscious" pathway. The dorsal surfaces of the thalami are free, forming the floor of the transverse fissure which separates the diencephalon from the overhanging cerebrum represented by the fornix and corpus callosum. Dorso-laterally, the thalamus is bounded by a groove which separates it from the tail of the caudate nucleus. This groove is overlaid by a lamina affixa and bears the vena terminalis, and serves for the attachment of the choroid plexus of the lateral ventricles. The medial surface is set off from the dorsal by the taenia thalami which serve for attachment of the choroid plexus of the third ventricle and is continuous with the epithalamus which includes the habenular trigone, striae medularis and pineal body. The lateral surface of the thalamus is bounded by a broad band of fibers, the internal capsule. Fibers from the thalamus filter out into it as the thalamic radiation and pass to the cerebral cortex. The hypothalamus lies below (Fig. 93).

The medial and anterior thalamic nuclei are olfactory centers, and may also mediate a crude indiscriminate consciousness. The lateral and posterior nuclei are sensory relays in the pathway for pain, temperature, touch and position. The pulvinar and lateral geniculate are in the optic path; the medial geniculate in the auditory path.

The hypothalamus includes the tuber cinereum, the infundibulum and hypophysis, the mammillary bodies. The latter

are nuclei in the olfactory tract and have connections by way of the fornix and the mammillo-thalamic tracts. The optic chiasma which lies immediately in front of the tuber cinereum, is considered a part of the telencephalon. Its fibers sweep upward to terminate in the pulvinar, lateral geniculate body and superior colliculus (Fig. 93).

The cerebral hemispheres are formed by evagination of the lateral walls of the telencephalon. The central cavities are the lateral ventricles. Each hemisphere consists of (1) a ventral rhinencephalon bearing the fibers and nuclei of the olfactory system; (2) a corpus striatum and (3) the dorsal pallium. The corpus striatum is continuous with the thalamus behind. The pallium is markedly convoluted and presents a frontal, parietal, temporal and occipital lobe. A rudimentary lobe, the insula, overlying the corpus striatum, is buried at the bottom of the Sylvian fissure by the overgrowth of the neighboring cortex (Fig. 93).

The two hemispheres are connected by (1) the membranous lamina terminalis and (2) septum pellucidum; (3) anterior commissure (4) fornix, fimbri and hippocampal commissure (5) the corpus callosum. The anterior and hippocampal commissures are fibers in the olfactory pathway. The corpus callosum is a broad thick band at the bottom of the longitudinal cerebral fissure which connects the various portions of the cortex of one side with those of the other by association fibers (Fig. 93).

The corpus striatum is formed of the caudate and lentiform nuclei and the complex compact fiber tract that separates them, the internal capsule. The caudate forms a portion of the lateral wall of the lateral ventricle. It is "tailed" and ends in the amygdaloid nucleus of the temporal lobe. The lentiform nucleus is pyramidal and compact. It lies between the caudate and the insula. Its outer base is the putamen and its inner two lobes form the globus pallidus. A thin outer gray strip, the claustrum, is interpolated between the putamen and the cortex. The internal capsule is of extreme importance

since it contains the sensory fibers from the thalamus to the cortex; the optic radiation from the pulvinar and lateral genic-

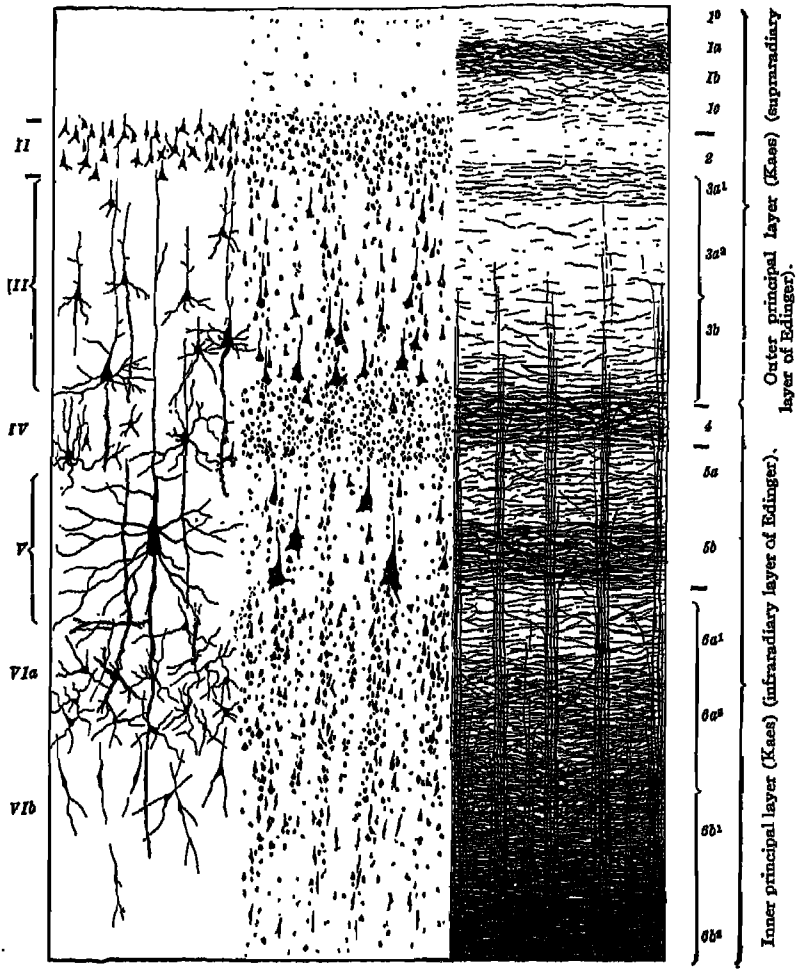

FIG. 95. Relation of the cell and fiber layers of the human cerebral cortex. Left, Golgi method; center, Nissl method; right, Weigert method. (After Brodmann, from Bailey.) *I*, lamina zonalis; *II*, lamina granularis externa; *III*, lamina pyramidalis; *IV*, lamina granularis interna; *V*, lamina ganglionaris; *VI*, lamina multiformis.

ulate body to the calcarine fissure; the acoustic radiation from the medial geniculate body to the transverse temporal gyrus;

the motor fibers of the corticospinal, corticobulbar, the corticopontine tracts (Fig. 93).

The cerebral cortex forms a convoluted gray lamina from 1.25 to 4 mm. in thickness and of about 200,000 square millimeters in extent. It is estimated to contain some 10,000,000,000 cells. The contained fibers are either cortipetal coming from distant cells or cortifugal, passing from local cells. Fibers that pass from one area of the hemisphere to another are association fibers; from one hemisphere to another, commissural fibers; and from the cortex to a lower center are projection fibers (Fig. 93).

Six layers are recognized in the cortex: (1) molecular, (2) small pyramidal, (3) large pyramidal, (4) stellate cell, (5) giant Betz cell, (6) polymorphic cell. By the Golgi method, the cells of the polygonal layer are small, fusiform or stellate with processes which course in the horizontal plane. The small, large and giant pyramidal cells all have a similar structure but vary in size. The small are 10 to 12μ in length; the large 20 to 30μ, and the giant 40 to 60μ. The cells are pyramidal or conical in shape with an axis cylinder arising from the inferior base and giving off a collateral brush. A single coarse dendritic process arises from the polar apex and branches profusely as it extends upward and into the molecular layer. Additional dendritic processes extend from the flange of the base. All bear spiny varicose sprouts. Only the Betz cells of the "motor area" have been definitely traced. Their axones form the pyramidal tract. The "inverted" cells of Martinotti occur in the third layer. They are fusiform in shape and the single axone is directed toward the molecular layer, in which they terminate in a horizontal brush.

The polymorphous cells are irregular or fusiform and angular.

The four outer layers of the cortex are probably receptive and associative in function; the two lower layers cortifugal and commissural. Sensory as well as motor localization has been shown in areas in the cortex, and visual and auditory receptive fields have been well established in aphasia (Fig. 95).

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