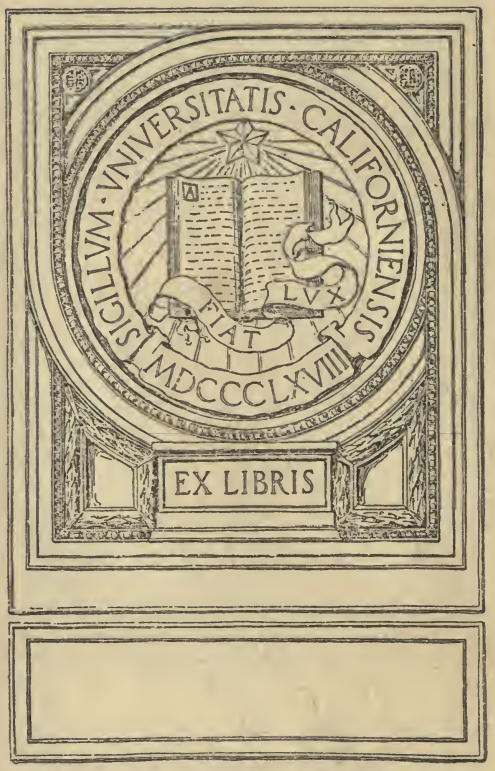
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LESSONS IN

PATHOLOGICAL HISTOLOGY

BY

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PREFACE.

This interesting and intensely practical little book is novel in almost every particular and has no parallel among the books offered to students of medicine.

It bears the same relation to pathologic histology that a "dissector" does to anatomy; it is a self-instructor, teaching the salient features of the tissues studied. It is not a text-book of pathology, nor can the student possibly suppose that it can take the place of one; it is not a hand-book of technic. It is a guide, and a very intelligible one, to the microscopic study of morbid tissues. It may not contain all of the sections that the student is called upon to study—they differ in different institutions—but it contains enough to teach him the correct method, and gives the most important facts, after which new material may be approached without hesitation and with full confidence that the same methods applied will yield the same satisfactory results.

The approach to the diagnosis is always systematically made: The student is first told what should be seen with the naked eye, then what is to be seen with the low-power lens, and finally, if necessary, what with the high-power lens.

Particular fields for examination with the higher powers are frequently indicated upon the drawing by lines inclosing small squares.

When the book is opened, the right-hand pages are found to show the beautiful drawings of M. Bessin, to which in this American edition have been added additional ones by Mr. Erwin Faber, so drawn as to correspond with the originals, from which it is impossible for one not in possession of the French copy to differentiate them. On the left-hand page is a text correlated with the illustration, and telling how one should proceed in studying it. Although brief, this text is descriptive, critical and diagnostic, and transforms the book from an atlas to a guide by being of a value equal to the illustrations.

J. McF.

LESSONS IN PATHOLOGICAL HISTOLOGY.

INTRODUCTION

At the beginning of this little book, intended to direct the student in his first steps in the study of pathological histology, are brought together a few elementary facts about practical microscopy. It is done as briefly as possible, in the hope that it will be appreciated by these for whom it is intended.

Certain details of histological technic are important in the successful interpretation of microscopic preparations.

Only the most important of them will be mentioned, especially as nearly all of the sections have been fixed and stained in the same manner.

It is indispensable to follow certain rules in the interpretation of histological slides, and it is through lack of knowing and observing them that beginners, too soon employing high-power lenses, lose themselves in the reading of the sections and commit the grossest errors of interpretation.

A histological diagnosis ought to be conducted much as a clinical diagnosis at the bedside. It is only after having exposed the patient and examined him in his entirety, that the clinician goes on to the successive methods of inspection, palpation, auscultation, etc.

Methods of Using the Microscope and Interpreting the Section.—A microscope consists of a stand, an optical system (objectives and oculars), and an illuminating apparatus comprising an Abbé parabolic condenser, a mirror and an iris diaphragm.

The *Abbé condenser* should not be employed with very low-power lenses whose magnification does not exceed that of a hand lens. Besides the diminution of the light that results

from its employment in such cases, images of the window, the wall and other objects are apt to appear in the field of vision. The condenser is, therefore, to be removed from the optical axis with such powers. It is, however, necessary with middle- and high-power lenses, but it ought to be placed at some distance from the object in order that the best illumination be obtained and distinctness of vision secured. The higher the magnification, the nearer the condenser must be brought to the stage; with an oil-immersion lens it should be in immediate contact with the slide.

The *mirror* has plane and concave sides, each of which subserves a special purpose. The concave side should be used when the source of light is small, as in artificial light; the plane side for natural light.

The *iris diaphragm* serves to cut out the excessively oblique rays of light when high-power lenses are used. How widely it should be open or how tightly closed is a matter that can only be learned by experience. As a matter of fact, the student should open and close it more or less with each change of magnification and with each different object examined, as with different degrees of light different structural details are brought out.

The Objectives and Oculars.—The microscopes used by students vary in different laboratories, some being provided with two, some with three objectives, according to the different character of the work to be done. When this is histological only, two objectives—a low power and a high power—are all that are required; if bacteriological or cytological work is to be included it may be necessary to add another—higher power—or even an oil-imersion lens. It will be supposed that the student using this manual finds his equipment to consist of two objectives—a low power and a high power. He usually also receives two oculars by which to reach the extremes of high and low powers within the range of his objectives. In general, however, it is best to work only with the low-power ocular as it affords the best definition.

The Low-power Objective.—It is with this magnification that the study of every microscopic section ought to be begun. It gives a general, that is, a topographical view of the whole section, and enables the different component tissues and their

relations to be determined, and the parts requiring further examination to be recognized. For example, in a section of a uniform structure, such as the pulmonary tissue, the low power enables sections of the bronchi and bloodvessels quickly to be found, and if there be any deeply-colored masses, such as bronchopneumonic areas or tubercles present, they quickly catch the eye. Again, in sections of any part of the wall of the alimentary tract it easily discovers any breach of surface continuity such as constitutes an ulceration.

The examination with the low-power lens ought, therefore, be continued for some time as it enables the trained eye not only to discover the organ concerned, but also to make a presumptive diagnosis of its principal lesions.

The Medium-power Objective.—Should there be a medium-power lens, its use will in most cases suffice to complete the diagnosis.

The High-power Objective.—This should only be employed to complete the observation. It shows but a very circumscribed field of the section, and its chief uses are for defining the cytological and nuclear structural details—protoplasmic granules, vibratory cilia, mitotic figures, etc.

THE ELEMENTARY PRINCIPLES OF HISTOLOGICAL TECHNIC.

Only the methods of fixing and staining indispensable to the interpretation of the sections described in this manual will be mentioned.

1. **Fixation.**—Pieces of tissue selected for histological examination should be immersed in a preserving fluid for the purpose of *fixing* their structure by coagulating the albumins with the least possible modification of their cells. According to the size and fixation of the blocks of tissue will their cellular characteristics be well preserved.

(*a*) Pieces of tissue obtained from surgical operations and fixed upon the spot may be regarded as in a state of perfect preservation.

(*b*) Pieces of tissue taken from autopsies made twenty-four hours after death will be found in a very unequal state of preservation. They have not only been subjected to the

disadvantages of putrefaction, but also to the action of autolytic enzymes, whose effects are especially marked upon the alimentary mucosa. The adrenal body and the cerebellum also rapidly show the effects of postmortem change.

In all such cases care must be taken not to confuse the results of the *postmortem changes* with the *pathological lesions*. In general, the cadaveric or postmortem changes are uniformly distributed throughout the entire section, all of the elements of the same kind being similarly affected and about to the same degree.

Among the fixatives most commonly used the following may be mentioned.

(*a*) *Formaldehyde.*—It is employed in a dilution of 1 part of the commercial 40 per cent solution with 9 parts of water.[1] It also forms the base of such other fixatives as Bouin's solution which is made up of 75 parts of a saturated solution of picric acid, 20 parts of formaldehyde and 5 parts of acetic acid. This solution, however, frequently imparts an undesirable yellowish color to the tissue.

(*b*) *Corrosive Sublimate.*—This may be employed in the form of a solution composed of corrosive sublimate 3 parts, acetic acid 1 part and distilled water 100 parts. It also enters into the composition of numerous other fixatives such as Domimici's solution which is made of a saturated aqueous solution of corrosive sublimate 100 cc, formaldehyde 15 cc and enough tincture of iodine to give the fluid a port-wine color.

Whenever solutions of corrosive sublimate are used as fixatives it is necessary to wash the tissue, after twelve to twenty-four hours' immersion, in running water for twenty-four hours. The chemical has the disadvantage of forming a combination with the albumins of the tissue which subsequently appears in the form of a black acicular crystalline deposit. This sometimes causes confusion with blood and other pigments naturally present, though its acicular form ought to enable it to be easily recognized. It is, however, best to remove it by adding tincture of iodine to the alcohols subsequently used for dehydration.

2. **Imbedding and Cutting.**—After fixation the blocks of tissue are subjected to washing, progressive dehydration by passage through alcohols of increasing strength, and are finally imbedded

[1] Better results result from the use of physiological salt solution instead of water as the diluent.

in some substance such as paraffine or celloidin that subsequently solidifies sufficiently to permit them to be cut into sections from 5 to 10 microns in thickness, with a microtome.

If the edge of the microtome knife is uneven the sections may present a striated appearance which deforms their structural elements. The parallel direction of these striæ enables them to be recognized as artefacts.

The colloid substance of the thyroid body commonly presents a "picket fence," or palisade appearance, but that is an artefact that depends rather upon the peculiar fragility of the substance itself than upon defects in the edge of the knife.

3. **Staining.**—The sections, fastened to the slides, are stained in various ways, of which only these most commonly used will be mentioned, as it is most important to simplify the technic as much as possible for beginners, and employ as nearly as as possible the same methods for all of the different tissues described.

Hematoxylon.—This is a basic dye extracted from logwood. It stains the nuclei of the cells a deep blue color.

Eosin.—This is an acid anilin dye. It stains connective-tissue fibers a pale rose color and striated and unstriated muscular fibers a bright red.

Van Giesen's Stain.—This consists of a solution made up as follows:

1 per cent aqueous solution of acid fuchsin	5 cc
Saturated aqueous solution of picric acid	100 cc

It is used as a counter-stain with iron hematoxylon. With the combination vascular connective tissue is stained intense red by the acid fuchsin, the protoplasm of the cells is colored yellow by the picric acid and the nuclei are black from the iron hematoxylon.

The method is especially appropriate for the demonstration of the vascular connective tissue in the study of the various scleroses—chronic nephritis, cirrhosis, pancreatitis, etc.

Acid Orcein.—This stain is composed of:

Orcein	1 gr.
Hydrochloric acid	1 cc
96 per cent alcohol	100 cc

The orcein has an elective affinity for the elastic tissue which it colors brown-black.

1. **Low-power Lens.**—The pulmonary tissue presents an alveolar appearance that is recognizable even to the naked eye, and depends upon the presence of numerous spaces, the *pulmonary alveoli*, of very similar size and shape in the normal lung.

These air spaces, irregularly lozenge shaped, are bounded by sinuous walls, the *interalveolar septæ.*

Here and there, as in the center of the drawing, bloodvessels and air tubes are seen cut transversely or longitudinally, and for the most part grouped together in the *connective-tissue trabeculæ* or *broncho-vascular axes* of the pulmonary structure.

Black patches, *anthracotic accumulations*, especially distinct in the neighborhood of the bronchial tubes, are almost constantly present in the lungs of the adult and the aged, and in the reading of the microscopic sections form a precious element in making the differential diagnosis of the organ. The lungs with their associated lymph nodes are the organs most frequently pigmented with carbon particles.

The alveoli, broncho-vascular axes and anthracotic collections form a triad that should always be looked for with care in recognizing the pulmonary parenchyma.

If the section reaches to the external surface of the lung it may include the pleura which is composed of a layer of vascular connective tissue covered by endothelium.

2. **High-power Lens.**—The structural details now become more distinct. The interalveolar septæ seem to be composed of cells of a shape varying in different cases. In lungs obtained at autopsy some of them are often found to have detached and to lie free in the air spaces. In certain areas the cells seem to be gathered together in masses—an appearance that results from the tangential sectioning of the wall of one or several alveoli.

In the interalveolar septæ there are capillary bloodvessels which in the normal state contain only one or two red blood corpuscles.

If the section be stained with orcein (as in Fig. 2) elastic fibers can be seen in the interalveolar septæ in the form of fine filaments of dark brown or black color, insinuating themselves between the cells and the capillaries and passing from one alveolus to another.

Cartilage in the bronchial wall.

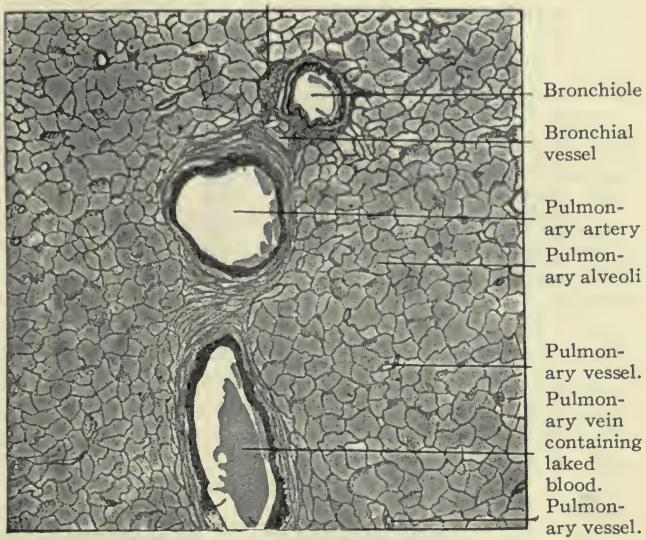


Fig. 1.—Normal lung. Lung of a suicide.

Stained with hematoxylon and eosin. Magnified 25 diameters.

This shows the characteristic triad upon the finding of which the diagnosis of the pulmonary tissue depends—the pulmonary alveoli, the vessels, which in this case contain some laked blood, and the bronchial tube with its supporting cartilage. The anthracotic accumulations cannot be easily recognized with this magnification.

In the neighborhood of the broncho-vascular apparatus the high-power lens enables one to recognize:

1. The *bronchioles*, or air tubes, with a cylindrical epithelial lining supported upon a connective-tissue wall, at the periphery of which, in those of middle and large size, there may be cartilaginous plates. These appear blue violet in sections stained with hematoxylon and eosin.

2. The *bloodvessels* which are easily recognized by their smooth endothelial lining, which contrasts strongly with the columnar epithelium so distinctly seen in the bronchial tubes.

The branches of the pulmonary artery can be distinguished from those of the pulmonary veins by the thickness of their walls, and by the fact that they are usually empty while the veins usually contain blood.

NOTE.—The anatomical unit of pulmonary structure is the *lobule*; but for its demonstration special methods of preparation—insufflation, injection of coagulable substances, serial sections, etc.—must be resorted to, so that it does not clearly appear in microscopic sections. It is of interest in enabling the morphological structure of the lung to be understood, but has very little importance in pathological histology.

In any section of a diseased lung the lesions of the alveoli, the bronchioles, the interalveolar septæ and the vessels are the important features for study, their lesions, through synthesis of the findings, enabling a diagnosis of the condition to be reached.

The pulmonary alveolus ought to be regarded as the unit of structure in pathological histology. It may be compressed or collapsed as in the fetus (*atelectasis*), distended to bursting (*emphysema*), or filled with morbid products (edematous fluid blood, fibrin, pus, etc.), in edema, infarction, pneumonia, or bronchopneumonia (*alveolitis serosa, hemorrhagica, fibrinosa, purulenta*, respectively). The same is true of the bronchial tubes.

It is only after study of the various elementary lesions and their distribution in the section that the whole can be interpreted, purely contingent lesions cast aside and proper evaluation given the most important.

The condition of the pleura should also be considered if the surface of the lung be included in the section.

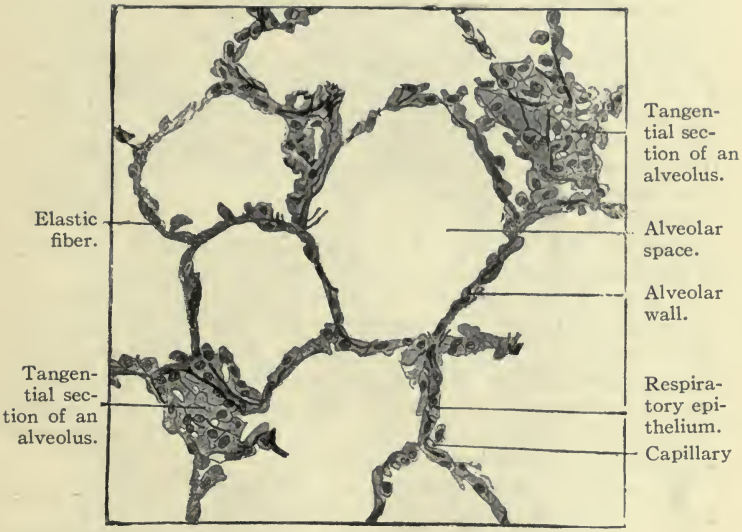


Fig. 2.—Normal lung. Lung of a suicide.

Stained with acid orcein. Magnified 250 diameters.

The reticulum of elastic fibers is shown colored black by the orcein. At two points, above and to the right, and below and to the left, the alveolar epithelium, seen in full face instead of in profile, seems to occur in plates. This is the result of tangential cutting of the section.

PULMONARY EMPHYSEMA AND CONGESTION.

The Diagnosis of the Organ.—This is easy to make: One recognizes the pulmonary alveoli and sees in the center of the drawing a section of a broncho-vascular axis containing a bronchial tube with its lining of cylindrical epithelial cells. A pulmonary artery and vein and patches of carbon particles are also shown.

The Diagnosis of the Lesion.—That which at once strikes the observer is the great size of certain of the air cells. There are all intermediate stages between normal alveoli and enormous cavities. Many of the alveolar walls have ruptured (emphysema), though they appear distinctly thicker than in the normal lung because of distention of the capillaries (*congestion*).

The air cells are almost entirely empty (contain air), but in some a few red blood corpuscles may be seen.

A higher power lens permits the alveolar walls to be studied. In sections stained with hematoxylon and eosin, they are almost entirely composed of extremely dilated capillaries containing numerous red blood corpuscles. Sometimes they make hernial protrusions into the alveolar cavity, and even rupture here and there, permitting the escape of the corpuscles into the air cells (*hemorrhagic alveolitis*).

The nuclei visible in the section belong, for the most part to the endothelial cells of the capillaries.

It is scarcely possible to find any of the alveolar epithelial cells, either because of pathological alteration (desquamation or degeneration), or because of cadaveric alteration (defective fixation of very fragile elements).

In sections especially stained with orcein (Fig. 5, B), which brings out the elastic-tissue network of the pulmonary structure, it is possible to study its alterations—fragmentation and extension—which are very important in emphysema.

The elastic tissue of the alveolar wall is found to be composed of delicate fibrillæ, colored black, mostly cut longitudinally and following a course that spreads out according to the obliquity of the section. To the right in the drawing a black stippling results from transverse section of the fibers. To the left a capillary in the alveolar wall distinctly shows its elastica. The interalveolar walls are stretched and thinned.

There are no changes in the microscopic appearance of the bronchial tubes.

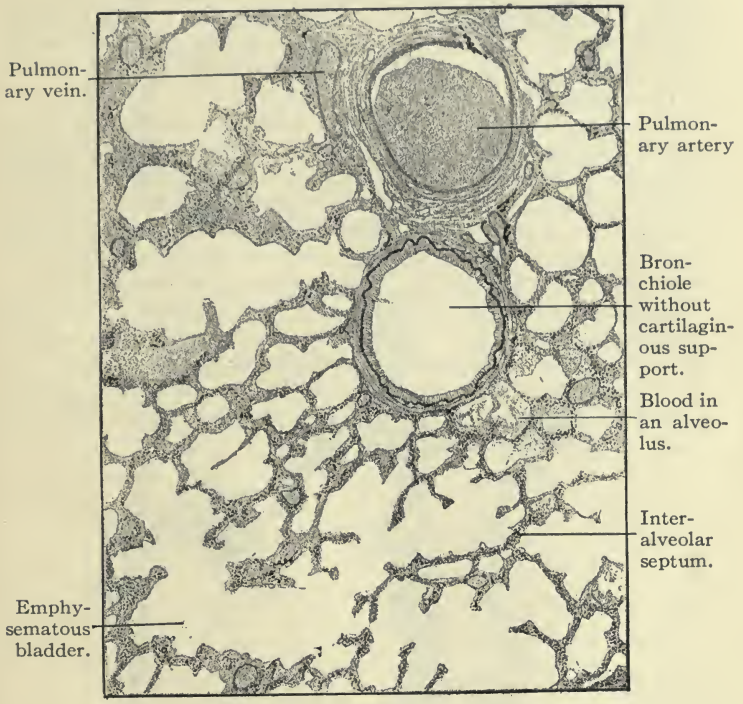


Fig. 3.—Pulmonary emphysema and congestion.

Staining with hematoxylon and eosin. Magnified 20 diameters.

It is the lung of an old man with chronic emphysema and congestion. The unequal size of the pulmonary alveoli, the rupture of the interalveolar septæ and the thickness of the alveolar walls from distention of the capillaries are to be particularly noted.

All of the bloodvessels, large and small, are dilated and distended with blood and show as bright red dots in the section. About the larger vessels there is a slight increase in the connective tissue (beginning sclerosis).

The condition corresponds with what is called *essential emphysema*, by which is meant that neither in the gross morbid specimen nor in the microscopic section can any explanation of the distention of the air cells be found.

In subsequent descriptions, and especially in that of bronchopneumonia, it will become evident that though emphysema sometimes occurs as a primary lesion, it also occurs in association with other important conditions such as fibrinous alveolitis, purulent alveolitis, hemorrhagic alveolitis and edema, which take precedence over it in importance in the interpretation of what is seen in the section and to which it is secondary.

Résumé.—Pulmonary emphysema with beginning sclerosis and intense congestion. The latter may be referred in part, if not altogether, to the agonal condition of the circulation. It is common in lungs removed at autopsy, and no importance should be attributed to it unless it is found in association with other conditions evincing its priority.

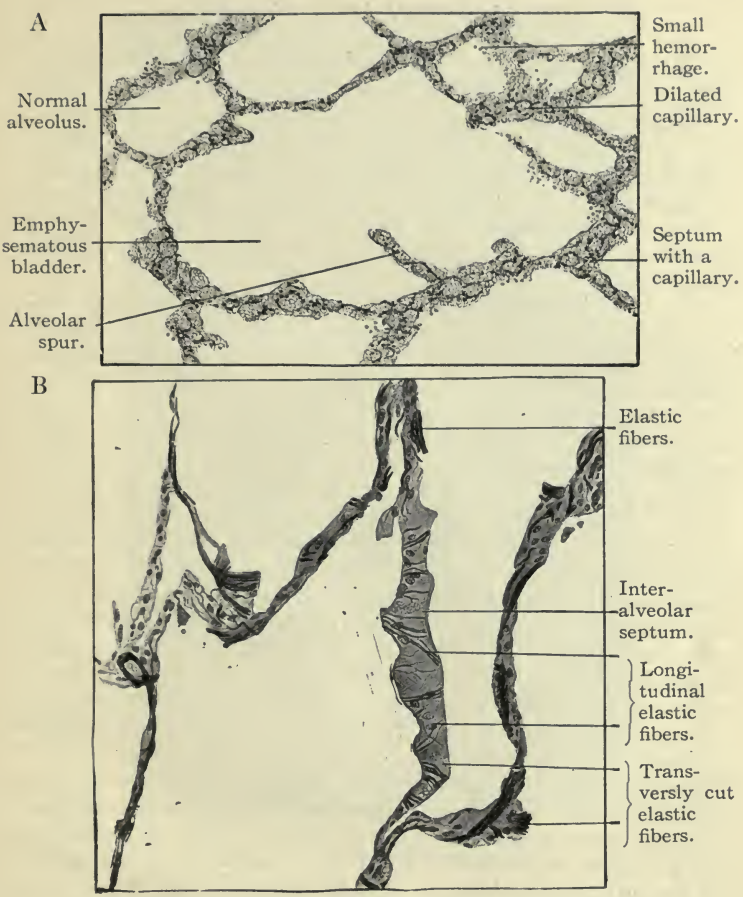


Fig. 4.—Pulmonary emphysema and congestion.

A.—*Stained with hematoxylon and eosin. Magnified* 200 *diameters. With this power the congestive changes of the interalveolar wall can be better appreciated.*

B.—*Stained with orcein. Magnified* 250 *diameters. With this stain the elastic fibers are brought out with distinctness on account of their black color.*

The section consists of a hemorrhagic focus and its immediate surroundings. To the naked eye it seems to be homogeneous.

Diagnosis of the Organ.—At the lower edge of the section one can make out the alveolar network, and by moving it about (under a low-power lens) can find sections of vessels and a bronchial tube (the last is not shown in the drawing).

1. *Low-power Lens.*—By passing from the center to the periphery of the hemorrhagic focus three zones may be distinguished:

(*a*) A central zone which is the seat of a hemorrhage that has effaced all the details of pulmonary structure, and appears to be composed of nothing but densely packed red blood corpuscles whose contours are still quite distinct. Occasional leukocytes appear, the nuclei of both lymphocytes and polymorphonuclears being stained blue by the hematoxylon. Disseminated throughout the area occasional blackish crystals of hematoidin, derived from the hemoglobin, may be seen.

(*b*) A median zone in which the alveolar contours can be distinguished though the air spaces are all filled with blood. The alveolar walls seem to have disappeared, their places being taken by blood pigment and cellular débris.

(*c*) An outer zone in which the pulmonary tissue has reacted —inflammatory zone. Here the alveoli are filled with a finely meshed fibrinous exudate (stained red), mononuclear leukocytes, desquamated endothelial cells and a great number of crystals of hematoidin either free or in the interior of mononuclear cells (*macrophages*).

In the upper right-hand fourth of the drawing the cause of the pulmonary hemorrhage appears as a branch of the pulmonary artery completely obliterated by a large clot adhering to the inner wall about its entire circumference, the result of thrombosis or embolism. The upper part of the thrombus is formed of red corpuscles densely packed together as in the hemorrhagic focus in the neighboring lung, but in the lower part its structure is less homogeneous and pigment crystals appear. Lastly, at the periphery of the thrombus there are minute vessels of new formation whose office it is to transform it into viable organized tissue (*organization of a thrombus*).

Résumé.—Pulmonary infarction from embolism. It is not recent as is shown by the transformation of the blood pigment and the penetration of new vessels into the thrombus.

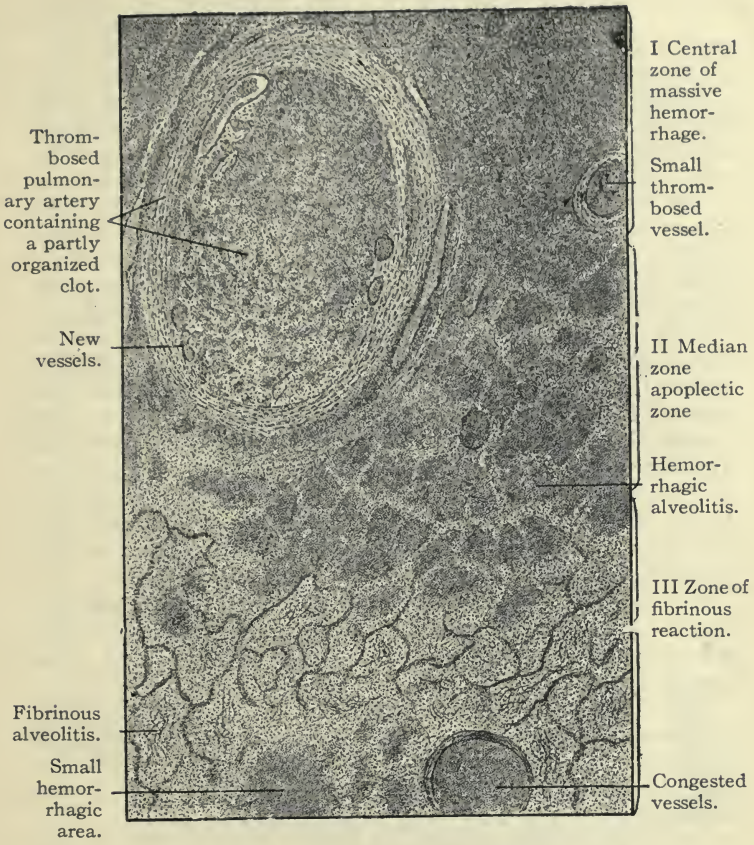


Fig. 5.—Pulmonary infarction.

Stained with hematoxylon and eosin. Magnified 25 diameters.

Embolic pulmonary apoplexy or infarction complicating acute endocarditis. The thrombus which closes the pulmonary artery is penetrated by newly-formed bloodvessels and is undergoing organization. Passing outward from the thrombosed artery as a center, the infarction shows three zones: I, a zone of massive hemorrhage; II, a zone of hemorrhage in which some of the alveolar walls can still be seen; and III, a zone of fibrinous alveolitis..

FIBRINOUS PNEUMONIA.

Croupous Pneumonia.

Diagnosis of the Organ.—This is difficult in consequence of the uniformity of the inflammatory reaction. The characteristic triad—alveolar network, vessels and bronchi and anthrocotic accumulations can be found only in the less atypical areas.

The lesion is very uniform and consists of a fibrinous exudate filling all of the alveoli, giving the pulmonary tissue a gross quality comparable to the liver, hence the term *hepatization*. From the red color resulting from the presence of large numbers of red corpuscles in the alveoli it is called *red hepatization*.

1. *Low-power Lens.*—The exudate consists of a network of fine meshes of eosin staining material, whose organized form contrasts with the red amorphous character of the serous fluid found in edema.

Sometimes the fibrinous meshwork is separated from the alveolar wall by a narrow interval, this appearance being caused by the contraction effected by the reagents used in fixing and preparing the tissue. Some of the bundles of filaments pass through ruptures in the alveolar walls and connect with exudate in neighboring air cells.

In the meshes of the network are numerous formed elements—large endothelial cells with abundant cytoplasm, polymorphonuclear and mononuclear leukocytes and red blood corpuscles.

The fibrin and red blood corpuscles characterize the stage of pneumonia called red hepatization (*fibrinous alveolitis*). In the subsequent stage the fibrin disappears, and polymorphonuclear leukocytes fill the alveoli—gray hepatization (*purulent alveolitis*).

In sections stained with methylene blue or by Gram's method numerous lanceolate diplococci—*pneumococci*—can be seen in the exudate.

The proportion of elements in the alveoli varies very slightly; the lesion is uniform and diffuse, and quite different from that found in bronchopneumonia (see Fig. 7) in which it occurs in scattered foci.

The respiratory epithelium is desquamated; the capillaries are much dilated, often ruptured, thus permitting the red corpuscles to escape into the exudate.

The smaller bronchi sometimes contain a serofibrinous exudate mixed with polymorphonuclear leukocytes.

Lastly, the pleura, not shown in the drawing, but often

affected in pneumonia, may be covered with a thick layer of fibrin (*false membrane*).

Résumé.—Fibrinous alveolitis, corresponding to the second stage of frank acute pneumonia. The uniformity of the lesion shows it to be diffuse and lobar, at least if the fragment was not taken from a nodule of bronchopneumonia, which histological examination alone does not enable one to determine.

Fig. 6.—Fibrinous pneumonia. (Fibrinous alveolitis.)

Stained with hematoxylon and eosin. Magnified 200 diameters.

Section made from a solid block of frank acute pneumonia in an adult whose other lung showed, at autopsy, the lesion of gray hepatization. The disturbance is precisely the same throughout the entire section and consists in fibrinous alveolitis, characterized by the presence of fibrinous reticula, red blood corpuscles, polymorphonuclear leukocytes and desquamated epithelium in the alveoli. It is the stage of red hepatization, the second stage of pneumonia.

Diagnosis of the Organ.—With a low-power lens one can recognize the alveolar network and sections of bronchi and vessels in the less affected pale parts of the section.

Diagnosing the Lesion.—That which at once attracts attention is the occurrence of the lesion in foci, indicated by scattered dark areas; nodules of peribronchial disturbance separated by healthy tissue.

Low-power Lens.—In the upper part of the drawing the débris of bronchial epithelium is recognizable by the columnar epithelium, arranged in palisade form, mixed with numerous abnormal polymorphonuclear leukocytes. Near the bronchial tube there is an arteriole. Both of these are in a broncho-vascular axis about which, according to the classical conception, the peribronchial nodule has developed. Passing from the center to the periphery, which is not always easy to recognize when the diseased areas are numerous and close together; the alveoli present extremely diverse appearances. But that which characterizes bronchopneumonia is the extreme variety of the alveolar lesions. These consist of:

1. *Fibrinous alveolitis*, much like that of fibrinous pneumonia, with network of fibrin enmeshing epithelial cells, leukocytes and red blood corpuscles.

2. *Purulent alveolitis*, where the fibrinous network has disappeared, giving place to an enormous number of partly degenerated polymorphonuclear leukocytes, with deeply staining nuclei from which the nuclear network has disappeared (*pycnosis*).

Sometimes the alveoli are filled with polymorphonuclear leukocytes mixed with desquamated epithelial cells and red blood corpuscles; sometimes they are bathed in serous fluid (*edematous alveolitis*); sometimes the alveolar walls have ruptured and large purulent cavities formed.

The large, middle-sized and small bronchial tubes are filled with pus—a condition constant in bronchopneumonia, but not a reliable character upon which to base a differential histological diagnosis between fibrinous and lobular or bronchopneumonia. It is the lobular distribution and the dissemination of the lesions that characterize bronchopneumonia.

In the zones of the pulmonary parenchyma that appear healthy (not shown in the drawing) contingent alveolar lesions may be observed—alveolar edema, emphysema, etc.

Résumé.—The extreme variety of the alveolar lesions, their

occurrence in disseminated foci and their frequent arrangement about the broncho-vascular axes are characters that permit the diagnosis of *acute bronchopneumonia*.

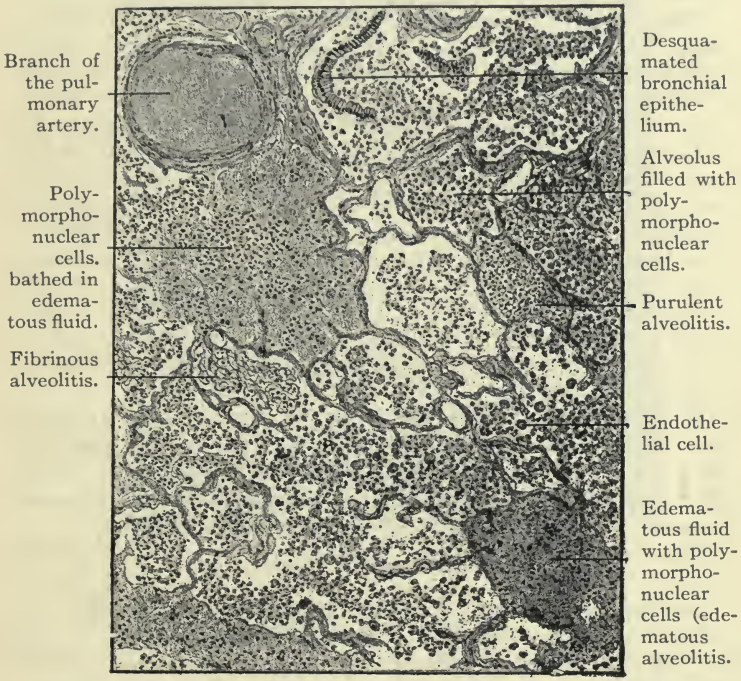


Fig. 7.—Acute bronchopneumonia.

Stained with hematoxylon and eosin. Magnified 150 diameters.

Bilateral nodular bronchopneumonia. The specimen was secured from the lung of a child that died of measles. With this magnification the peribronchial distribution of the areas does not appear. The diversity of the alveolar changes, which vary from edematous to purulent infiltration is to be noted. There are also marked changes in the bronchial epithelium.

With the naked eye the rose-colored centers of small dark patches the size of millet seeds can easily be distinguished.

Diagnosis of the Organ.—With a low magnification the *diagnosis of the organ* can easily be made through the presence of the pulmonary alveoli, vessels and bronchial tubes,

Diagnosis of the Lesion.—The dark patches are formed of dense rose-violet masses, the topography of which is quite irregular and without the peribronchial arrangement seen in bronchopneumonia. Examination of the nodules shows them to be *miliary tubercles* in different stages of development.

In some the center is occupied by one or more giant cells and is surrounded by a zone of epithelioid cells, large and transparent, with elongated and frequently bilobed nuclei; while the periphery is composed of lymphoid cells whose nuclei, colored a deep blue, are surrounded by a very small amount of protoplasm.

In others the center is caseous, with occasional fissures brought about through the action of the fixing reagents. The giant cells are then crowded to the periphery or absent.

Sometimes the tubercles tend to fuse into conglomerate masses of much greater size.

In the upper left-hand portion of the drawing (Fig. 8) there is a structure that can easily be confounded with a tubercle. It is rounded and has a central lumen limited by a very indistinct undulating line. It is a small artery with a thickened diseased wall. Such *arteritis* is frequent in tuberculosis.

Between the tubercles the pulmonary parenchyma shows a variety of lesions:

(*a*) *Catarrhal alveolitis* with desquamated epithelial cells and some red blood corpuscles escaped through rupture of the alveolar capillaries, which are everywhere dilated and filled with blood.

(*b*) *Purulent alveolitis*, characterized by accumulations of polymorphonuclear leukocytes in alveoli with normal or ruptured walls.

(*c*) *Edematous alveolitis*, characterized by the presence of serous fluid in the air cells.

There are no lesions of the bronchial tubes, the epithelium of whose walls is intact.

Résumé.—*Pulmonary tuberculosis* in which the tubercles are fairly discrete and in various stages of development, some already having undergone caseation in the center: *Miliary Tuberculosis.*

Fig. 8.—Miliary tuberculosis of the lung.

Stained with hematoxylon and eosin. Magnified 100 diameters.

It is a case of bilateral miliary tuberculosis of the lungs in an adult. The tubercles visible to the naked eye are a little larger than the fine gray granules of the granulia.[1] *Further they are distributed in loose clusters about the bronchi, and not at hazard as are the granulia. The dissemination of the tuberculous areas is to be noted. All are about the same size, but not all contain giant cells. Between the tubercles the alveoli show contingent lesions such as edematous and catarrhal alveolitis.*

[1] Granulia is a name given by Empis for an inflammatory condition that like tuberculosis is characterized by the presence of small granulations upon the serous surfaces and in the organs. It is not recognized in America, and the term is almost never heard.

The tubercle selected as the type was taken from a section of pulmonary tuberculosis.

Diagnosis of the Organ.—This is easily made through the presence of an alveolus which shows in the upper left-hand part of the drawing, and a part of a bronchial wall seen in the upper right-hand corner.

Diagnosis of the Lesion.—With the low-power lens the tubercle can be divided schematically into three zones.

1. A central part of a more or less bright rose color.

2. A median part composed of a crown of pale cells and of giant cells.

3. A peripheral part, dense and formed of blue cells.

This is the miliary tubercle in the stage of its full development, *i. e.*, with central caseation. In the same section some can be found in less advanced stages with or without central giant cells, and almost entirely composed of lymphocytes.

With the high-power lens the same tubercle shows:

1. The central zone formed of caseous material and structureless or finely granular, taking the eosine strongly, with occasional cracks caused by retraction during fixation.

2. The middle zone composed of epithelioid and giant cells. The *giant cells* are of very irregular shape, and frequently of indefinite outline because their prolongations insinuate themselves between the neighboring cellular elements. The protoplasm is granular, homogeneous and acidophil; the nuclei are numerous, sometimes 20 or 30, in general arranged near the periphery of the cell in the form of a coronet when complete, or a horse-shoe when incomplete.

The *giant cells of tumors* (giant-cell sarcoma) do not have the peripheral arrangement of the nuclei and their cytoplasm is basophilic, *i. e.*, colored by the hematoxylon. The *foreign-body giant cells* may have the nuclei pushed out toward the periphery, but the cytoplasm is always basophilic in reaction.

The epithelioid cells surround the central caseous mass as a bluish ring. They are polyhedral cells with abundant distinct protoplasm, and an elongated, often bilobed, nucleus. The lymphocytes insinuate themselves in greater or smaller numbers between them. Through pressure the epithelioid cells become fused into masses that eventuate in giant cells.

In sections stained by Ziehl's method, tubercle bacilli may be seen in the centers of the giant cells and between the epithelioid cells.

3. The peripheral zone of lymphocytes contrasts with the

preceding both by its density and by its color. The nuclei are small, dark and are surrounded by very scanty cytoplasm.

If the central area of caseation be large the softened and liquified material may be evacuated through a neighboring bronchial tube in the form of a sudden profuse expectoration (*vomica*) and a *cavity* thus be formed.

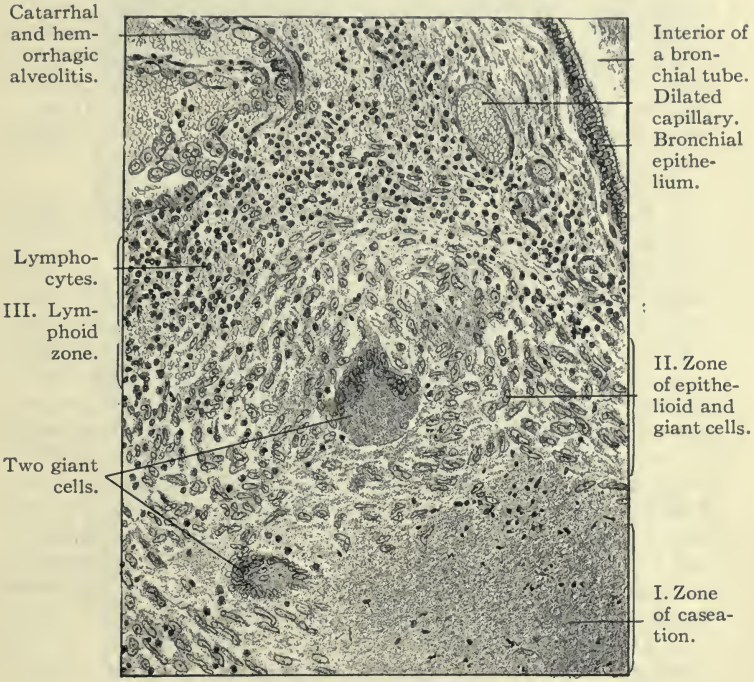


Fig. 9.—Miliary tubercle

Stained with hematoxylon and eosin. Magnified 300 diameters.

The figure shows under a high magnification a part of a tubercle taken from a case of ulcerative tuberculosis of the pulmonary apex. It shows the different zones of the miliary tubercle very distinctly. I. Zone of central caseation. II. Zone of epithelioid and giant cells. III. Zone of lymphoid cells. About the tubercle, desquamation of the alveolar epithelium (catarrhal alveolitis), and dilated capillaries with blood in the alveoli (hemorrhagic alveolitis), both of which are contingent lesions.

TUBERCULOUS BRONCHOPNEUMONIA.

Naked-eye Examination.—This shows a series of dark patches scattered over a clear field.

Diagnosis of the Organ.—This is made by the recognition of the alveolar network, the bronchial tubes (almost normal), and of the bloodvessels.

Diagnosis of the Lesions.—*Low-power Lens.*—The patches riddling the pulmonary parenchyma resemble those of the ordinary bronchopneumonia, but differ from them in that their staining reaction varies from the center to the periphery. They are most frequently grouped about the bronchial tubes.

High-power Lens.—Here are found for study:

1. The inflammatory areas.
2. The bronchi and alveoli in the intermediate zones, with their principal and contingent lesions.

1. The Inflammatory Areas: These consist of rounded formations having the structure of miliary tubercles, with caseous centers, giant cells, epithelioid cells and lymphocytes.

Besides these, above and to the left, above the bronchial tube, in the drawing, there are conglomerate tubercles, closely pressed together. Such an assembly of small rounded grayish tubercles in the lung is visible to the naked eye. It is composed of young tubercles without central caseation.

In the middle of the drawing there are two dark patches consisting of structureless caseous granular masses, colored bright red by the eosin. About them are giant cells, epithelioid cells and lymphocytes. When the process of caseation becomes more advanced the caseous material is eliminated by the bronchi and gives rise to the tuberculous cavities.

2. The Pulmonary Parenchyma: At the periphery of less confluent tuberculous masses the pulmonary alveoli are found distended, with the walls ruptured (emphysema), either empty, or filled with serous fluid (edema).

Elsewhere, but not shown in the drawing, there may be alveolar catarrh, with desquamation of the epithelial cells, hemorrhagic alveolitis, fibrinous alveolitis with delicate network of fibrin fibrillæ containing desquamated epithelial cells and leukocytes—purulent alveolitis in which the alveoli are filled with degenerated polymorphonuclear leukocytes.

The bronchioles are normal.

Résumé.—The distribution of the lesion in foci about the bronchi permits the diagnosis of bronchopneumonia; the presence of the caseation and giant cells, that of tuberculosis: *Tuberculous bronchopneumonia.*

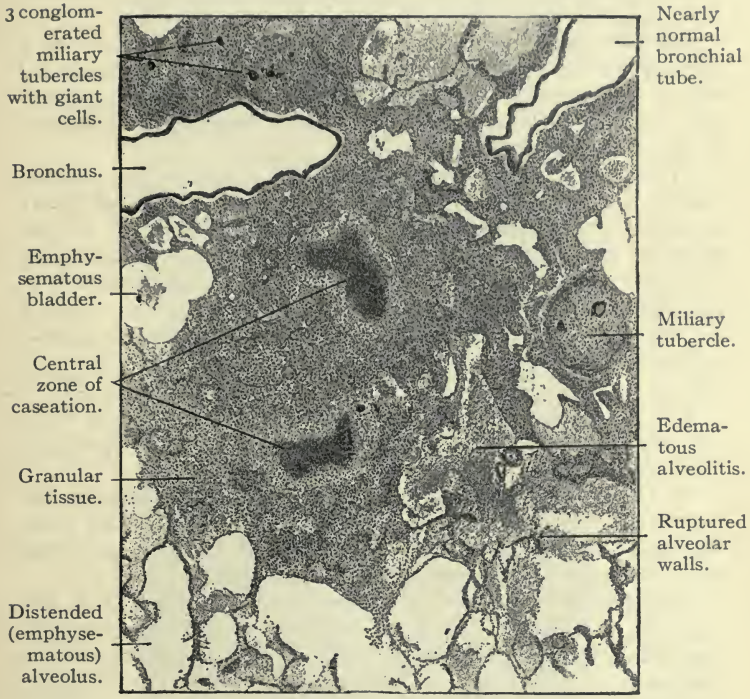


Fig. 10.—Tuberculous catarrhal pneumonia.

Stained with hematoxylon and eosin. Magnified 50 diameters.

It is a case of chronic tuberculous bronchopneumonia in an old man. Note the peribronchial arrangement of the bronchopneumonic nodule, the zones of caseation (of which there are two), and the numerous young miliary tubercles with giant cells. The bronchi are normal.

Diagnosis of the Organ.—This is difficult to make as the whole section is formed of a compact and uniform mass. An experienced eye, however, is able to recognize the alveolar reticulum at several points. It is ill-defined and badly colored but recognizable.

The most striking feature of the lesion is the presence of a finely granular substance colored red by eosin, a character by which the caseous tuberculous substance can be recognized. But here one has to do with a diffused caseation not localized in the central part of a tubercle.

This caseous mass occupies the median zone of the section. Below, a fine bluish reticulum shows against a reddish background. It is formed of elastic fibers, the skeletons of the alveolar walls that have resisted the process of caseation, strongly stained by the hematoxylon. They are grouped in parallel fasciculi, free, without branchings, distinctly limited to the periphery of alveoli in which all the other elements—epithelial cells, capillaries, etc.—are subject to the necrotic change.

The alveolar spaces contain filaments of fibrin and some scarcely recognizable elements, such as desquamated epithelial cells and leukocytes.

In the upper part of the drawing the reaction zone of the pulmonary parenchyma can be seen, following the usual commonplace type of catarrhal, fibrinous and purulent alveolitis with dilatation of the interalveolar capillaries.

Between this zone of commonplace pneumonia and the massive caseation there is a transition zone which explains the histogenesis of the principal lesion. The fibrinous exudate disappears; polymorphonuclear leukocytes and desquamated epithelial cells fill the alveoli. All of these elements, as well as the interalveolar walls lose their staining properties, and little by little take on the uniform rose tint of the complete caseation.

Résumé.—The nature of the lesion with necrosis terminating in complete caseation shows that we have to do with a massive caseous pneumonia. The extent of the caseous foci proved to be such by histological study confirmed by anatomo-clinical knowledge, permits us to speak of a *caseous pneumonia.* The absence of giant cells should throw no doubt upon its nature, as the caseation is evidence of its tuberculous origin; but in proof it is easy to demonstrate the presence of tubercle bacilli by staining other sections by Ziehl's method.

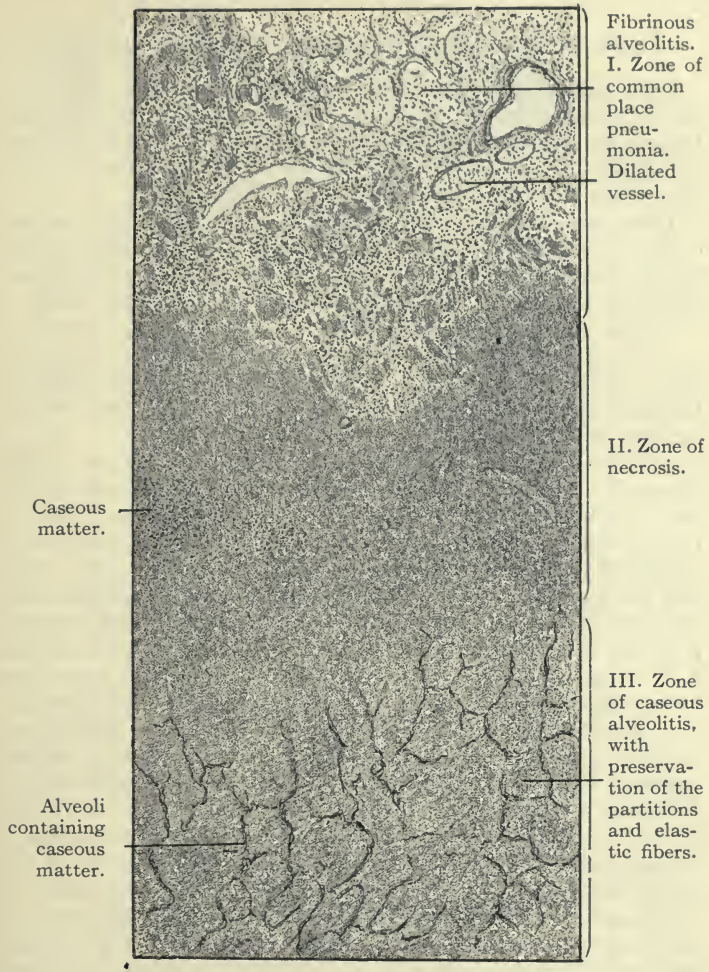


Fig. 11.—Massive caseous pneumonia.

Stained with hematoxylon and eosin. Magnified 30 diameters.

A section taken from the periphery of a mass of caseous pneumonia in a case of tabes dying with large pulmonary cavities.

TUBERCULOUS SEROFIBRINOUS PLEURISY.

Diagnosis of the Organ.—This is difficult as the pulmonary parenchyma is greatly modified. It is arrived at, however, by finding the pulmonary reticulum (in a part of the section not shown in the drawing), some débris of bronchial epithelium and numerous anthracotic granules.

Diagnosis of the Lesion.—The red edge at the upper border of the drawing corresponds to the visceral layer of the pleura, much thickened, transformed and covered with false membrane. Below this the pulmonary tissue is greatly modified.

Let us study the section from above downward.

1. A frayed-out surface, granular and somewhat homogeneous, represents the false membrane consisting of fibrin, a frequent form of reaction on the part of the pleural endothelium against noxious agents.

2. Below this, a very thick zone of granular tissue: little blue cells—lymphocytes—distributed throughout a loose reticulum; epithelioid cells mixed up with lymphocytes and lastly a caseous mass with numerous tuberculous giant cells with nuclei in horse-shoe arrangement. These giant cells must not be confused with the numerous dilated capillaries distributed throughout the section, and are usually readily recognized by the presence of red blood corpuscles in their interiors.

In many areas lymphocytes, epithelioid cells and giant cells are arranged in such manner as to form typical miliary tubercles.

3. Beneath the zone of the inflamed pleura the pulmonary tissue is greatly changed. There are numerous newly formed capillary vessels, with or without carbon particles around them. Between them the pulmonary tissue is formed of indifferent connective-tissue cells lost in the meshes of a fine reticulum of collogen and elastic-tissue fibers. All of the elements of the pulmonary tissue have disappeared or been transformed.

Résumé.—Tuberculous serofibrinous pleurisy with pulmonary sclerosis and atelectasis. This is a classic form of pleurisy and is frequently spoken of as "afebrile "(*a frigore*) pleurisy, and is in reality always of tuberculous origin. To make the diagnosis certain sections may be stained by Ziehl's method for demonstrating the tubercle bacillus.

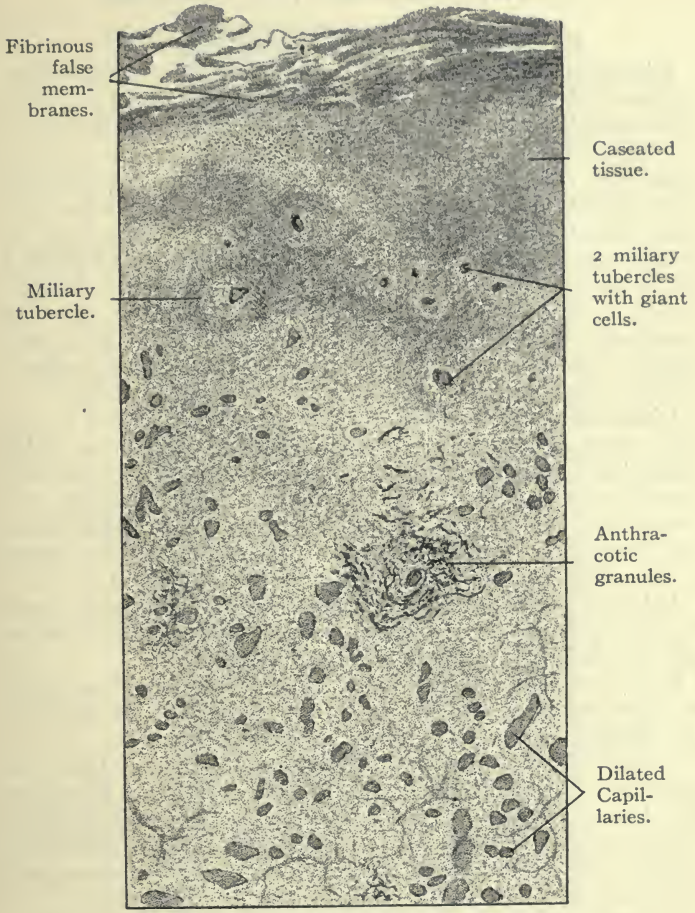


Fig. 12.—Tuberculous pleurisy.

Stained with hematoxylon and eosin. Magnified 25 diameters.

It is from a case of tuberculous pleurisy with large serofibrinous effusion, dying of asystole.

EPITHELIOMA OF THE TONGUE.

Carcinoma Spinocellulare with Epithelial Pearls.

Diagnosis of the Organ.—The section includes two portions: That in the upper part of the drawing, uniform in appearance, represents the normal organ; the other, below, the lesion.

In the normal portion it is possible to recognize a stratified squamous epithelium with its papillary layer, whose basal cells are separated from the underlying muscular tissue by a thin corium. The muscle tissue is easily recognized by the dense cytoplasm, the cross striations and the excentric position of the nuclei. The muscle fibers are cut transversely, longitudinally and obliquely. This last point, together with the nature of the covering epithelium and the absence of fat cells enables one to recognize the buccal mucosa and to make a tentative diagnosis of the *tongue.*

Diagnosis of the Lesion.—In that portion considered as normal, there is keratinization of the superficial layers of the epithelium: Fine lamina of the cornified substance exfoliate as from the surface of the skin. This marks the position of a plaque of lingual *leukoplakia*, such as is common among smokers, and in syphilis. At the edge of this plaque, which some regard as the precancerous stage, the cancer has developed.

If the epithelium be followed from above downward it is seen to thicken and change its staining affinities, becoming a deeper red, and descending deeply into the tissue.

These processes and extensions of the epithelium thrust their multiple ramifications along the interstitial spaces and into the muscles—a characteristic of malignant tumors.

In the centers of many of the epithelial masses there are epithelial pearls—cornified cells formed layer upon layer like the skins of an onion. This may be regarded as a perversion of the normal transformation of the epiderm, whose outer cells normally cornify and are shed. In the cancer masses desquamation is impossible and the cornified cells are retained.

Between and about the epithelial masses there is connective tissue forming a stroma in which mononuclear and polymorphonuclear leukocytes occur in considerable numbers—*inflammatory infiltration*—whose presence is to be referred to the ulceration of the cancer and its subsequent infection.

Résumé.—(1) The presence of the epithelial processes penetrating in every direction into the depths and breaking through the limits of the basal membrane (the separation between epiderm and corium), (2) the presence of the epithelial pearls, and (3) the presence of atypical cells with monstrous nuclei are sufficient to permit the diagnosis of *squamous-cell carcinoma of the tongue.*

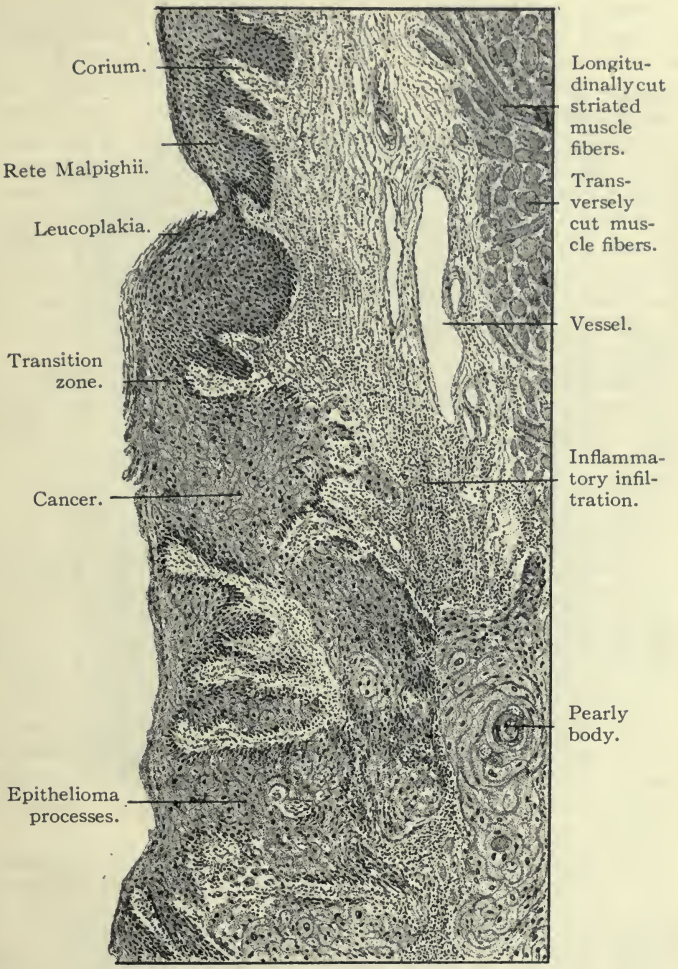


Fig. 13.—Epithelioma of the tongue.

Stained with hematoxylon and eosin. Magnified 75 diameters.

A fragment of a non-ulcerated cancer on the point of the tongue, removed at operation. The upper part of the drawing shows the normal tongue; the lower part, the tumor invading the submucous and muscular layers.

Diagnosis of the Organ.—When the section is examined with the naked eye or with a low-power lens it is found to be formed of a homogeneous tissue, one edge of which is covered by a deeply stained border. A stronger magnification shows the border to be composed of a stratified squamous epithelium, separated by a thin connective-tissue layer from a thick mass of interlacing striated muscle fibers. The epithelium shows a cornified surface layer throughout the greater part of its extent. As in the preceding illustration, we have to do with a lesion in an epithelial covered tissue without adipose tissue and with a structure composed of striated muscle fibers passing in every direction. These are sufficient evidence that we have to do with the mucous membrane of the cheek or tongue—at any rate, of the mouth.

Diagnosis of the Lesion.—Let us consider the different layers passing from the surface downward. The superficial horny layer of the epithelium is seen to take the stain badly, though with a uniform color, and without showing individual cellular elements. It is composed of thin layers, some of which are in process of desquamation, and keratinization of the epithelium—leukoplakia lingualis. The epithelium sends descending processes between the papillæ, which penetrate more deeply than normal—*acanthosis*—in consequence of an inflammatory reaction.

Infiltrating the corium, and even penetrating into the muscular layer, are a great number of small round cells—lymphocytes.

In the depths of the corium, and even occurring as deeply as the muscular layer, are a number of rounded formations—miliary tubercles—recognizable through the presence of numerous giant cells, epithelioid cells and lymphocytes. These do not show any central caseation.

This histological lesion corresponds clinically to the indurated leukoplacic patches of the tongue so often superimposed upon an indurated base, and makes one hesitate to make a differential diagnosis between tuberculosis and cancer.

This reminds us that the clinical diagnosis can be very difficult and is often subject to serious error. Also that it is often necessary to remove a fragment of tissue from the living subject in order to make a diagnosis and institute the appropriate treatment.

Résumé.—*Lingual tuberculosis* without ulceration, as the covering epithelium, is complete everywhere, and shows only leukoplakia.

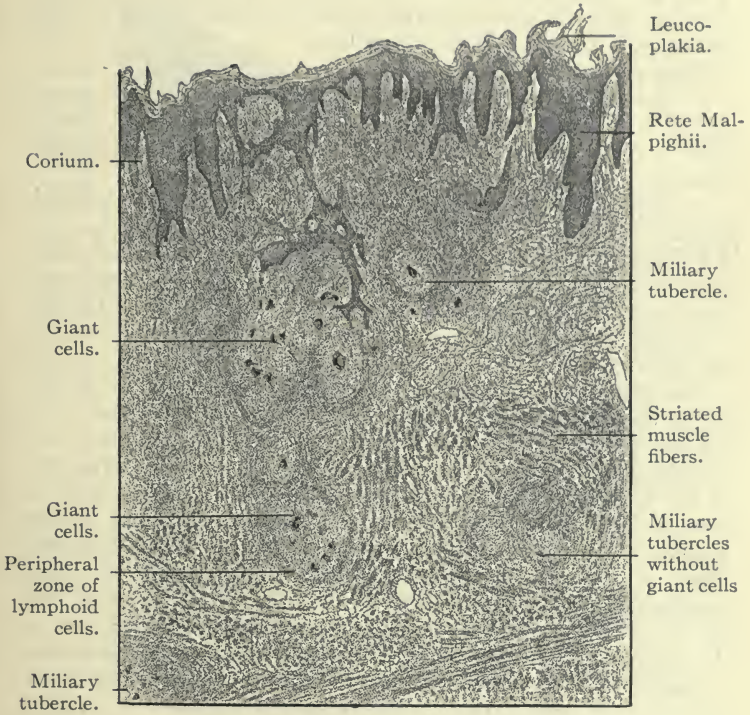


Fig. 14.—Tuberculosis of the tongue.

Stained with hematoxylon and eosin. Magnified 20 diameters.

A fragment taken from the edge of a large patch of induration which simulated cancer. The microscopic examination showed the tuberculous nature of the lesion. Above is the surface of the tongue with some leukoplakia, below are seen the miliary tubercles, with numerous giant cells.

The section is sufficiently broad to include a part of the wall of the stomach on each side of the ulcer. In the center of the drawing there is an excavation with vertical border. This corresponds to the seat of ulceration.

Diagnosis of the Organ.—One notes the following:

1. The *epithelial cells* of the *gastric mucosa.* These are cylindrical, with elongated nuclei, and are arranged in a single layer upon a connective-tissue stroma, into which bifurcating glandular tubules penetrate deeply.

2. Below the gastric glands there are occasional *lymphoid follicles*—less numerous than in the intestine.

3. The *submucosa,* formed of dense connective-tissue fibers, separating the mucosa from the muscularis, which is here thick and forms a true sphincter and is not separated into distinct layers.

4. The *serosa,* which does not concern us except as a part of the thickness of the section.

The epithelium and muscularis make one think of the structure of the digestive apparatus; the absence of villi cause us to exclude the duodenum and small intestines; the complexity of the glandular structure is not compatible with the structure of the large intestine, so we are probably concerned with a portion of the stomach. The absence of parietal cells in the tubular glands show us that the tissue does not come from the fundus, and the mucosa being formed exclusively of clear undifferentiated cells, we see that we have to do with the pylorus. The thickness of the muscular layer finally gives us the diagnosis of the precise topography, the *pyloric sphincter.*

Diagnosis of the Lesion.—The borders of the ulceration are covered with epithelial cells that tend to disappear in proportion as one approaches the bottom of the ulcer. The glands also become less distinct and are stuffed with an enormous number of round cells—leukocytes. At the bottom of the ulcer the mucosa is completely absent. The smooth fibers of the muscular coat, covered by a thin serous exudate containing a few pus cells, are scarcely recognizable; they are transformed into a granulation tissue. On each side the muscular tissue resumes its normal appearance.

The serous coat consists of dense and compressed connective-tissue fibers formed through a defensive inflammatory reaction, resulting in sclerosis by which the gastric wall is locally thickened and its perforation prevented.

Résumé.—*Simple ulcer of the pylorus:* a common, non-specific subacute inflammatory lesion.

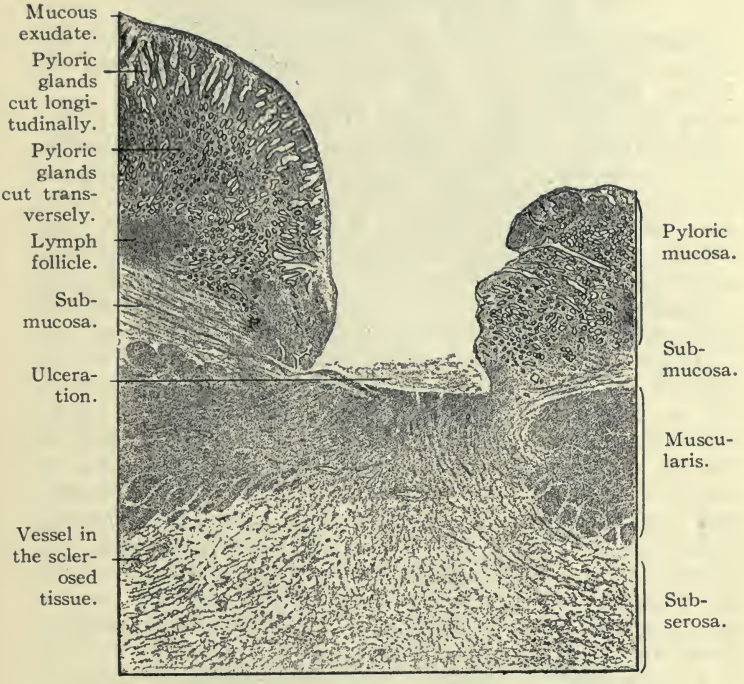


Fig. 15.—Simple ulcer of the pylorus.

Stained with hematoxylon and eosin. Magnified 20 diameters.

A small ulcer of the pyloric region of the lesser curvature found at autopsy. The base of the ulcer is shown in the center of the figure. To the right and left the borders seem to be cut out of the mucosa as with a punch. Numerous glands of Brunner can be seen in the mucosa. Beneath the ulceration there is reactive inflammation of a defensive character.

CANCER OF THE PYLORUS.

Beginning Epithelioma.

Diagnosis of the Organ.—The section divides itself into two distinct layers, one blue, the mucosa; the other bright red and thicker, the muscularis.

To the right in the drawing—the normal part—there is a simple layer of epithelial cells, contiguous to, and descending into the mucosa to form tubular glands. In the mucous layer, which is of the gastro-intestinal type, the absence of villi shows that the section does not come from the duodenum or small intestine; the absence of the cells differentiated into chief cells and parietal cells, the fundus of the stomach. The presence of glands of the serous type and the thickness of the muscular coat—sphincter—show that the section comes from the *pylorus*.

Diagnosis of the Lesion.—If we begin the study of the section under a low-power lens and follow the mucosa from right to left we find that at a certain point the arrangement of the cells into glands disappears, the tubular glands themselves become unrecognizable and are replaced by irregular masses of cells with transparent nuclei that sometimes bud and extend into the muscular coat. This is not a simple inflammatory infiltration of cells in which one scarcely sees anything but nuclei, but is composed of cells that more or less closely resemble the glandular cells themselves. In certain foci they may be seen originating at the expense of the gland cells. It is not, therefore, an inflammation but a neoplasm.

At one point the neoplasmic cells pass through the muscularis and infiltrate the subjacent tissue, hence the cancer—a malignant tumor that progressively invades and destroys the neighboring tissues—is formed.

In the submucosa there are lymph vessels with very thin walls filled with cells identical with the primitive neoplasmic cells—lymphatic neoplasmic emboli—cells of the cancer transported by the vessels to colonize at a distance.

Résumé.—A tumor developed from the pyloric glands in which one can find all the stages of transformation, that is to say, *beginning glandular epithelioma*, of which the malignant nature of the growth is already shown by the invasion of the wall of the stomach, and by the probable formation of metastases as indicated by the cancer cell emboli in the lymph vessels.

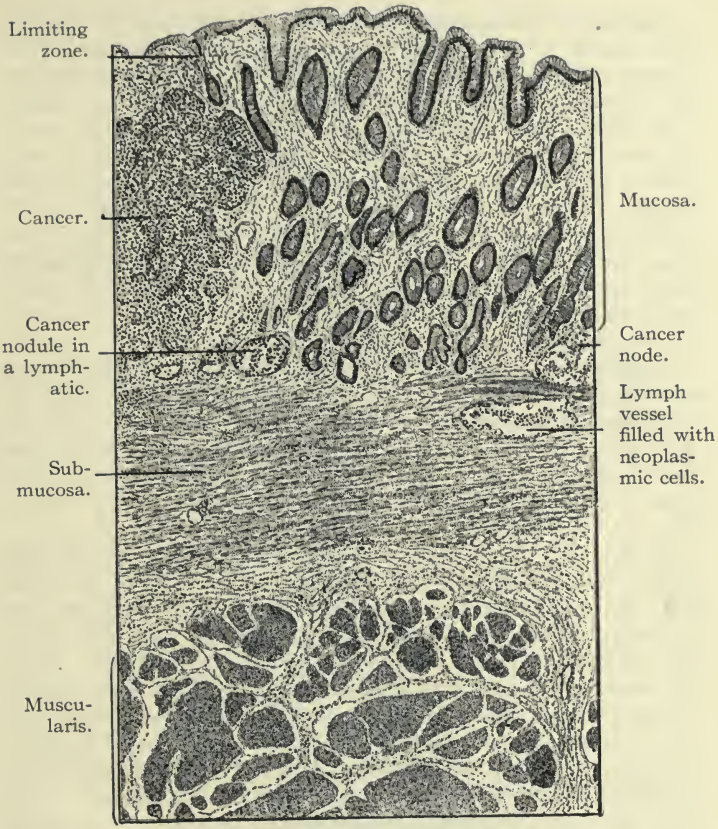


Fig. 16.—Beginning cancer of the pylorus.

Stained with hematoxylon and eosin. Magnified 45 diameters.

The fragment of tissue was surgically removed during pylorectomy. From above downward the drawing shows the mucosa with its glands, the submucosa and the muscularis. Above and to the left of the mucosa is seen the beginning of the glandular epithelioma. The submucosa shows cancer emboli in the lymphatics.

TYPHOID ULCERATION OF THE INTESTINE.

Diagnosis of the Organ.—At one extremity of the section, that shown at the bottom of the drawing, one can distinguish a mucous membrane of the intestinal type whose epithelial cells and nuclei are scarcely visible on account of postmortem change. The glands of Lieberkühn, together with the villi, enable the small intestine to be recognized. The epithelium rests upon a delicate corium which separates it from the *muscularis mucosa*. Beneath it is a vascular layer, the submucosa. In it there are no glands of Brunner, hence the tissue cannot come from the duodenum. Below the submucosa are two definite muscular layers which form the muscularis. The internal of these runs transversely, the outer longitudinally. The organ is, therefore, the *small intestine*.

Diagnosis of the Lesion.—Following the mucosa from above downward it is found to flatten little by little, its villosities disappearing. Further down the glands and villi reappear. A careful study of the flattened part of the section shows that the change does not depend upon postmortem maceration, but upon a true pathological lesion of inflammatory nature—ulceration.

As the edge of the ulceration is approached the villi crumble away, the cells show a dull staining and their pycnotic nuclei dissolve in the cytoplasm. Most of the capillaries are considerably dilated and their eosin-stained red corpuscles stand out distinctly against the dark blue of the mucosa. All of the tissue of the mucosa is infiltrated with an enormous quantity of small round cells. In the normal intestinal wall such small round cells are collected in aggregations of varying size in the mucosa, where they form the solitary follicles and Peyer's patches. Their abundance and diffused infiltration in this case indicate ulceration of one of Peyer's patches. The bottom of the ulceration is formed of a granulation tissue in which are seen occasional scarcely-recognizable vestiges of the epithelial cells of the glands of Lieberkühn. The tissue is very vascular and has many capillaries, some of which project above the surface of the ulceration.

Résumé.—The microscopic examination permits the diagnosis of inflammatory ulceration of the small intestine, but does not enable us to go further through histological study alone. But the frequence of typhoid fever and the ulcerations that characterize it justify the opinion that the lesion is *typhoid ulceration*. The final and definite diagnosis can be made only through the information gained from the clinical notes of the case and the bacteriological examination.

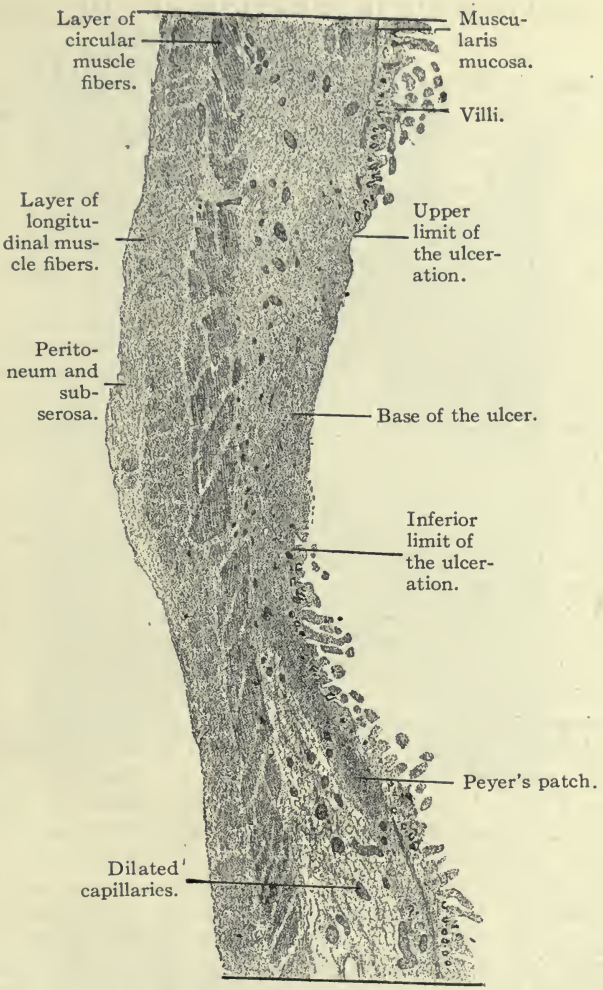


Fig. 17.—Typhoid ulcer of the intestine.

Stained with hematoxylon and eosin. Magnified 15 diameters.

The right-hand side of the drawing shows the mucosa, subnormal above and below, and ulcerated in the middle. To the left are the deeper layers and the peritoneal covering.

TUBERCULOUS ULCERATION OF THE SMALL INTESTINE.

Diagnosis of the Organ.—Two parts are distinguishable: The one thin, dark-colored and upon which intestinal villa can be seen, the mucosa; the other, thicker and distinct, the muscularis. The concave lower surface of the figure corresponds to the peritoneal surface covered by the serosa; the convex upper surface to the mucosa. This curvature, easily seen with the naked eye, is the result of the unequal retraction of the tissue in the fixing reagents, and in seeking to make the diagnosis of the organ no attention should be paid to it.

The normal mucosa, well-preserved at the left hand of the illustration, is covered by a single layer of columnar epithelium with elongated nuclei. Here and there a goblet cell shows as a clear vesicle between the regular columnar cells. The epitheium dips down to form crypts—glands of Lieberkühn. Scattered in large numbers through the corium, and occasionally gathered together in masses, are large numbers of small round cells. These are the normal lymphoid cells and their aggregations are the solitary glands of the small intestine.

Beneath the mucosa is the muscularis mucosa and the submucosa in which the absence of Brunner's glands indicates that the tissue does not come from the duodenum. The presence of villi on the other hand shows that we have to do with the jujenum or ileum. Beneath all these are the muscularis and finally the serosa.

Diagnosis of the Lesion.—Following the mucosa from left to right of the illustration it is found to entirely disappear at the extreme right. This is because of ulceration, of which only a part is represented. All of the bottom of the ulcer and a great part of the submucosa consists of an infiltration of miliary tubercles with caseous centers and more or less numerous giant cells.

Résumé.—The grouping and distinctly follicular arrangement of the infiltration, and the large number of giant cells, permit one to affirm the tuberculous nature of the ulceration. The final proof—the demonstration of the tubercle bacilli in the lesion—should present no difficulties when the appropriate staining is performed.

The lesion is, therefore, *tuberculous ulceration of the small intestine.*

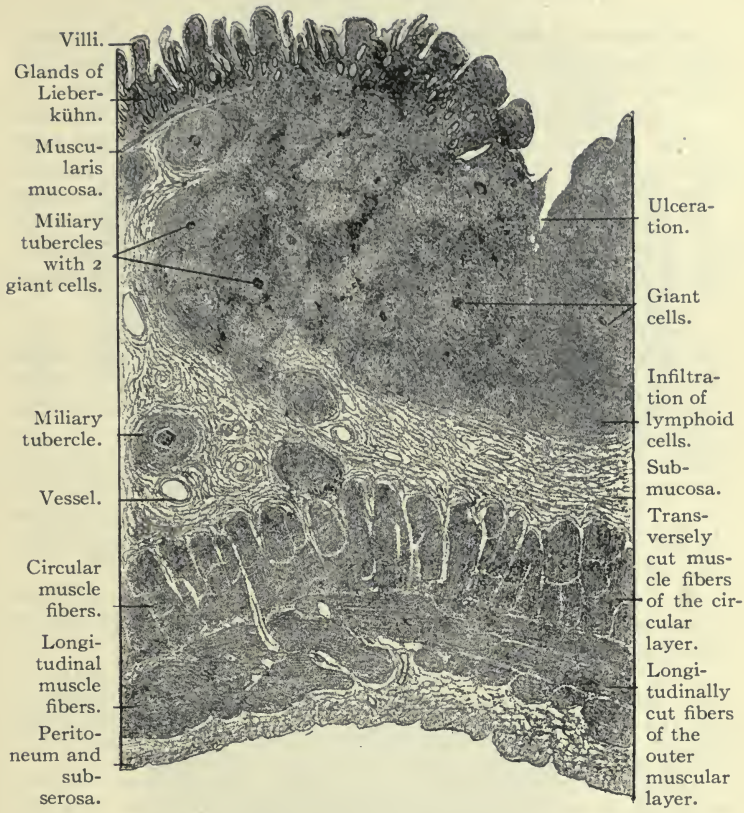


Fig. 18.—Tuberculous ulcer of the small intestine.

Stained with hematoxylon and eosin. Magnified 20 diameters.

It is a fragment of a tuberculous ulceration of the terminal portion of the small intestine, the cecum and vermiform appendix (with invasion of the peritoneum) removed at operation. Above, and to the left, is the surface of the mucosa with normal villi, above and to the right, the ulcer. Below the mucosa are numerous miliary tubercles with giant cells.

NORMAL VERMIFORM APPENDIX.

Naked-eye Examination.—The section shows a circular organ with a small central lumen and thick walls. If we examine the various layers from within outward we find the following:

1. *The Mucosa.*—This is formed of an epithelium composed of tall cells placed side by side, with occasional goblet cells between them, and resembling those of the intestinal mucosa. From it, prolongations descend into the deeper layers between collections of lymphoid tissue to form glands, some of which are cut transversely, some longitudinally. The former appear as small rounded cell collections isolated from the surface. The cavity of the organ is small and empty.

2. *The Submucosa.*—Below the mucosa the corium or submucosa shows an enormous infiltration of lymphoid cells. Many of these are collected into definite groups, of rounded shape, with pale centers—germinal centers—and comprise the solitary lymphoid follicles. These, similar to those of the other lymphoid organs—tonsils, lymph nodes, etc.—serve as precious elements in the diagnosis of the appendix vermiformis.

3. *The Muscularis.*—This coat is much less in evidence but it and the submucosa are arranged as in the sections of the wall of the small intestine.

4. *The Serosa.*—At the periphery is the peritoneum with its subserosa, from one point upon which the attachment of the meso-appendix can be seen to arise.

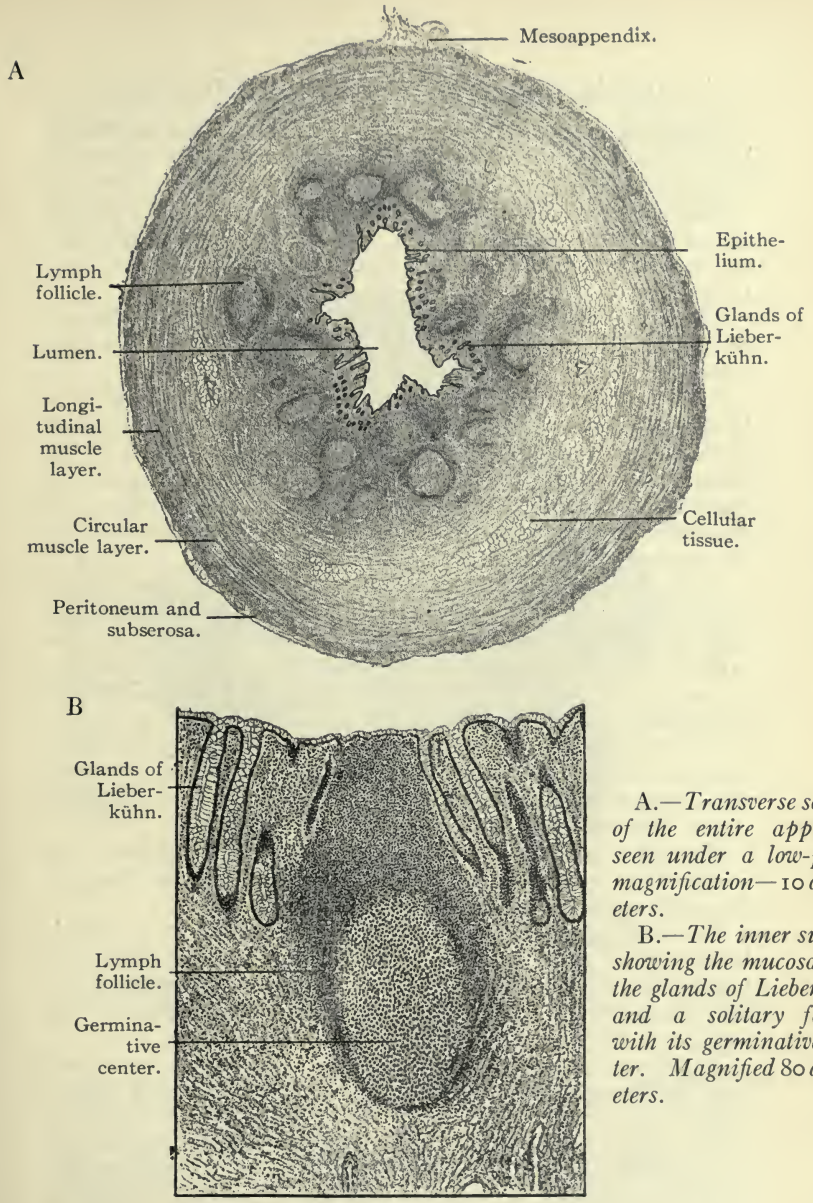
The small size of the lumen, the regularly circular shape of the section, the abundance of the lymphoid deposits, and finally the structure of the walls enable the diagnosis of the *vermiform appendix* to be made.

The absence of mucopus in the interior, the perfect preservation of the epithelial layer, the regular arrangement of the follicles which show no trace of hemorrhage and the absence of polymorphonuclear leukocytes among the lymphocytes in the mucous corium show that there are no inflammatory lesions, either acute or chronic.

Differential Diagnosis.—1. An artery or vein—aorta or vena cava—can at once be differentiated by the absence of an epithelial and the presence of the endothelium lining, as well as by the absence of lymphoid collections from the walls.

2. A section of the esophagus is easily differentiated by its interior lining of stratified squamous epithelium.

3. A section of a large bronchial tube is easily recognized by the cartilaginous support that its wall contains, though the lining epithelium is of the same columnar type as that in the vermiform appendix.



A.—*Transverse section of the entire appendix seen under a low-power magnification*—10 *diameters.*

B.—*The inner surface showing the mucosa with the glands of Lieberkühn and a solitary follicle with its germinative center. Magnified* 80 *diameters.*

Fig. 19.—Normal vermiform appendix.

Stained with hematoxylon and eosin. Organ removed at operation.

Diagnosis of the Organ.—This is easily made if attention has been paid to the differential points given in the discussion of the preceding section.

Diagnosis of the Lesion.—That which at once attracts attention is the communication between the interior and the exterior shown in the upper left-hand portion of the drawing. It is a perforation.

The epithelium is slightly altered but at certain points, notably in the neighborhood of the perforation, it has disappeared.

In the lumen of the appendix there is a serous exudate containing pus cells—polymorphonuclear leukocytes and some mononuclear leukocytes with altered nuclei. There is no foreign body in the interior, nor is there any accumulation of agglomerated or inspissated fecal matter, nor a calculus, nor any parasite—*oxyuris*—such as are frequently encountered in the appendix when the seat of pathological change.

If the epithelial layer does not show any pathological alteration it is not the same with respect to the lymphoid deposits. One cannot help being struck by the small number of pale germinal centers that are present; there are not more than two or three such to be found. There seems to be complete disarrangement of the lymphoid cells which are mixed up with a considerable number of polymorphonuclear leukocytes. The lesions of these follicles are very important and are the point of departure of the disturbance of neighboring tissues—notably of the peritoneum.

The inflammatory cells, polymorphonuclears, mononuclear leukocytes and lymphocytes infiltrate the entire thickness of the wall, even to the meso-appendix itself.

The capillaries are very much dilated and often ruptured, but not much attention is to be paid to that, as it is commonly present in operative cases (false hemorrhagic appendicitis), and is caused by traumatic injury done to the tissues by the forceps or the fingers at the time of the operation.

The peritoneal coat is roughened and is more or less covered with false membranous deposits—fibrin—infiltrated with leukocytes.

The edges of the perforation have a necrotic appearance and scarcely show any normal structure on account of the enormous collection of leukocytes by which they are infiltrated.

Résumé.—The presence of mucopus in the interior of the appendix, the excellent preservation of the epithelial lining

(except at the point of perforation) and the striking changes in the lymphoid structures of the walls indicate the lesion to be *acute perforative appendicitis.* It would be difficult if not impossible to say from the examination of the section whether or not this lesion had occurred in an appendix already the seat of chronic appendicitis.

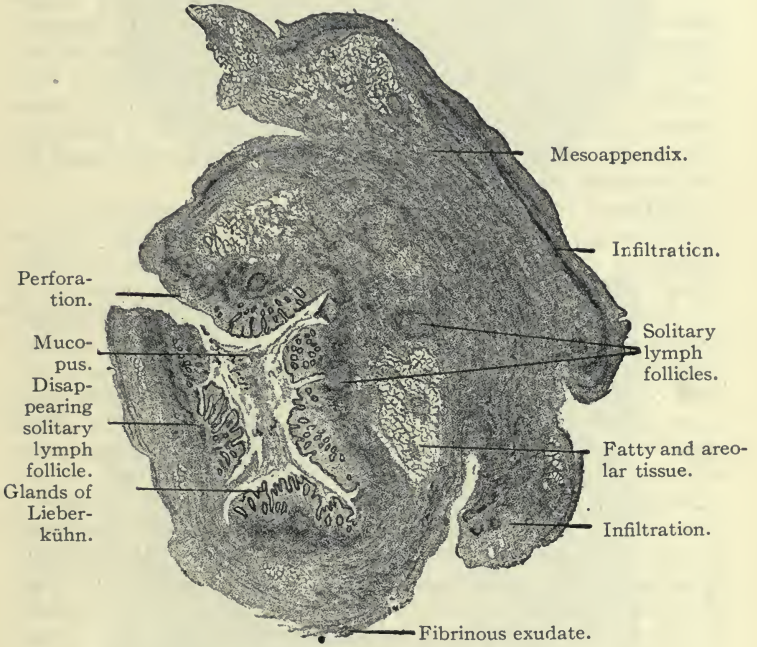


Fig. 20.—Acute appendicitis with perforation.

Removed at operation. Stained with hematoxylon and eosin. Magnified 10 diameters.

The perforation is seen above and to the left. The contrast between the extensive vascular and connective-tissue lesions and the well-preserved epithelium is to be noted. The solitary glands have almost entirely disappeared. The interior contains pus, the exterior is covered with fibrinous false membranes. The mesoappendix, especially at its attachment is greatly infiltrated with inflammatory cells.

CHRONIC OBLITERATIVE APPENDICITIS.

Diagnosis of the Organs.—This is difficult to make.

Examination with a low-power lens shows a section of a cylinder, or tube, whose interior is completely filled up. Its walls are formed of smooth muscular tissue arranged in two layers and about which there is a serous coat. The center of the tube is formed of connective tissue and of cells whose nature this magnification does not permit to be recognized. The arrangement of the muscular tissue and the absence of any elastic layer enables us to eliminate a bloodvessel from consideration and makes us suspect a section of some other obliterated tube such as as the vermiform appendix or a Fallopian tube. Knowledge of the clinical source of the material must be be depended upon for a correct final diagnosis.

Diagnosis of the Lesion.—The general architecture of the organ being completely upset, a greater magnification must be employed to determine the lesion. Having learned that the tissue is vermiform appendix, the first thing that strikes us is the absence of a lumen, of a lining epithelium and of the glands belonging to the epithelium, as well as the goblet cells usually so numerous among them. Another element equally characteristic of the vermiform appendix has equally disappeared, that is, the lymphoid tissue with its follicles. In the place of all of these elements one finds only a dense connective tissue filled with cells of an embryonal appearance—lymphocytes. It is a granulation tissue and contains numerous young bloodvessels—arterioles with thick walls and capillaries—of new formation. Finally, at various points there are groups of fat cells of adult type which give somewhat the appearance of minute openings punched in the tissue. Their presence is referred to metaplasia of the connective tissue caused by the inflammation. Under the influence of chronic inflammation of the organ the mucous corium has proliferated, crowding out the epithelial and lymphoid formations. The sclerosis even extends to the muscularis, in which the fibers can be seen to be more or less dissociated, so that the tunic has a striated appearance comparable to that seen in the mesarterium of atheromatous arteries. The peritoneal coat—serosa—is unchanged.

Résumé.—The absence of all epithelial and lymphoid elements, the disappearance of the central lumen and its replacement by connective tissue of embryonal character lead to the diagnosis of *chronic obliterative appendicitis.*

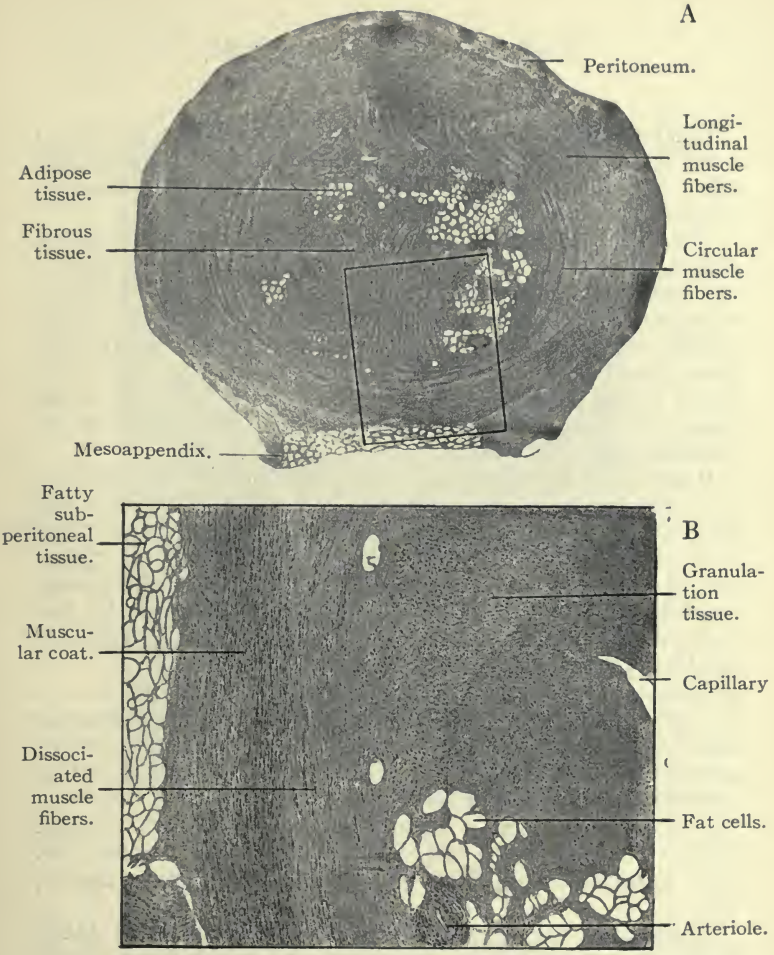


Fig. 21.—Chronic obliterative appendicitis.

Stained with hematoxylon and eosin.

A.—*Entire section of the appendix magnified* 15 *diameters. The portion included in the rectangle is shown in Fig.* B.

B.—*A portion of the muscular wall showing the details of connective-tissue proliferation which end in the complete obliteration of the appendix. Magnified about* 150 *diameters.*

CANCER OF THE CECUM.

Cylindrical Cell Carcinoma.

Diagnosis of the Organ.—At the upper part of the figure there is a mucous membrane of the intestinal type; in the lower part, numerous tubular formations recalling the structure of tubular glands.

The entire thickness of the mucosa is formed of tubular glands side by side—glands of Lieberkühn—resembling those of the small intestine. In the thickness of the corium there are numerous lymphoid deposits; follicles like those seen in the normal small intestine. The muscularis mucosa distinctly separates the mucosa from the subjacent formations. The other layers of the intestinal wall are not distinct. The size of the glands of Lieberkühn and the absence of villi enable us to recognize the large intestine—*colon.*

Diagnosis of the Lesion.—So long as a neoplasm, even though it be large, respects the muscularis mucosa as a boundary and develops only upon one side of it, the tumor is benign. But if the boundary of the muscularis be passed and the tumor propagates itself by contiguity throughout the thickness of the intestinal wall the tumor is malignant—cancer. In this case the muscularis mucosa is passed and the whole thickness of the intestinal wall is invaded.

The tumor is a *typical glandular epithelioma*, that is to say, a tumor that deviates but slightly from the original glandular type of the tissue from which it grows, in the arrangement or grouping of its cells. It is composed of cylindrical tubes, somewhat irregular, and giving the general effect of ramifying and branching glands. Sometimes the spaces lack distinct walls. The cells have atypical structure and functions, and show hypertrophy of the nuclei, nucleoli, karyokinetic figures, etc.

These cancerous formations are to be found in the entire thickness of the intestinal wall as well as between the muscular fibers as in the submucosa.

Résumé.—*Typical glandular epithelioma of the colon*, infiltrating the wall but not ulcerating upon the surface. It is a form of infiltrating cancer of the intestine, different from the large cauliflower masses that ulcerate and bleed upon the slightest contact—the ulcero-vegetative form.

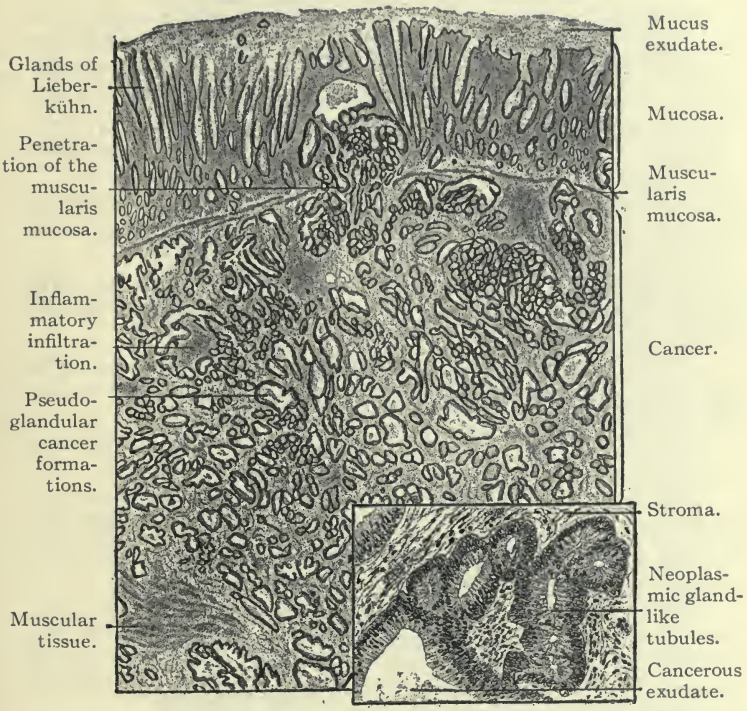


Fig. 22.—Cancer of the cecum.

Stained with hematoxylon and eosin. Magnified 15 diameters.

A large infiltrating tumor of the cecum without either vegetations or ulcerations. In the upper part of the drawing is shown the mucosa separated from the tumor by the muscularis mucosa, in the center of which there is a breach of continuity and an invasion of the cellular tissue by the neoplasmic tubules. Below and to the right, in the square the appearance of the neoplasmic tubules is shown in a magnification of 150 *diameters.*

CHRONIC PASSIVE CONGESTION OF THE LIVER.

Liver of Chronic Heart Disease.

Diagnosis of the Organ.—Under a low-power magnification the tissue appears to be formed of strands arranged like the spokes of a wheel about central points composed of various elements. Sometimes these are constituted by a single vessel—hepatic vein—sometimes, on the contrary, of a series of elements enclosed in connective tissue—portal space—in which are found the following:

1. A *venule*, a ramification of the portal vein, with flattened lumen and thin musculo-elastic tunic. In the interior a few red blood corpuscles may be seen.

2. One or more *branches of the hepatic artery*, circular, with thicker walls than the branches of the portal vein, and usually empty of blood.

3. *Bile capillaries*, single or multiple, having about the same diameter as the hepatic artery, but lined with a cuboidal epithelium (colored blue with hematoxylon).

Lastly, in the periportal tissue, sections of the nerves and lymphatics.

The columns of cells arranged like the spokes of a wheel, the central or subhepatic veins and the periportal spaces constitute characteristic elements forming a tripod upon which the diagnosis of the liver depends.

The student, of course, knows that the liver is formed of a series of histological units, the hepatic lobules. The subhepatic vein represents the center of the lobule—the central zone. The periportal connective tissue is at the periphery of of the lobule—peripheral zone.

Diagnosis of the Lesion.—With the aid of a low-power magnification considerable modifications can be detected in the hepatic parenchyma. Even with the naked eye or a hand lens the section can be seen to be made up of a series of zones alternately dark and pale. The dark zones comprise the hepatic trabeculæ colored rose-violet by the eosin and hematoxylon and corresponding to the periportal or peripheral zones of the lobules. The pale areas, on the other hand, scarcely contain any of the columns of liver cells, but are formed by a considerable hemorrhagic exudation about the branches of the subhepatic veins—central area of the lobule. This arrangement, a little schematic, corresponds to the naked eye appearance of the liver of chronic passive congestion, in which the eye differ-

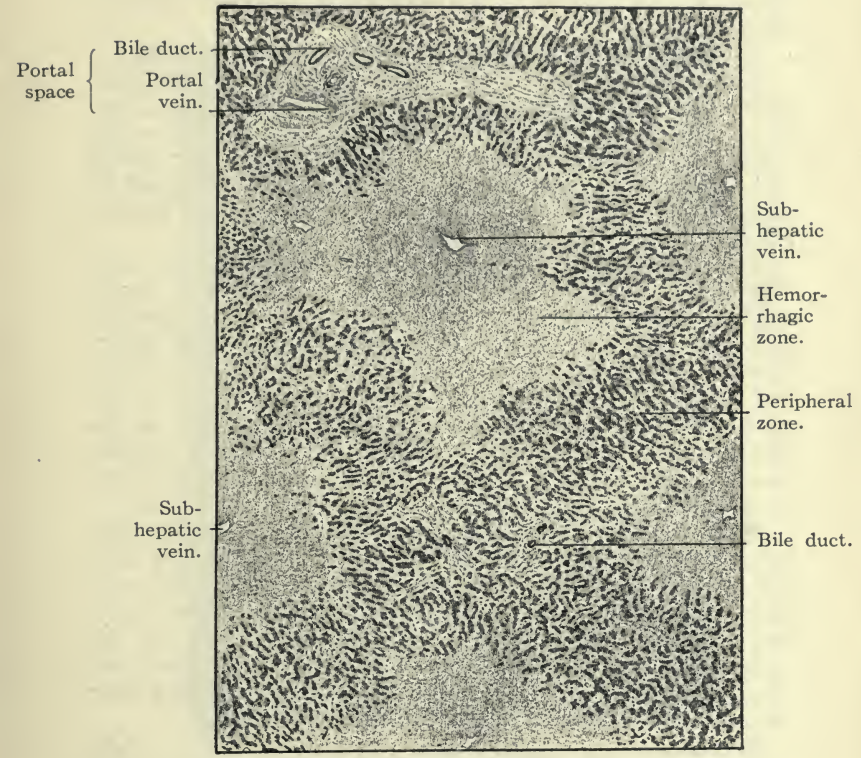


Fig. 23.—Chronic passive congestion of the liver—liver of heart disease.

Stained with hematoxylon and eosin. Magnified 100 diameters.

Section made from an enlarged liver showing the nutmeg appearance, removed at autopsy from a patient dead of asystole. The parenchyma is differentiated into a portal zone in which the hepatic cell columns are still recognizable and perihepatic zones in which the parenchyma is destroyed by hemorrhage.

entiates dark zones—blood—and pale yellowish zones—liver tissue—the alternation of colors giving the tissue the so-called *nutmeg appearance.*

The topographical arrangement seen in the drawing (Fig. 23) is then as follows: a zone of hepatic parenchyma, relatively healthy, is surrounded on all sides by hemorrhagic areas from which all the parenchymatous tissue has disappeared. The result is an entirely changed appearance of the liver lobule which seems to center about a periportal space instead of about a subhepatic vein. This has been called an *inverted lobule.*

If the examination be continued with a higher power lens (Fig. 24) the following becomes apparent: Leaving the portal space (near the center of the drawing), the columns of liver cells radiate like the spokes of a wheel from a central point. Close to the periportal tissue the liver cells appear healthy and separated from one another by scarcely dilated blood-vessels (capillaries). But in proportion as we pass from the portal space the columns of hepatic cells appear to become shorter, dissociated and separated from one another by closely packed red blood corpuscles.

Still further toward the center of the lobule the blood capillaries become larger and larger to the detriment of the liver cells, which eventually form only narrow cellular columns, flattened, stretched and composed of only two or three cells, and finally of single cells—*monocellular dislocation.* In the upper right-hand portion of the drawing there are considerable areas of recent hemorrhage in which the red corpuscles have escaped from some of the ruptured dilated capillaries.

Examination with a still higher power lens enables an estimate of the nature and severity of the cellular changes to be made. The protoplasm is found to be homogeneous or to contain fatty or pigmentary granules; the nuclei are pycnotic, fragmented or have disappeared. These lesions are especially marked as the central vein is approached.

Résumé.—Intense congestion of the hepatic parenchyma, preponderating in the center of the lobules where the blood stasis tends to cause dilatation of the capillaries, separation and dissociation of the columns of liver cells, and ends by causing hemorrhage. Such are the lesions of hepatic congestion in heart disease—*hepatic asystole.*

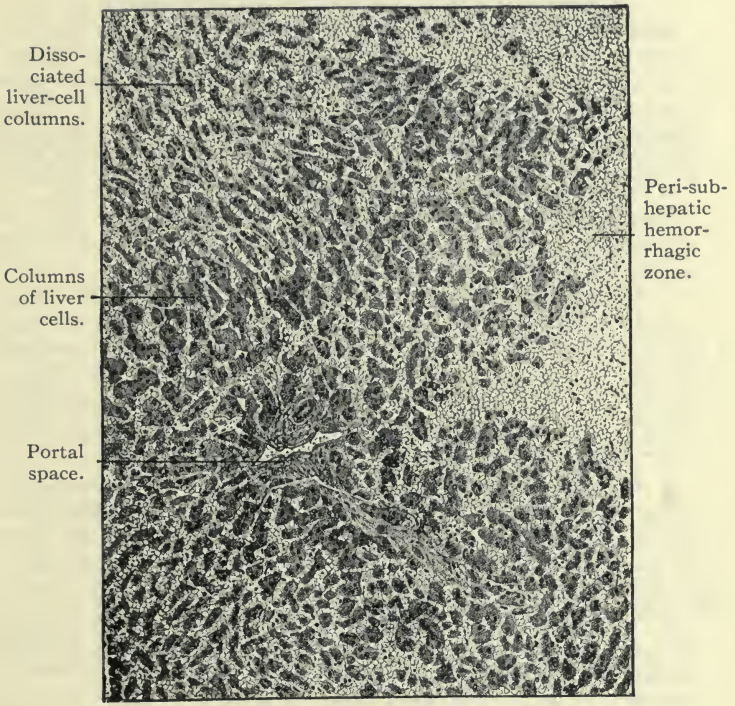


Fig. 24.—Chronic passive congestion of the liver.

Stained with hematoxylon and eosin. Magnified 100 diameters.

The same section from which the preceding drawing was made, showing the edge of a hemorrhagic zone—to the right—and the still preserved parenchyma with cell columns separated by the dilated capillaries—to the left.

THE FATTY AND CONGESTED LIVER.

Liver of Heart Disease and Tuberculosis.

Diagnosis of the Organ.—With the low-power lens the columns of liver cells are recognized, radiating like the spokes of a wheel from the central—subhepatic—veins. In the lighter colored areas the periportal connective tissue, with its usual inclosed sections of the portal vein, hepatic artery and bile ducts, are easily found—the artery with its thick wall by which it is recognized, the bile duct with its cuboidal epithelium.

Diagnosis of the Lesion.—One is at once struck by the appearance of dark central zones separated by broad stretches of pale tissue in which the portal vessels occur.

1. In the central area—zone about the central vein—there are alterations in the columns of liver cells which are sometimes separated widely by dilated capillaries, sometimes reduced to small groups of cells or to single cells (mononuclear dislocation). In the hepatic cells themselves there are small, nonconfluent fatty granules. These cells frequently have badly colored or invisible nuclei.

2. In the peripheral zones—periportal zones—there are important fatty changes. In order to comprehend the histological appearances it is necessary to recall that every part of the tissue from which the section was cut was immersed for a time in reagents—xylol, alcohol, chloroform, ether, etc.—which are fat solvents. It is on this account that the fat does not occur in the form of drops; it is only the outlines of the spaces that formerly contained the fat that show (a negative image). The little droplets seem to coalesce to form larger and larger drops until some of the cells contain large transparent vesicles that displace the nuclei to the periphery of the cell (seal-ring appearance), or may determine that they cannot be seen. The hepatic tissue is thus gradually replaced by adipose tissue not unlike that normally occurring beneath the skin. The areas of fatty change are arranged about the periportal tissue whose vessels and ducts are otherwise normal.

Résumé.—Liver showing two types of lesion, well systematized as regards topography.

1. A pronounced congestion without hemorrhage situated about the central vein and affecting only the central area of the lobules. 2. Fatty disease localized in the periportal areas.

These together make the diagnosis *fatty and congested liver.*

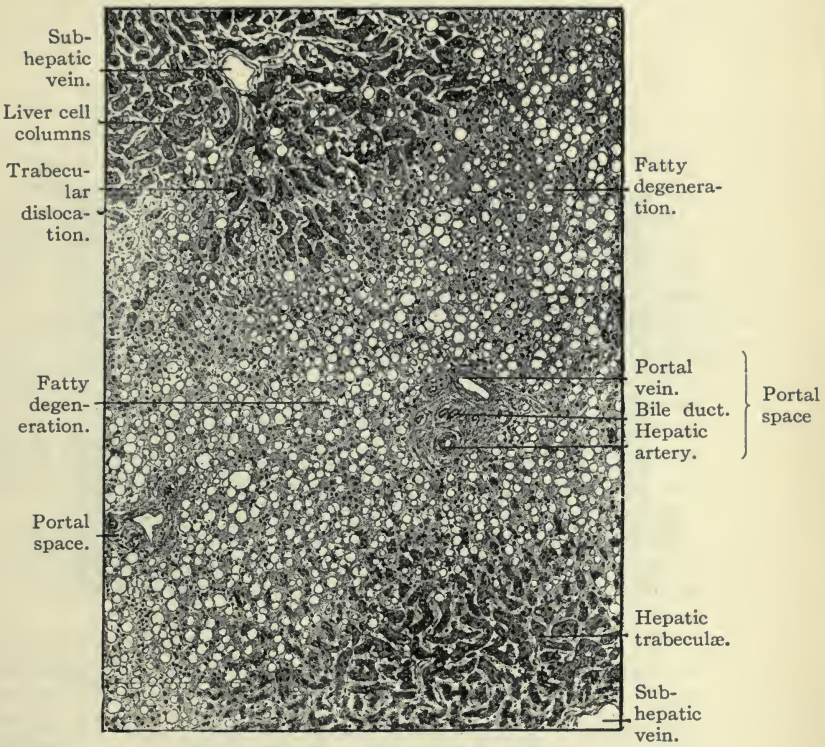


Fig. 25.—Fatty and congested liver.

Stained with hematoxylon and eosin. Magnified 100 diameters.

A section of a large, flabby, reddish-yellow liver removed at autopsy from a case of pulmonary tuberculosis. In the center and a little to the right there is a portal space surrounded by an extensive zone of fatty degeneration. Above and below it are columns of hepatic cells separated by dilated capillaries centering about a subhepatic vein.

FATTY DEGENERATION OF THE LIVER.

The liver was removed from the body of a patient dying of sarcoma, with profound anemia affecting all of the viscera.

Diagnosis of the Organ.—This can at once be made, as in the preceding case, by observing the columns of liver cells and the arrangement of the bloodvessels and bile ducts in the periportal connective tissue.

Diagnosis of the Lesion.—A little to the left and slightly below the middle of the drawing there is an opening which, being single, thin-walled and without surrounding connective tissue, can be recognized as a central vein. From it, in all directions, radiate columns of liver cells like the spokes of a wheel. But all of the cells for a considerable distance from the central vein are scarcely recognizable because of contained transparent, highly refracting vacuoles—fat droplets.

It will be observed that the distribution of the fatty deposit in this case is exactly the reverse of that in the preceding illustration. There it was at the periphery of the lobule, here it is at its center.

The meaning of visible fat in the cells is not sufficiently clear to enable positive inferences to be drawn, but it is supposed that in the preceding case the fat brought to the liver in the portal blood not being quickly oxidized collected in the adjacent cells pending combustion. In the present case, however, it is supposed that the malnutrition arising from the impoverished condition of the blood has been followed by retrogressive changes in the liver cells with partial chemical dissolution of the protoplasm and the setting free of its combined fat.

Résumé.—Centrally situated fatty change of the liver cells—*fatty metamorphosis.*

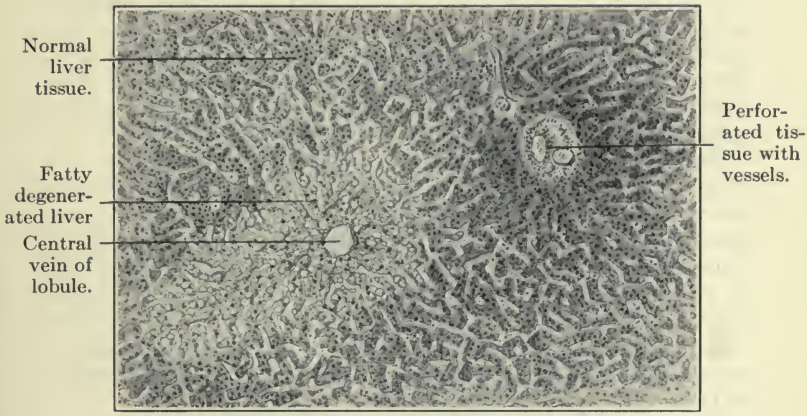


Fig. 26.—Fatty degeneration of the liver.

Stained with hematoxylin and eosin. Magnified 200 diameters.

From a man dying of sarcoma, with profound anemia of the viscera.

AMYLOID INFILTRATION OF THE LIVER.

Section of a portion of a large firm dark-colored liver from a case of chronic pulmonary tuberculosis.

Diagnosis of the Organ.—This is not easy on account of the advanced degree of the morbid process present. But careful examination of the right-hand margin of the drawing will show cells arranged in columns and of the appearance most commonly seen in the liver. Near the center of the drawing there is a section of a single, thin-walled vessel, probably a central vein. By moving the section about it may be possible to find periportal connective tissue with sections of the hepatic artery, subportal vein and bile ducts.

Diagnosis of the Lesion.—That which at once strikes the observer is the fact that the greater part of the sketch represents a structureless, waxy, amorphous, pink-stained substance that seems to have taken the place of the liver cells. Upon careful examination one can scarcely escape the impression that this is a new substance that has infiltrated between the liver cells and crowded them out. In many places small (atrophic) liver cells may be seen caught between the masses of infiltrating substance. Thus separated from their fellows and from their nutrient supply such are doomed to extinction.

This new homogeneous substance, because of a fancied resemblance to boiled starch and because it sometimes gives a blue color with iodine and sulphuric acid, is called *amyloid.* It has no relation to the starches, however, but is a conjugated protein. With Lugol's solution it gives a mahogany red-brown color, with gentian violet (1 per cent aqueous solution) a pink color. It stains pink with eosin as in the case under observation.

Supposing that the vessel near the center of the drawing is a central vein, one can make out that the amyloid deposit occupies a distribution intermediate between a central and a peripheral zone. This is, however, rarely as clearly shown as in this drawing.

Résumé.—Infiltration of the intermediate zone of the liver lobule by a translucent waxy substance with affinity for iodine and gentian violet—*amyloid infiltration.*

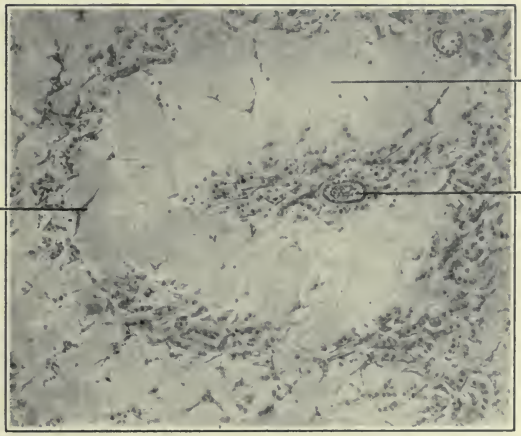


Fig. 27.—Amyloid infiltration of the liver.

Stained with hematoxylin and eosin. Magnified 100 diameters.

LAENNEC'S ATROPHIC CIRRHOSIS OF THE LIVER.

Diagnosis of the Organ.—In spite of the transformation of the architecture of the organ, the liver is easily recognized, thanks to the triad of diagnostic features already given: portal spaces, central veins and columns of liver cells.

Diagnosis of the Lesion.—One is at once struck by the presence of bands of fibrillar tissue that divide the hepatic tissue into a series of islands. These are best demonstrated in sections stained by Van Giesen's method in which they appear bright red.

The abnormal development of the connective tissue is sufficient to lead to the opinion that in this case we have to do with a sclerosis, or, what comes to the same thing, an annular cirrhosis of the liver.

With the higher magnification the more or less thick bands of connective tissue are found to be formed of fine and feebly undulating fibrillæ, in the meshes of which there are small dots representing the nuclei of fixed connective-tissue cells. At certain points, as, for example, in the upper left-hand part of the drawing, these round cells occur in patches which often preponderate in the portal spaces or beneath the capsule of the liver (not visible here).

Among the bile ducts some are large enough to show the cuboidal epithelium, but a great many are serpentine strands of cells without appreciable lumen. It is a mistake to regard these latter as canaliculi or bile capillaries of new formation. More likely they are columns of atrophic liver cells that are compressed between the fibers of the connective tissue—*pseudo-canaliculi.*

The columns of liver cells are confused in their relations and in their structure. They no longer seem to radiate from the central vein like the spokes of a wheel. Furthermore, many of the liver cells are in a state of fatty disease.

Résumé.—Annular cirrhosis of the liver also called the *bivenous cirrhosis* because the bands of connective tissue connect the central vein and the periportal veins and penetrate into the lobules. This type of annular cirrhosis corresponds, from the microscopic point of view, either with the atrophic cirrhosis of Laennec or with the hypertrophic cirrhosis of alcoholism.

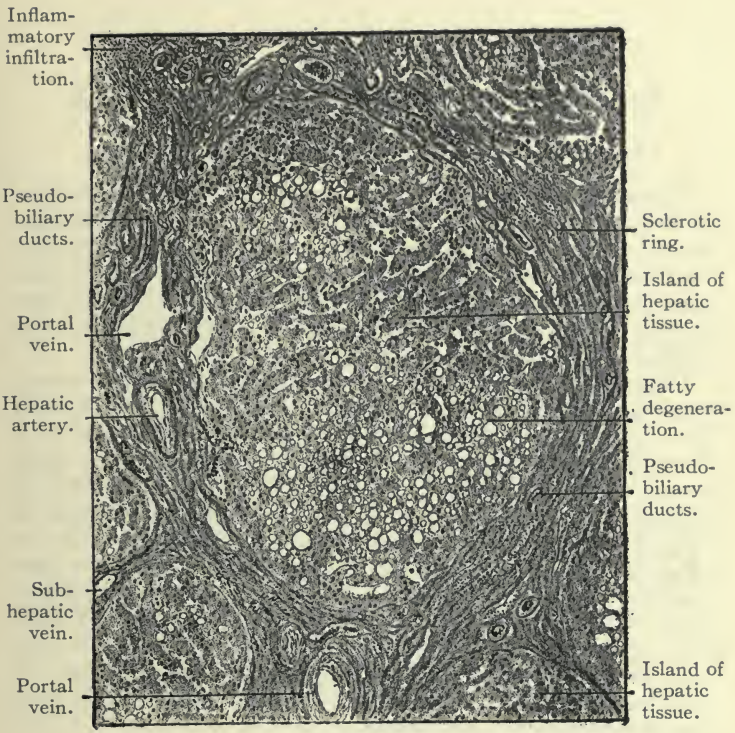


Fig. 28.—Atrophic cirrhosis of the liver.

Stained by Van Giesen's method. Magnified 100 diameters.

The liver from which this section was made was removed at autopsy. It was atrophied, irregular, nodular (hob-nail), and upon section showed bands of sclerotic tissue throughout its substance. In the center of the drawing a large island of the hepatic parenchyma is shown surrounded by a thick ring of connective tissue (annular cirrhosis). Portions of other similar islands are seen at the periphery.

BILIARY PIGMENTATION OF THE LIVER.

From a Case of Chronic Obstruction of the Bile Ducts.

Diagnosis of the Organ.—Under the high power so limited an area of the liver tissue is shown as to make the diagnosis a matter of doubt. One should confirm his suspicion that the organ is the liver by using a low-power lens and finding central veins with radiating columns of liver cells and periportal connective tissue with hepatic artery, subportal vein and bile ducts.

Diagnosis of the Lesion.—In the upper right-hand corner and elsewhere throughout the tissue represented in the drawing there are some normal liver cells. But the greater number of liver cells are modified through the presence of granules, single or in groups, of varying size and a color varying in intensity to opaque dark green. Here and there, between the columns of liver cells, in spaces supposed to be bile capillaries, there are larger and coarser masses of the same substance, sometimes rounded, sometimes clavate, sometimes dumb-bell in shape. These are composed of inspissated and more or less oxidized bile pigments and in the bile capillaries are surrounded by amorphous translucent matter which is probably a protein constituent of the bile condensed by the obstructive process and precipitated by the reagents.

The seat of biliary obstruction is not shown in the section. It may have affected the duct system low down, even entirely outside of the liver proper, but its effect has been the retention of the bile in the ducts and capillaries, with resulting separation of the pigment and its disposition in the distribution figured.

Résumé.—Biliary pigmentation of the liver from obstruction of the ducts.

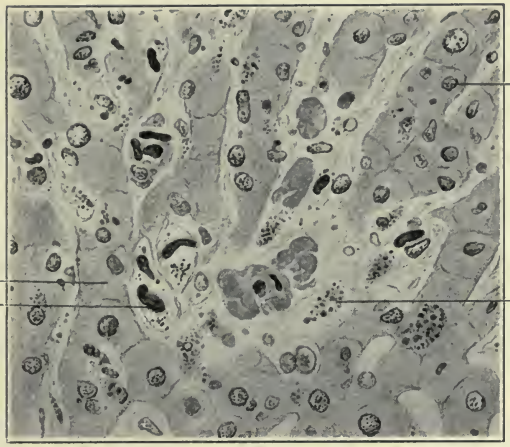


Fig. 29.—Bile ducts containing inspissated bile, from a case of biliary obstruction.

Stained with hematoxylin and eosin. Magnfied 500 diameters.

MALARIAL PIGMENTATION OF THE LIVER.

From a Case of Chronic Paludism.

Diagnosis of the Organ.—This cannot be certainly made from the limited extent of tissue shown in the drawing. In most cases the arrangement of polyhedral cells in columns such as shown here is sufficient to make the diagnosis, but the student should not be satisfied. What he first thought liver might turn out to be part of the adrenal or part of a corpus luteum of pregnancy. By moving the section about under a lower magnification, however, the central veins with radiating columns of liver cells and peripheral connective tissue with sections of the renal arteries, subportal veins and bile ducts ought to be found to complete the diagnosis.

Diagnosis of the Lesion.—The liver cells in this case show no distinct abnormality. But between them and in the capillary plexuses—hepatic sinusoids—there are numbers of cells of irregular shape and unequal size whose protoplasm is filled with black granules of fairly uniform size to such an extent as to make it difficult to discover the rather darkly stained ovoid vesicular nuclei. These are the cells of Kupffer, and are phagocytes. The black pigment they contain is *hemozoin*, or melanin, a metabolic product of the malarial plasmodium which is set free in the circulation at the time of sporulation and is subsequently taken up by phagocytic cells, among which are these cells of Kupffer in the liver. The cells react similarly to other minute particles in the circulation.

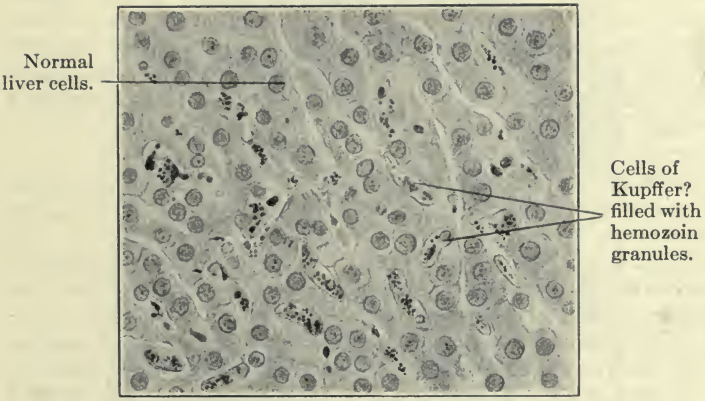


Fig. 30.—Malarial pigmentation of the liver in a case of chronic paladism.

Stained with hematoxylin and eosin. Magnified 350 diameters.

CAVERNOUS ANGIOMA OF THE LIVER.

In the substance of hepatic parenchyma without other definite disturbance the naked eye discovers a large bright red patch (Fig. 31, A). Under the low power of the microscope this is found to be composed of large spaces whose inner walls are lined with a delicate endothelium. These cavities are filled with blood. They are, in fact, blood spaces, whose walls are formed of a connective tissue that is mostly fibrous and contains very few cells. A few capillaries can be seen here and there in the connective-tissue partitions which form a vast network with coarse meshes, marking out the spaces which freely intercommunicate with one another, forming a veritable cavernous tissue similar to that of the corpus cavernosum of the penis in the state of erection.

The occurrence of such a tissue in the liver constitutes an *angioma—cavernous angioma*—a benign tumor, never giving metastasis.

At the periphery of the angioma the cavernous tissue is separated from the hepatic parenchyma by a layer of connective tissue, as is the rule with benign tumors. There are no compressed columns of liver cells at the edge of the tumor such as one sees at the borders of cancer nodules. The absence of all signs of compression is explained by the very slow growth of the tumor which is of congenital origin.

Differential Diagnosis.—It is important not to confound the tumor with a hemorrhage: If it were such the trabeculæ would be dissociated and the hemorrhagic foci would not be so nicely delimited by endothelium.

In *capillary angioma* there are no large blood spaces, but, on the contrary, very small spaces corresponding in size with the capillaries themselves compacted in considerable numbers. Capillary angioma is almost never encountered in the liver, but occurs in the skin where it is known as *nevus vasculosus*.

Résumé.—*Cavernous angioma of the liver*, a small benign tumor, sometimes single, sometimes multiple, and constituting a not uncommon and rarely important autopsy finding.

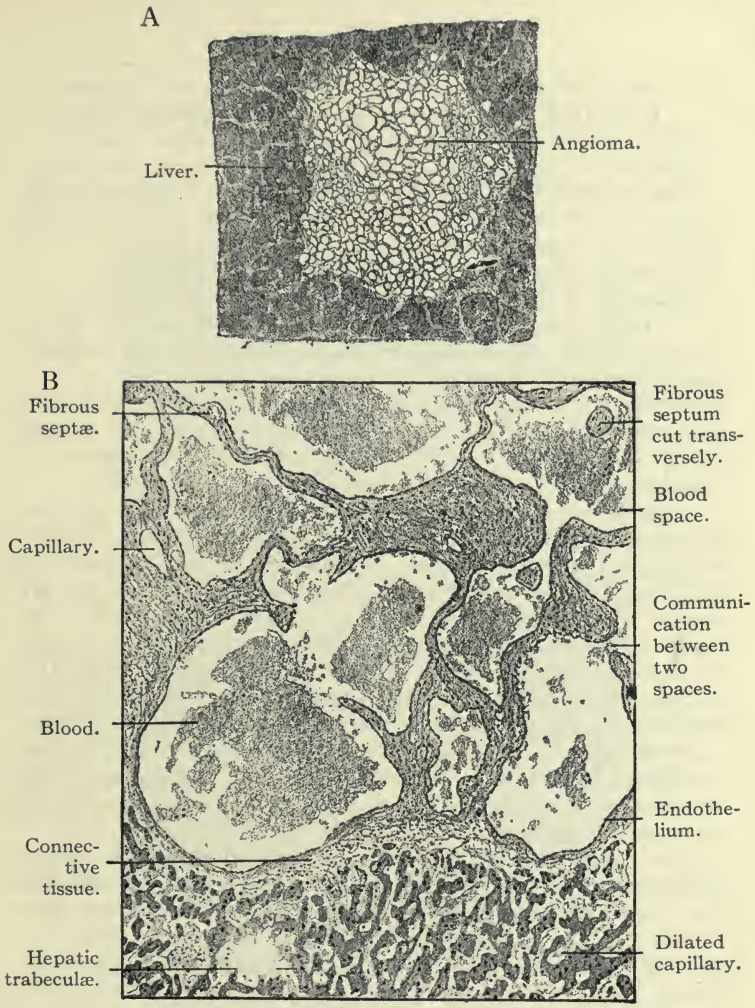


Fig. 31. Cavernous angioma of the liver.

Stained with hematoxylon and eosin.

A.—*A section of the entire tumor, surrounded on all sides by the liver tissue. It was unexpectedly found at autopsy.*

B.—*Drawing showing the appearance of the margin of the tumor and the adjacent liver substance. Magnified 80 diameters.*

BILIARY ABSCESS OF THE LIVER WITH CIRRHOSIS.

Diagnosis of the Organ.—It is quite easy to recognize the section as coming from the liver because of the visible columns of liver cells and the distinct periportal connective tissue with its usual accompaniment of vein, artery and bile ducts.

Diagnosis of the Lesion.—Two things attract attention:

1. Dark colored oval patches, two of which show in the drawing and sharply contrast their dark blue color with the generally rose-red color of the section. These are the abscesses.

2. The excess of connective tissue in the form of islets that concentrate about the periportal tissue and send out narrow bands between the hepatic parenchyma, dissecting apart its columns of cells. This is the indication of the cirrhosis.

Under a higher power the dark-colored, homogeneous patches show themselves to be composed of aggregated cellular elements with nuclei of variable form. Some of these are elongated and of large size and correspond to the mononuclears; others are smaller and many-lobed, and evidently polynuclears. The nuclei are in the condition of pycnosis, that is to say, in process of degeneration, and show only as blue masses of chromatin without any visible finer structural details. The protoplasm itself is not altered, but the cellular outlines are distinguished with difficulty. These cells are pus cells, formed of white blood corpuscles in a state of degeneration, whose aggregation forms *microscopic abscesses*. At the edge of the abscess are fine strands of young connective tissue.

The connective tissue islets are particularly dense in the neighborhood of the bile ducts, in the periportal spaces. The bile canaliculi have a lining of cuboidal epithelium, well preserved, though in the center of some of them there may be a few desquamated cells and polymorphonuclear leukocytes. About the bile ducts the lesions of periangiocholitis are shown by concentric sheaths composed of layers of connective tissue and inflammatory collections of cells of blue color. In this connective tissue are many pseudocanaliculi—false bile ducts—that call attention to themselves by a double layer of cells and potential but not distinct lumina. These are signs of endo- and pericholangitis. Occasional collections of bile pigment in the portal connective tissue indicate retention of bile. The

columns of liver cells are dissociated; the cells here and there in a state of fatty degeneration.

Résumé.—*Multiple abscess of the liver*, of which the biliary origin is shown by the lesions of the bile canaliculi (angiocholitis), by the retention of bile and the periductal sclerosis.

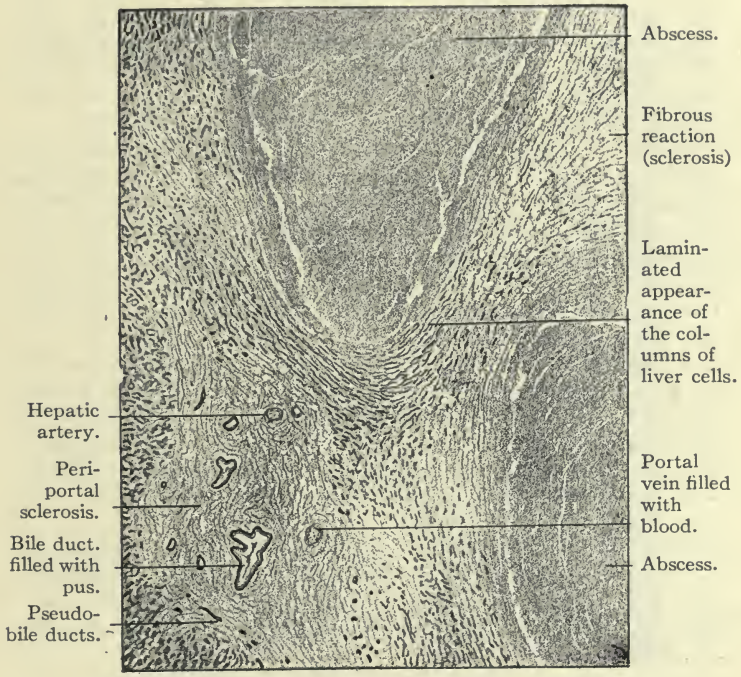


Fig. 32.—Biliary abscess of the liver with cirrhosis.

Stained with hematoxylon and eosin. Magnified 30 diameters.

Cirrhotic liver of an old woman with cholelithiasis. The organ was crowded with little abscesses most of which were visible to the naked eye, and had become a spongy mass filled with pus. The drawing shows two of the abscesses surrounded by reactive inflammation (sclerosis), and columns of liver cells separate and compressed.

SECONDARY CANCER OF THE LIVER.

Diagnosis of the Organ.—This is quite easy in the lower part of the drawing where the columns of liver cells show distinctly.

Diagnosis of the Lesion.—An examination by the naked eye or with a low-power lens shows distinct masses of a dark color and varying size, sharply separated from the more pale and uniform part of the section. These masses are composed of epithelial cells often arranged in the form of glandular acini. Some narrow strands of connective tissue carry the nutrient bloodvessels of the tumor and at the same time its stroma.

Under a higher magnification the nature of the tumor can be better made out. The cells are columnar and arranged in columns or acini. The nuclei are elongated and not infrequently show karyokinetic figures, indicating abnormal cellular activity. Amorphous matter frequently fills the spaces—products of secretion. The cells, both by grouping and structure suggest those of a glandular mucosa such as might occur in some part of the alimentary canal—stomach or intestin.

At the periphery of the nodules are small cellular masses of the same type as those of the principal tumor which is thus shown to be infiltrating the organ. In the hepatic parenchyma itself (far to the right and low down in the drawing) a mass of the tumor cells (cancer embolus) can be seen in a portal vein. It is by the vessels and notably by the portal vein that the distribution of the cancer cells takes place.

From the examination of this section one quickly grasps the two principal and most important features of malignant tumors: the destructive invasion and the metastasis, characters that joined to the signs of cellular activity enable one to say at once that he has to do with a cancer.

Is it a primary cancer developed on the spot through malignant transformation of the columns of liver cells, or bile ducts, or is it a secondary cancer?

The type of cells found does not suggest hepatic cells. On the contrary, their arrangement in glandular acini and the absence of transition between the hepatic parenchyma and the cancer make us incline to the opinion that the tumor is secondary.

At the periphery of the cancer nodule there is no connective-tissue separation as is found in the benign tumors. The trabeculæ are compressed and reduced to thin lamellæ.

There is also a contingent lesion in the form of congestion that chiefly centers about the central veins.

Résumé.—*Secondary cancer of the liver. Cylindrical epithelioma,* or *adenocarcinoma,* the primary seat of which seems to be some part of the alimentary canal.

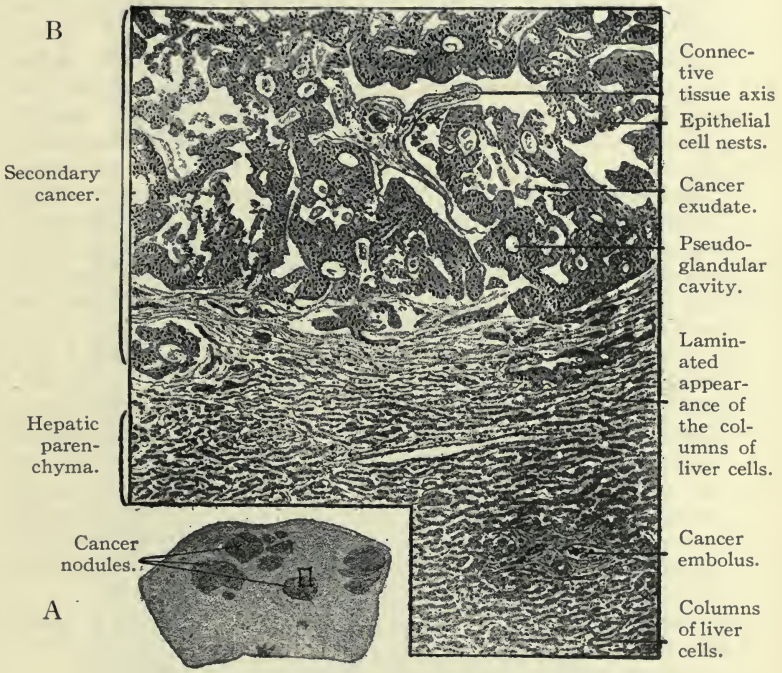


Fig. 33.—Secondary cancer of the liver.

Stained with hematoxylon and eosin. Magnified 90 diameters.

Secondary cancer of the liver characterized by the occurrence of numerous tumor nodules secondary to cancer of the pylorus.

A.—*Fragment of tissue showing numerous nodules, natural size.*

B.—*Periphery of one of the nodules shown in A magnified* 90 *diameters, and showing the hepatic parenchyma with the columns of liver cells separated and compressed.*

WALL OF AN ECHINOCOCCUS CYST OF THE LIVER.

Diagnosis of the Organ.—This is absolutely impossible. There is no liver tissue in the section which is altogether made up of a pathological new formation. For the diagnosis, therefore, we must depend upon information obtained from the pathological anatomical clinic where the specimen was obtained. This informs us that the specimen was a fragment of an echinococcus cyst of the liver.

Diagnosis of the Lesion.—The upper figure, A, shown under a low magnification, gives the general topography of the wall of the cyst. In the interior of the concavity, turned toward the left, there is nothing more than débris of a fibrinopurulent character. Nothing remains either of the membrane or of the cyst contents. The wall of the cyst consists of a rather thick composed of adult fibrous connective tissue. This wall represents a defensive reaction against the parasite (echinococcus) formed at the expense of the connective tissue of the organ in which the cyst developed, in this case the liver, which, as has been said, is not visible in the section.

Under a higher magnification (see B.) the structure of the wall itself is shown. That which should at once strike the observer is the great number of eosinophilic cells it contains. These are polymorphonuclear leukocytes that contain great numbers of granules—acidophilic granules—that have affinity for acid aniline dyes such as eosine. Several of these cells seem to contain two nuclei, but this is only an appearance that results from the close approximation of cells whose limits cannot be accurately defined. Here and there eosinophilic granules may be seen free in the stroma.

The stroma itself, as shown in the drawing, includes a capillary bloodvessel and connective-tissue cells, some of which are elongated, others irregular—fixed cells.

The intensity of the local eosinophilia parallels that found when the blood is examined, for *eosinophilia* is almost constantly found in parasitic affections, especially in cases of infestation by the echinococcus. In this very case the eosinophiles in the circulating blood were from 4 to 6 per cent, as contrasted with the 1 per cent which is supposed to be normal.

Résumé.—Subacute inflammatory reaction constituting the wall of an *echinococcus* or *hydatid cyst*, with eosinophilia both local and in the circulating blood.

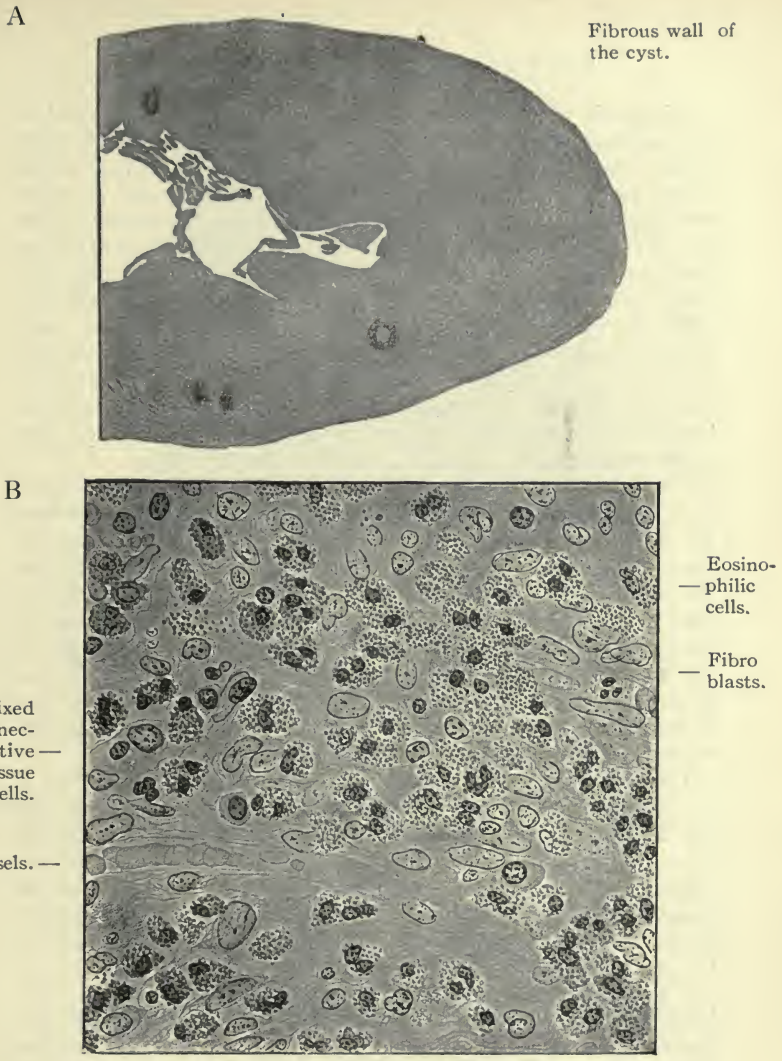


Fig. 34.—Wall of a hyatid cyst.

Stained with hematoxylon and eosin.

A.—*About one-half of the cyst magnified twice, and showing its wall and fibrinous contents.*

B.—*Part of the wall magnified* 200 *diameters, and showing the great number of eosinophilic cells it contains.*

Diagnosis of the Organ.—Under a low-power magnification the parenchyma of the organ seems to be formed of small masses of glandular cells disposed about a potential rather than distinctly visible central cavity. The finely granular structure of the protoplasm, deeply colored by the hematoxylon, the circular arrangement of the cells, the excentric position of their nuclei and the very small size of the cavity of the acini make one think of a gland in full activity and of the salivary gland in particular—parotid, for example. But upon more careful inspection it is found that there are certain small pale areas distributed throughout the parenchyma—the islands of Langerhans. In these one finds pale or dark nuclei distributed throughout a protoplasmic mass not distinctly divided into cells—syncytial or plasmodial mass.

The glandular acini plus the islands of Langerhans enable the diagnosis of the *pancreas* to be made. The acini represent the organ of external secretion, the islands of Langerhans, the organ of internal secretion. Between these two formations there are various intermediates which correspond to transition stages. The acini can transform themselves into islands of Langerhans and *vice versa*. In the interior of the gland, in the substance of the connective-tissue partitions, the presence of ducts is to be noted. These are branches of the ducts of Wirsung and Santorini and are composed of small cubical cells supported by a dense basement membrane.

Diagnosis of the Lesion.—That which attracts attention is the thickness of the bands of connective tissue that pass through the tissue in all directions, dividing it into lobules. There are even points at which little islands of the acinous tissue are separated from the main mass and lost in the substance of the connective-tissue partitions. Here we see some correspondence with what was found in the liver in Laennec's cirrhosis; but the nature of the parenchyma differs.

The sclerosis is at the same time peri- and intralobular. The large bands of connective tissue divide the gland into lobules; the finer bands of the same tissue penetrate into the lobules and dislocate the glandular acini—*periacinous sclerosis*, and even in some cases *monocellular sclerosis*.

The ducts contain a number of desquamated cells which either betray the inflammatory nature of the process, or may be the result of errors in fixation and treatment.

Résumé.—Chronic inflammation of the pancreas: *chronic sclerotic pancreatitis*.

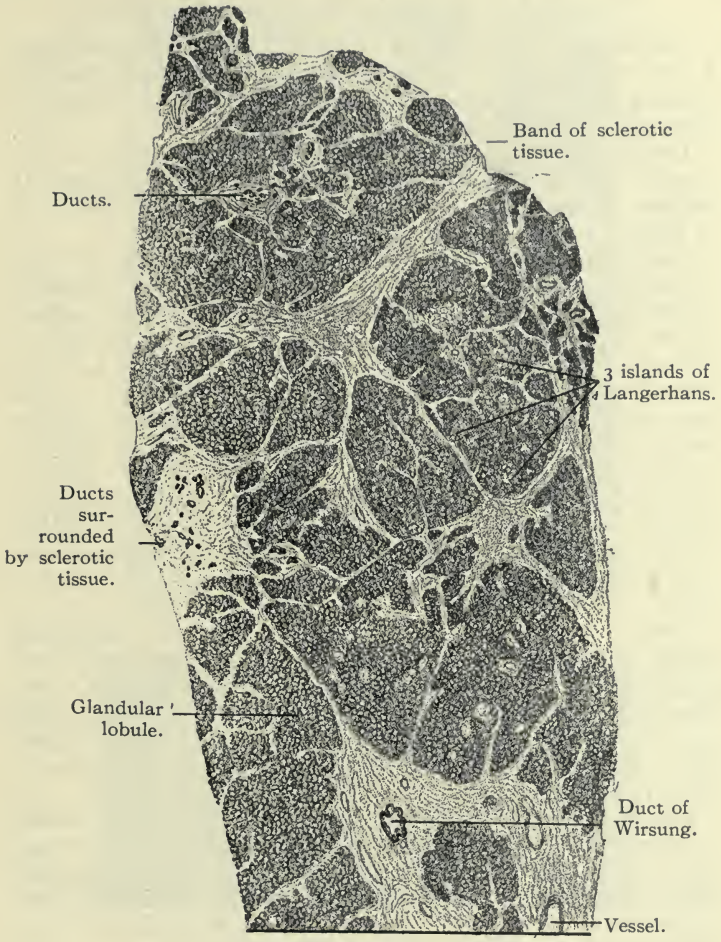


Fig. 35.—Chronic pancreatis.

Stained with hematoxylon and eosin. Magnified 8 diameters.

Sclerosis of the pancreas in a case of chronic pancreatitis consecutive upon cholelithiasis in an old man.

ADENOCARCINOMA OF THE PANCREAS.

The section shows both the cancer and the healthy gland and is, therefore, composed of two distinct parts that differ in their staining qualities: the one dark colored and blue, the other a great deal paler and more rose colored.

Diagnosis of the Organ.—In the upper drawing (Fig. 36, A), the dark part to the right can easily be recognized as pancreas because of the presence of the glandular acini and the island of Langerhans.

Diagnosis of the Lesion.—To the left in the same drawing, in the pale-colored area, one may see some of the islands of Langerhans and pancreatic acini, but cannot fail to be struck by the disorderly arrangement. Instead of being composed of cells regularly arranged about a central cavity there are long tubes, more or less attenuated, with a lumen scarcely visible and often, indeed, entirely absent. At other points, on the contrary, the central cavity may be very obvious. In many of the dilated acini there are masses of finely granular material coagulated by the reagents. Finally, and this is most characteristic, the neoplasmic cells escape into the stroma, no longer adopting an acinous arrangement and resemble the fixed connective-tissue cells except for their larger size and more spherical shape.

Under a low-power lens the tumor seems to be completely separated from the normal gland, but under a high power one is surprised to find at various points, in what appears to be otherwise normal parenchyma, some areas in which the cells become atypical, show the same appearance as in the tumor (zone of invasion) and reproduce the same atypical cellular arrangement as in the cancer properly so called.

Differential Diagnosis.—Interstitial pancreatitis with mononuclear sclerosis can be mistaken for cancer; but in the case before us the difference in the staining properties, the almost perfect preservation of the normal parenchyma and finally the occurrence of occasional cellular monstrosities make us throw aside the idea of simple sclerosis in favor of cancer.

The dislocation of the glandular acini, the arrangement of the cells in tubules, their peculiar staining affinities, which all differ from the normal, enable us to say that the lesion is *cancer of the pancreas* developed from the cells of the acini, and which has in some places reached the point of actual infiltration.

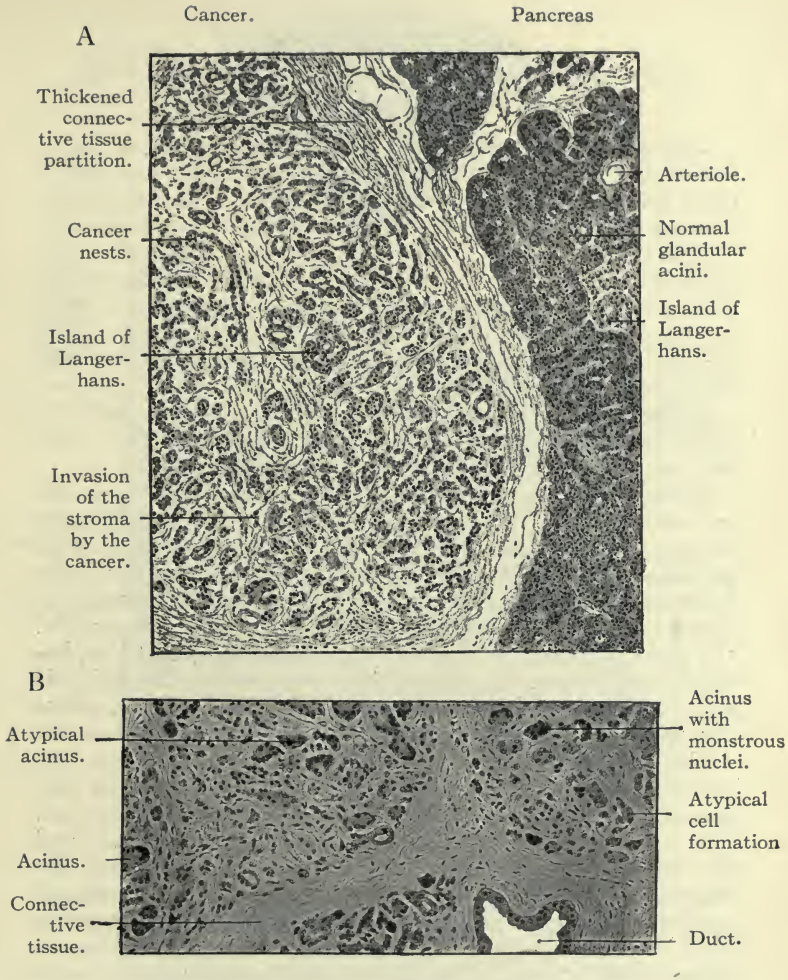


Fig. 36.—Cancer of the pancreas.

Stained with hematoxylon and eosin.

Fragment removed at operation. Death shortly after followed from obstruction of the common bile duct.

A.—*Magnification of* 100 *diameters, showing the separation between the cancer and the normal pancreas.*

B.—*Magnification of* 300 *diameters, showing the cancer zone.*

CHRONIC PASSIVE CONGESTION OF THE SPLEEN.

Diagnosis of the Organ.—To the naked eye the section is found to consist of a pale background, distributed over which there are a number of dark points. With a medium-power lens the background is found to be composed of a pale tissue in which nuclei and red blood corpuscles are mixed up. The dark points are found to be masses of lymphoid tissue, nearly always centered about a small bloodvessel—arteriole. These are the Malpighian bodies characteristic of the spleen. The pale substance of the background is the *red pulp;* the dark points and the Malpighian corpuscles the *white pulp.*

A greater magnification shows a Malpighian corpuscle in which is a section of an arteriole near the periphery. The cells are nearly all of the type of lymphocytes.

Elsewhere in the section other Malpighian corpuscles can be found. These do not always show the central arteriole and are sometimes entirely without the vessel, appearing as lymphatic ganglia in the paler background of splenic pulp. Between the Malpighian corpuscles the red pulp is formed of a pale tissue in which various elements are easily recognizable. The most numerous are the red blood corpuscles, next lymphocytes, then occasional polymorphonuclear leukocytes and cells with budding nuclei. Finally, separating these elements there is a reticulum comparable to that seen in the lymph nodes.

Diagnosis of the Lesion.—In the section itself, the red pulp is differentiated from the white pulp, with a distinctness that causes the Malpighian corpuscles to stand out prominently. This is because of the extreme congestion of the red pulp and the consequent predominance of the red corpuscles over the lymphocytes. The red corpuscles are numerous and so massed together that there are small areas of actual hemorrhage in which brownish masses of blood pigment—hematoidin—can be distinguished. Some of the pigment is contained in the interior of large cells—*mononuclear phagocytes.*

Attention must be again called to the connective tissue partitions—trabeculæ—which indicate a pronounced sclerosis.

Résumé.—The enormous number of red blood corpuscles in the pulp, the presence of the small hemorrhagic areas, the numerous collections of pigment and the intensity of the connective-tissue reaction enable the diagnosis of *chronic passive congestion of the spleen*—cardiac spleen—to be made.

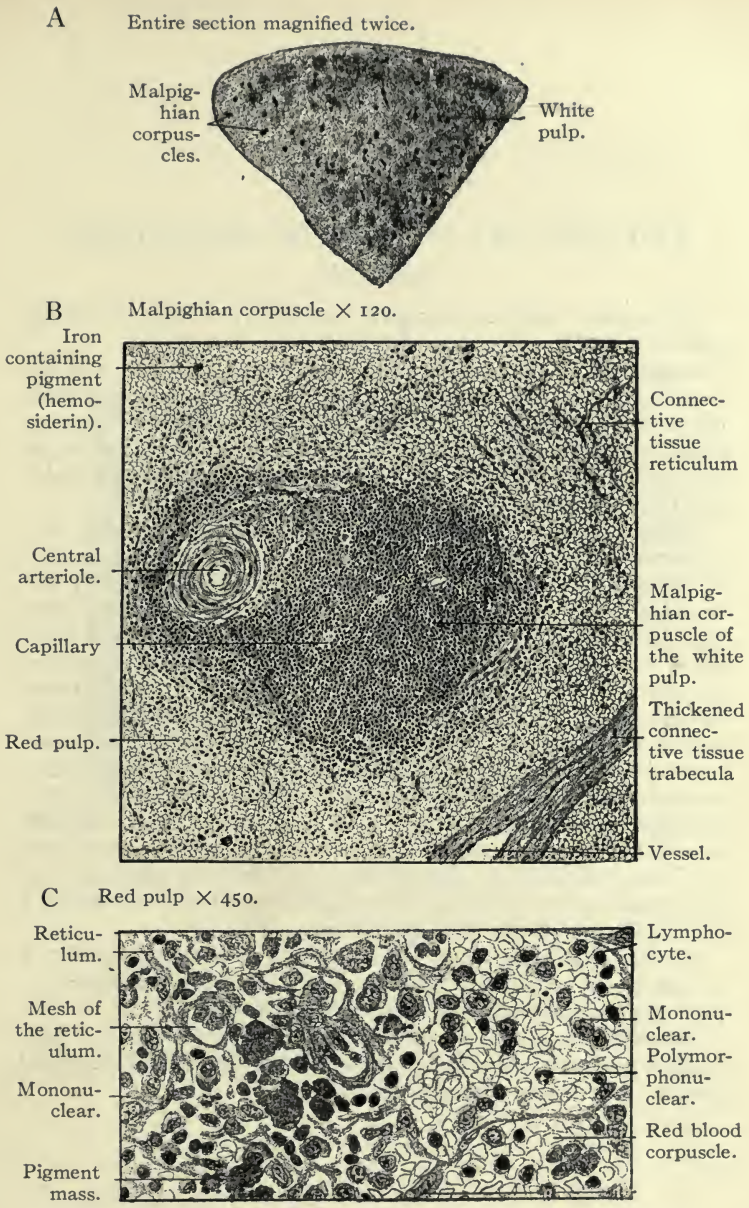


Fig. 37.—Chronic passive congestion of the spleen, in an old man dying of asystole.

AMYLOID INFILTRATION OF THE SPLEEN.

Sago Spleen.

The spleen, slightly enlarged, was removed from a patient dead of chronic pulmonary tuberculosis.

Diagnosis of the Organ.—This is difficult to make without examining more of the section than is shown in the drawing. By so doing it is easily possible to recognize the red pulp and locate the white pulp, some of which is not changed and occurs as typical Malpighian bodies with the associated arterioles and the numerous fibromuscular trabeculæ.

Diagnosis of the Lesion.—To the right of the drawing is a rounded formation, at the center of which a transverse section of an arteriole occurs. The presence of the vessel and the rounded shape of the body suggest a Malpighian body, but the small size and resemblance to the surrounding red pulp show that if it be such, it is distinctly pathological. Moreover, instead of being composed of lymphoid cells, it is largely made up of masses of translucent waxy substance, taking a pinkish color with the eosin stain. These are *amyloid*, a conjugated proteid composed of protein and condroitin sulphuric acid, deposited between the cells with resulting atrophy and disappearance of many of them. The peculiar shapes of the amyloid deposits, some of which are rounded, some sigmoid and some serpentine, suggest that the amyloid substance, as is commonly the case, has first infiltrated about the walls of the capillaries of the Malpighian body.

By the application of Lugol's solution to amyloid substance a mahogany red-brown color is produced. Gentian violet (1 per cent aqueous solution) colors amyloid pink.

Résumé.—Deposits of homogeneous waxy substance about capillary vessels, striking characteristic colors with iodine and gentian violet—*amyloid infiltration.*

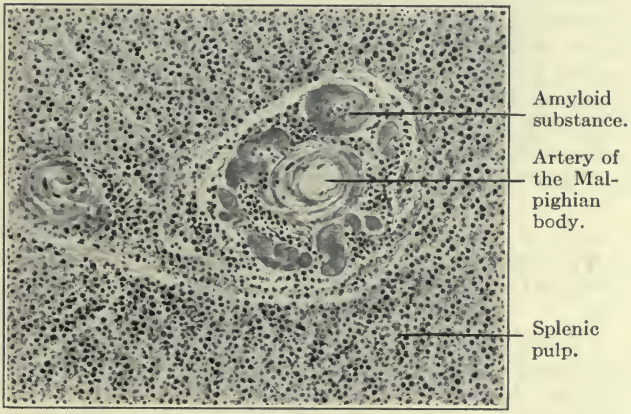


Fig. 38.—Amyloid infiltration of a malpighian body in the spleen. From a patient dying of chronic pulmonary tuberculosis.

Stained with hematoxylin and eosin. Magnified 200 diameters.

TUBERCULOSIS OF THE SPLEEN.

Diagnosis of the Organ.—The spleen can be recognized by the dark dotting of the Malpighian corpuscles upon the background of almost homogeneous paler pulp (Fig. 39, A).

Diagnosis of the Lesion.—That which at once strikes the observer is the presence of four or five spots of the color of "dregs of wine," scattered about irregularly, having the size of millet seeds and of no particular shape. Let us take one of these and subject it to a higher power for more careful study (Fig. 39, B).

1. At the right-hand part of the drawing, at a part corresponding very nearly to the center of one of the spots designated above, we see an amorphous granular tissue in which minute nuclear fragments are disseminated. This is easily recognized to be caseous substance. At the periphery of this substance there is a considerable mass of a black pigment. This is an artefact and results from the action of bichloride of mercury, in which the tissue was fixed, upon its proteins.

2. To the left of this caseous zone there is a second zone of cells of the type known as epithelioid cells. They have pale protoplasm, are of variable shape and their nuclei are not infrequently elongated. Between them are occasional giant cells.

3. Finally there is a third zone, at the extreme left of the drawing, in which appear a considerable number of lymphocytes, grouped about a central point, usually corresponding to the position of an arteriole. In these one recognizes the Malpighian corpuscles.

The rarity of the element often, but wrongly, considered to be characteristic of tubercle—the giant cell—might confuse a beginner as to the tuberculous nature of the lesion. But the epithelioid inflammatory reaction, added to the intense and precocious caseous transformation and the tendency to nodular formation, speak only in favor of the tuberculous nature of the lesion.

Résumé.—From the histological characteristics it may be concluded that we have to do with a *caseous tuberculosis of the spleen*, but, of course, it requires a bacteriological examination and the demonstration of the bacillus to confirm the diagnosis.

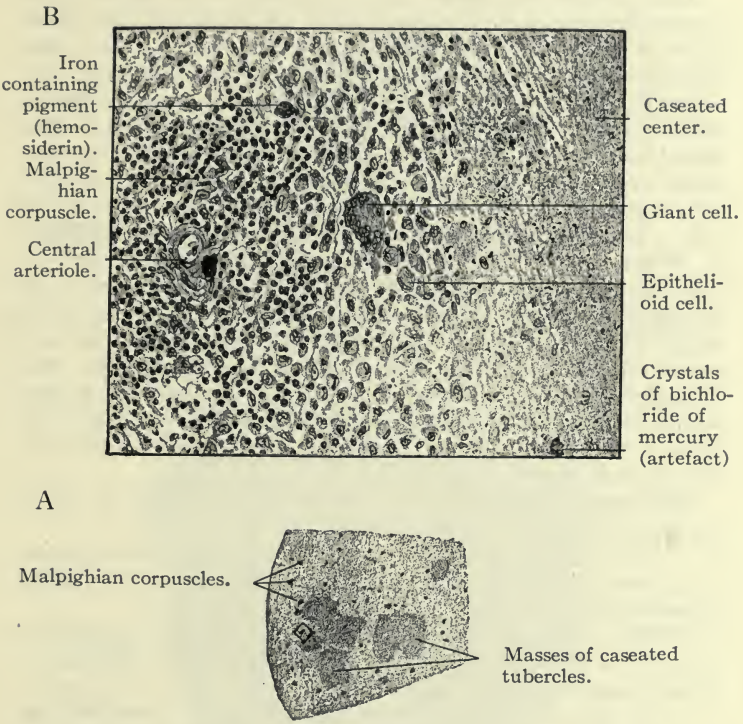


Fig. 39.—Tuberculosis of the spleen.

Stained with hematoxylon and eosin.

Tuberculosis of the spleen in a woman, aged forty-five years, dying of tuberculous meningitis following pulmonary tuberculosis with cavity formation.

A.—*Fragment of the spleen twice natural size, showing the distribution of the lesions, and a square showing the area from which* B *was taken.*

B.—*The caseous center and periphery of a tuberculous mass magnified* 250 *diameters.*

Diagnosis of the Organ.—To the naked eye or under a low-power lens the section appears oval and shows at one of its poles a greater amount of pale substance than at the other. The lower part of the section, seen in the drawing (Fig. 40), is a reticulated lymphoid tissue composed of a great number of small deeply staining cells, and under a low power can be divided into two different portions. One of these, below the capsule, sends prolongations into the depths of the organ. It is formed of a loose tissue composed of a reticulum poor in nuclei and is the *lacunar substance.* The other, composed of cells arranged in dense masses, with pale centers—germinative centers—is the follicular substance. The oval shape of the organ, the presence of the reticulated and follicular substance permits the diagnosis of lymph node. The differentiation into two kinds of substance—the one pale and lacunar, the other dense and follicular—ought to be easily recognized by the student, though beginners frequently mistake the pale germinal centers of the follicles for a pathological condition and suppose the node to be the seat of secondary cancer.

Differential Diagnosis.—Certain lymphoid organs are to be distinguished from the lymph node:

1. The *spleen* is recognized by the presence of the Malpighian corpuscles which are lymphoid-cell aggregations in the center of which there is an arteriole.

2. The *tonsils* can be recognized by the squamous epithelium that covers them by their crypts with glands and by the absence of any connective-tissue capsule.

3. The *thymus* is recognized by the absence of closed follicles and by the presence of the corpuscles of Hassal which are characteristic.

4. The *appendix* is easily recognized by the glandular crypts and the presence of columnar epithelium.

Diagnosis of the Lesion.—In the upper part of the figure the collection of pale-colored areas recalls the general appearance of the miliary tubercles already seen in other sections, especially the lung. The caseous centers are easily found and there are numerous giant cells surrounded by coronets of epithelioid cells with the usual abundant protoplasm, large pale nuclei and the peripheral zone of lymphocytes.

Résumé.—*Miliary tuberculosis of a lymph node* in an early stage. Later this might terminate in suppuration in which one would find nothing but a central caseous mass without structural details and surrounded by a fibrous envelope.

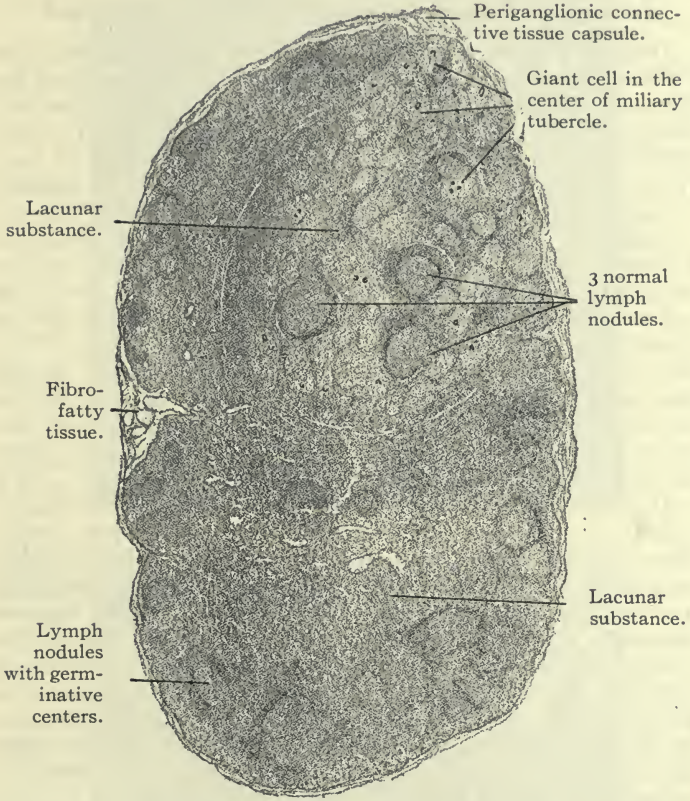


Fig. 40.—Tuberculosis of a lymph node.

Stained with hematoxylon and eosin. Magnified 16 diameters.

An iliac lymph node removed at an operation upon a case of ulcerative tuberculosis of the cecum. The lower part of the node is normal and shows the lymph nodules with germinative centers; the upper part contains numerous miliary tubercles with giant cells.

CANCER OF A LYMPH NODE.

Metastatic Epithelioma, Secondary to a Cancer of the Stomach.

Diagnosis of the Organ.—This is difficult if not impossible to make. One is forced to have recourse to information from the clinic or autopsy, from which we learn that the structure is a lymph node from the lesser curvature of the stomach. The only indications that permit us to suppose the structure to be a lymph node are the presence of lymphoid tissue and the surrounding connective-tissue capsule.

Diagnosis of the Lesion.—The greater part of the section is formed of cellular aggregations, pale in color, with insignificant masses of lymphoid tissue between them. In this case it is not to be expected that one could separate the gland into its classical elements, lacunar and ganglionic. We have to do with a pathological condition of some special nature, as the pale areas do not present any reticular aspect, but, on the contrary, are formed of cells with abundant protoplasm, disposed in long branching processes of epithelial cells—the cancer nests.

Under a higher power (Fig. 41, B) one sees all of the cytological modifications of malignant tumors; budding nuclei, often multiple in the same cell; numerous and often atypical mitotic figures, etc. The arrangement of the cells is anarchical, and nothing, apart from the rough draughts of acini, suggests the organ from which the cells were derived—atypical epithelioma. Nothing but their epitheliomatous character is recognizable. However, in other cases it is sometimes possible to find in the secondary tumors in lymphatic nodes an arrangement of the cells that indicates the structure of the organ from which the cells are derived, through a preservation of the primitive arrangement of the cells as in the original organ.

Résumé.—We have to do with an epithelial tumor developed in a lymph node, that is to say, a lymphatic metastasis. The cancer cells transported by the currents of fluid have arrived in the lymph node where they have grown and multiplied before going further. The arrangement and nature of the cancer cells here is very atypical and does not permit one to say from what organ they originally came, and in what organ the tumor originally started. The acinous outlines, however, suggest it to be from a glandular organ. To make sure, it is necessary to depend upon information derived from the autopsy or from the clinic.

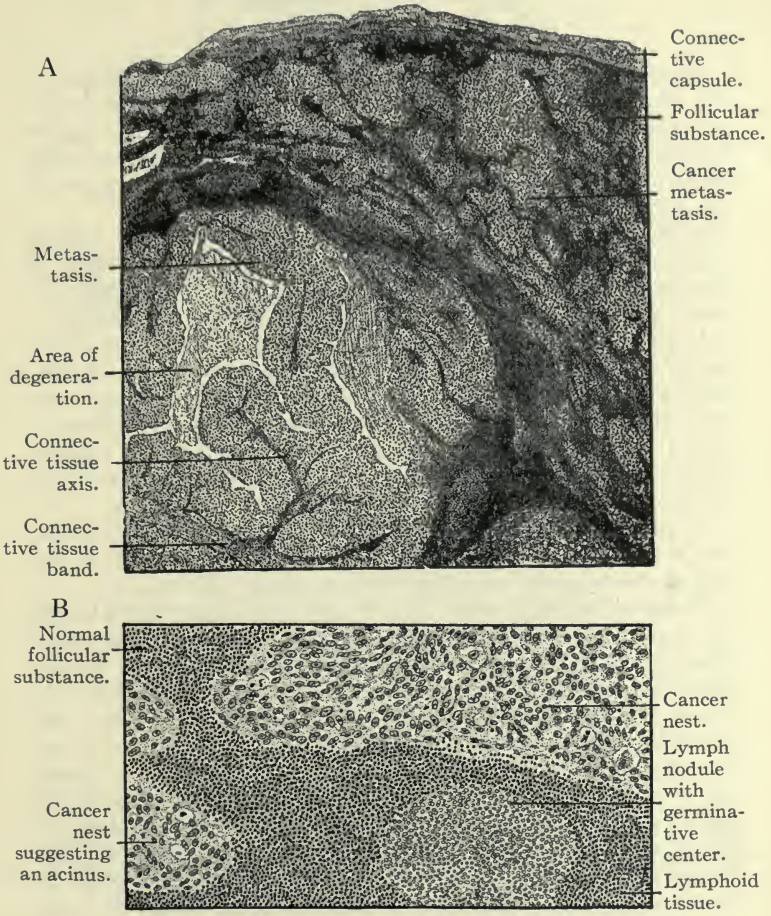


Fig. 41.—Secondary cancer of a lymph node.

Stained with hematoxylon and eosin.

The node was removed from the lesser curvature of the stomach in a case of cancer of the pylorus.

A.—*Magnified* 25 *diameters, and showing the appearance of the periphery of the node.*

B.—*Magnified* 150 *diameters, and showing the epithelial cell masses with their monstrous cells.*

CHRONIC MYOCARDITIS.

Fibrous Plaques on the Myocardium.

Diagnosis of the Organ.—If a section of the wall of one of the ventricles of the heart be examined with the naked eye, it is found to be limited on the external surface by an almost straight line and on the internal by a very sinuous one with large promontories and occasional islets which are sections of the muscular bundles.

If the section be examined with low-power lens the central portion is found to be composed of the muscular tissue of the myocardium, the cells of which are easily recognizable by their centrally situated nuclei and their Y-like branchings.

If we now turn to the part of the section shown in the drawing (Fig. 42) we see that at its superior part (A), which corresponds to its external surface, the myocardial fibers are covered with a thin layer of adipose tissue, above which there is a thin band of fibrillar connective tissue which is the visceral layer of the pericardium—the epicardium, of great importance in orienting one's self in studying sections of the heart.

If the entire thickness of the section was shown the festooned line with its promontories and islets, which corresponds to the endocardium, would be at the bottom of the drawing.

Diagnosis of the Lesion.—Here and there strands and bands of connective tissue penetrate into the muscular tissue and separate its fibers. They appear pale rose colored, the muscle being distinctly red. The connective tissue forms considerable masses—the fibrous patches of the myocardium—that can be distinctly seen with the naked eye. When the fibrous tissue is viewed with a higher magnification it is found to be composed of collagenous fibrillæ, with some cells of which the nuclei are visible. These are fixed cells of the connective tissue and betray an inflammatory reaction. Starting from the large plaques, the fibrous tissue infiltrates fasciculi in bundles of varying thickness—*interfascicular sclerosis*—and sometimes even between the cardiac cells—*interfibrillar sclerosis*. Under the high-power lens the myocardial fibers may show degeneration; they become pale, the protoplasm becomes finely granular and here and there there may be transverse fragmentation—*segmentary dislocation of the fibers*, long considered to be characteristic of cardiac degeneration, but now looked upon as an artefact of cadaverization. Attention must be called to accumulations of pigment granules surrounding the nuclei of the cardiac cells—pigmentary degeneration.

Résumé.—*Chronic myocarditis:* sclerosis or formation of fibrous patches in the myocardium, very common in the aged.

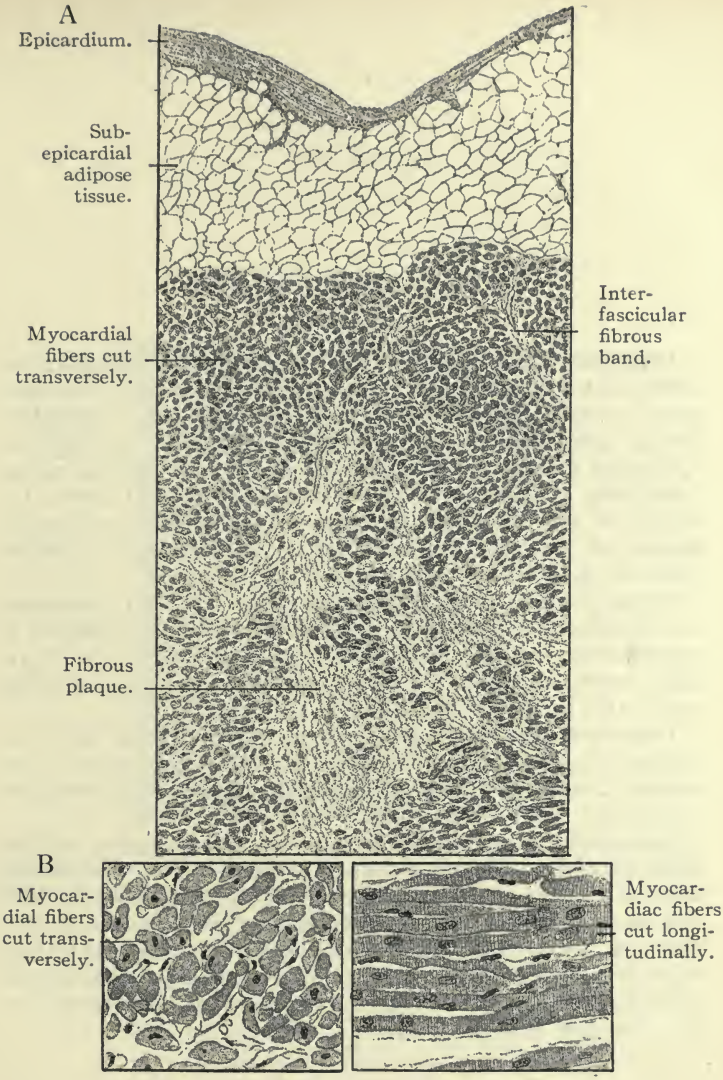


Fig. 42.—Chronic myocarditis.

Stained with hematoxylon and eosin.

A fibrous plaque in the right ventricle of the heart of a case of Bright's disease.

A.—*Magnified* 25 *diameters.*

B.—*Magnified* 120 *diameters.*

COR ADIPOSUM.

Obese Heart.

Diagnosis of the Organ.—Under the low magnification represented in the drawing this is scarcely possible. At the extreme lower margin the section passes perpendicularly through a fibrous and vascular membrane which is the epicardium. Ascending from this we reach a thick layer of adipose tissue containing a vessel, and above this, beginning at about the middle of the drawing there appear irregularly-shaped aggregations of red dots, while in the upper third of the section there are groups of horizontal wavy red lines.

Employing a higher magnification these latter can be resolved into bundles of transversely striated muscle fibers, made up of quadrilateral segments with centrally situated nuclei and lateral anastomoses by which the cardiac muscle can at once be recognized, and the tissue diagnosed as the heart.

Diagnosis of the Lesion.—Three things should at once impress the student as peculiar: (1) The large quantity of adipose tissue; (2) its distribution among the muscle bundles and fibers; (3) the small size of the muscle fibers.

The heart was removed from an obese individual who suffered from shortness of breath upon exertion. The microscopic findings explain, at least in part, the symptoms mentioned. The increase in the subepicardial adipose tissue and its descent between the muscle bundles and fibers has separated them so as to interfere with conjoint action and diminish their power, as well as compressing them so that many of them atrophy—*i. e.*, become smaller in size.

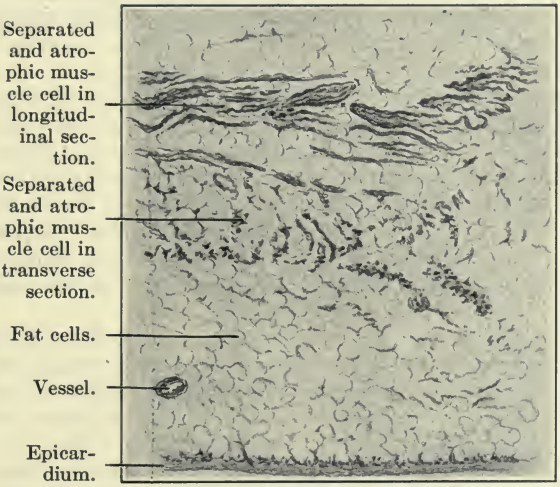


Fig. 43.—Cor adiposum—adipose heart. Heart suffering from fatty infiltration of the intermuscular connective tissue, with resulting separation and atrophy of the muscular fibers.

Magnified 25 diameters.

ACUTE FIBRINOUS PERICARDITIS.

Diagnosis of the Organ.—The section, as seen in the drawing (Fig. 44) is composed of two compact lamina, bound together by a loose tissue of very atypical appearance. At the extreme inferior portion the fibers of the myocardium, with their central nuclei can be recognized. Covering the myocardium there is a thin layer of adipose tissue between it and a thick fibrous band—the pericardium. The presence of these structures enables us to recognize the outer surface of the heart.

Diagnosis of the Lesion.—In the lower part of the drawing, in the adipose tissue, there are some large vessels, about which are collections of small cells. The epicardial layer is reduced to the condition of granulation tissue, a type of inflammatory tissue with dilated capillaries and lymphocytes, of which the whole forms a dark layer above the subepicardial adipose tissue. The endothelium limiting the pericardium is replaced by a fine fibrillar tissue which takes the red color of the eosin with avidity—this is fibrin.

The extreme upper edge of the drawing represents the parietal layer of the pericardium. It is formed of parallel bands and fasciculi of connective tissue, accompanied by vessels and nerves. At its middle portion one finds granulation tissue and infiltration comparable to that in the epicardium. The endothelium of the parietal layer, like that of the visceral layer has given place to a fibrinous exudate. Between the two principal structures in the drawing—the epicardium and the pericardium—and binding them together, there is a broad zone of lamellar tissue formed of fibrillæ with a few nuclei. These are false membranes of fibrin. At certain points the fibrin is organizing as is shown by the appearance of a few new vessels. The organization is, however, only beginning as the patient died of the pericarditis before permanent adhesions had time to form.

Résumé.—*Acute fibrinous pericarditis.* Information derived from the bacteriological laboratory showed that the disease was caused by the pneumococcus.

Fig. 44.—Acute fibrinous pericarditis.

Stained with hematoxylon and eosin. Magnified 10 diameters.

Pneumococcic acute serofibrinous pericarditis with resolving exudate.

Diagnosis of the Organ.—The section can easily be recognized as the wall of the heart by the features already pointed out. By knowing the normal thickness of the ventricular walls it can easily be guessed that the section includes the entire cardiac wall. Three portions are selected for special examination and are indicated by the three small rectangles shown in the drawing (A).

Diagnosis of the Lesion.—To facilitate the examination the selected portions will be considered from above downward.

1. The peripheral, or epicardial portion (Fig. 45, B).

Passing from the outer portion of the section toward the deeper tissues, we find first the epicardium, a dense fibrillar tissue of considerable thickness. Below it there is a layer of adipose tissue and below it the muscle of the myocardium.

The only abnormality is the presence in the adipose and muscular tissues of a considerable number of inflammatory small round cells.

2. The central or myocardial portion (Fig. 45, C),

In this one sees, at once, the presence of strands of dense homogeneous connective tissue—plaques and bands of fibrous myocarditis. To the left in the drawing there is an arteriole with a very thick wall. Above and to the right the fibers of the myocardium are dissociated and separated from one another by fine bands of sclerosis. Examination with a high power may, in well-fixed and prepared tissues, permit the various stages of the muscular degeneration to be made out. They are characterized by a homogeneous staining of the protoplasm, disappearance of the striæ and of the nucleus, etc.

3. The part shown in Fig. 45 (D) corresponds to the endocardial surface. As the surface is approached the entire tissue is found to be infiltrated with cells of various types: lymphocytes, mononuclears and polymorphonuclears. The last-mentioned are rather rare. At the extreme lower portion of the section, the lower ragged edge in the drawing, the color becomes dark blue. This is granulation tissue in which numerous mononuclear and polymorphonuclear cells well advanced in degeneration can be seen. There are also numerous small reddish bands with a finely fibrillar appearance composed of fibrinous exudate. All of the endothelial covering has disappeared, and the lesion forms a true ulceration.

Résumé.—*Acute ulcerative endocarditis.* The section shows the ventricular wall of the heart, in which the disturbance is almost limited to the endocardial surface.

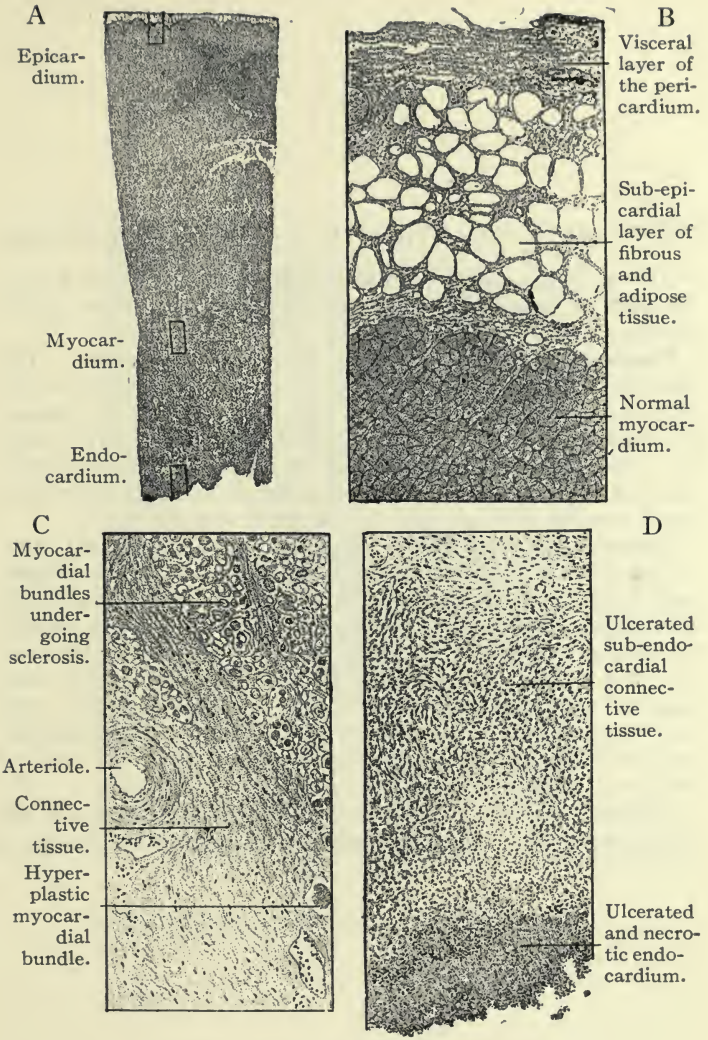


Fig. 45.—Ulcero-vegetative endocarditis.

Stained with hematoxylon and eosin.

Entire thickness of the ventricular wall twice magnified, with small rectangles showing where fragments B, C and D were taken for further examination.

FATTY DEGENERATION OF THE HEART MUSCLE.

The section is a longitudinal one passing through the wall of the heart of a case of "tabby-mottling," occurring in pernicious anemia.

Diagnosis of the Organ.—This should not be difficult. The tissue is composed of longitudinal bundles of a fibrillar structure with distinct longitudinal and transverse striations (not shown in such distinctly diseased parts as that selected for the drawing). It is also composed of irregularly quadrilateral segments that can be recognized as cardiac muscle cells, both by the occasional anastomosing fasciculi and the centrally placed nuclei.

Diagnosis of the Lesion.—Examination under a high magnification shows that in many of the fibers the original transversely striated fibrillar structure and the nuclei have disappeared, and in their place are collections of granules which are colored black with the osmic acid. These are fatty droplets, the result of the degeneration of the muscle following malnutrition or intoxication. Their presence, together with the degenerative changes with which they are associated, explains the yellow-gray speckled appearance of the wall of the heart.

Résumé.—Fatty degeneration of the muscle fibers of the ventricular wall—*fatty degeneration of the heart.*

Fig. 46.—Fatty degeneration of the heart muscle. From a case of pernicious anemia.

Stained with osmic acid. Magnified 750 diameters.

OBLITERATIVE ENDARTERITIS.

Endarteritis Obliterans.

Diagnosis of the Organ.—The section is of a tube whose wall is divisible into an external zone that stains a deep red—*tunica media*—and an internal zone of paler color—*tunica interna*—separated by a thin undulating membrane, the *internal limiting membrane*, a landmark important both in making the diagnosis of the organ and of the lesion. Outside of this elastic limiting membrane the unstriated muscular fibers can be recognized by their elongated nuclei. To bring out the elastic fibers recourse must be had to staining by one of the specific stains of Mallory or Weigert, or the orcein stain. In the lumen of the tube there are a number of red blood corpuscles that confirm the suspicion that the tube is a bloodvessel. The external tunic, the adventitia lacking in this section, being represented only by the connective tissue forming the stroma of the organ in which the vessel was contained. The distinctness of the undulating membrane shows that the vessel is an artery; in this case a visceral artery of middle size.

Diagnosis of the Lesion.—The inner coat is very thick. Instead of being composed of an endothelium with a thin layer of subjacent connective tissue, it has undergone an enormous thickening through hyperplasia of the tunic beneath the endothelium which forms a very thick stratified connective tissue, with occasional elongated nuclei, particularly numerous in the neighborhood of the lumen. In proportion, as we remove from the lumen toward the muscular coat, the nuclei little by little lose their staining properties and become as pale as the surrounding tissue. The connective tissue of the endarterium becomes structureless, colorless and devoid of fibrillar structure—*hyaline degeneration*—which frequently complicates areas of endarteritis in the visceral vessels, as well as occurring in atheromatous degeneration of the aorta and great peripheral arterial vessels.

The tunica media—the musculo-elastic tunic—does not show any notable alterations. The lumen of the artery, though diminished in size is not yet closed.

Résumé.—Arteritis chiefly confined to the internal tunic, hence *endarteritis*, and with a tendency to obliteration.

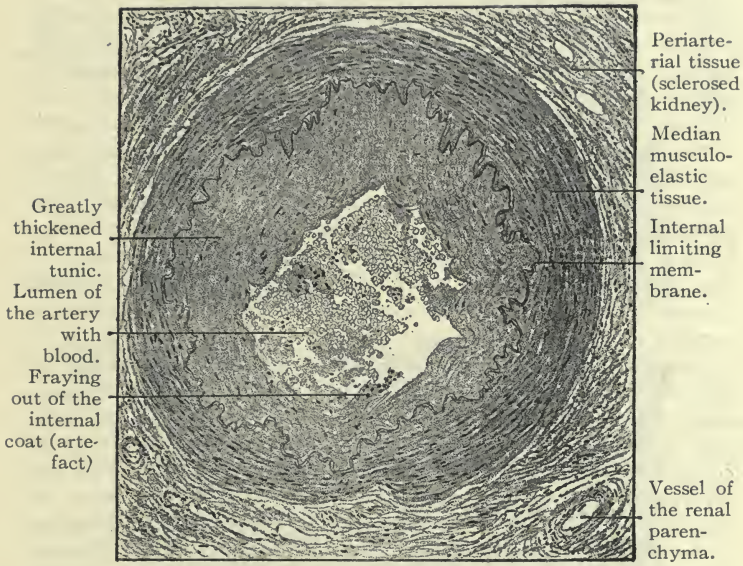


Fig. 47.—Endarteritis obliterans.

Stained with hematoxylon and eosin. Magnified 100 diameters.

Section of an artery in the kidney of a case of chronic interstitial nephritis with pronounced vascular lesions. The great thickening of the inner coat, inside of the festooned line of the internal limiting membrane, effecting an incomplete obliteration of the lumen of the vessel, is to be carefully noted.

ENDARTERITIS OBLITERANS.

Stained with Orcein.

Diagnosis of the Organ.—Again we have to do with a transverse section of a cylindrical tube, slightly flattened and having a lumen that is slightly excentric. The drawing A represents one-half of the entire section. At first glance it is difficult to make a diagnosis of the organ because of the special method of staining adopted (orcein); nevertheless, the circular character of the organ, the absence of epithelium and of lymphoid tissue, and above all the presence of the sinuous blue-black line—*elastica*—permit one to recognize an artery. The sinuous line pointed out is nothing more than the internal elastic limiting lamina separating the endarterium from the mesarterium. The elastic fibers become more and more thick until they form a dense feltwork. They consist of long black filaments running parallel with one another and showing distinct undulations.

Diagnosis of the Lesion.—There are no notable disturbances in either the external or middle tunics. All of the pathological alterations take place inside of the internal limiting elastics, that is to say, in the endarterium. Instead of consisting of an endothelial layer superimposed upon a thin layer of connective tissue, as can be seen in the right-hand lower corner of the drawing (Fig. 48, A), it has undergone enormous thickening in the form of a hyperplasia of the subendothelial fibrillar layer. At certain points, and especially at the internal limiting elastic membrane, the endarterium assumes a pale areolar and fragmented appearance—hyaline degeneration corresponding to the beginning of the formation of an atheromatous area (Fig. 48, B).

The lumen of the artery is extremely diminished and seems to have undergone an excentric displacement. This appearance is due to the fact that the plaque of endarteritis does not extend all around the vessel. The lumen still permits the passage of blood, but it is so reduced that except for the anastomotic branches, the territory of its distribution is menaced by ischemic gangrene.

Résumé.—*Endarteritis obliterans* of the superior mesenteric artery. It resulted in an infarct of the intestine and the death of a woman aged seventy years.

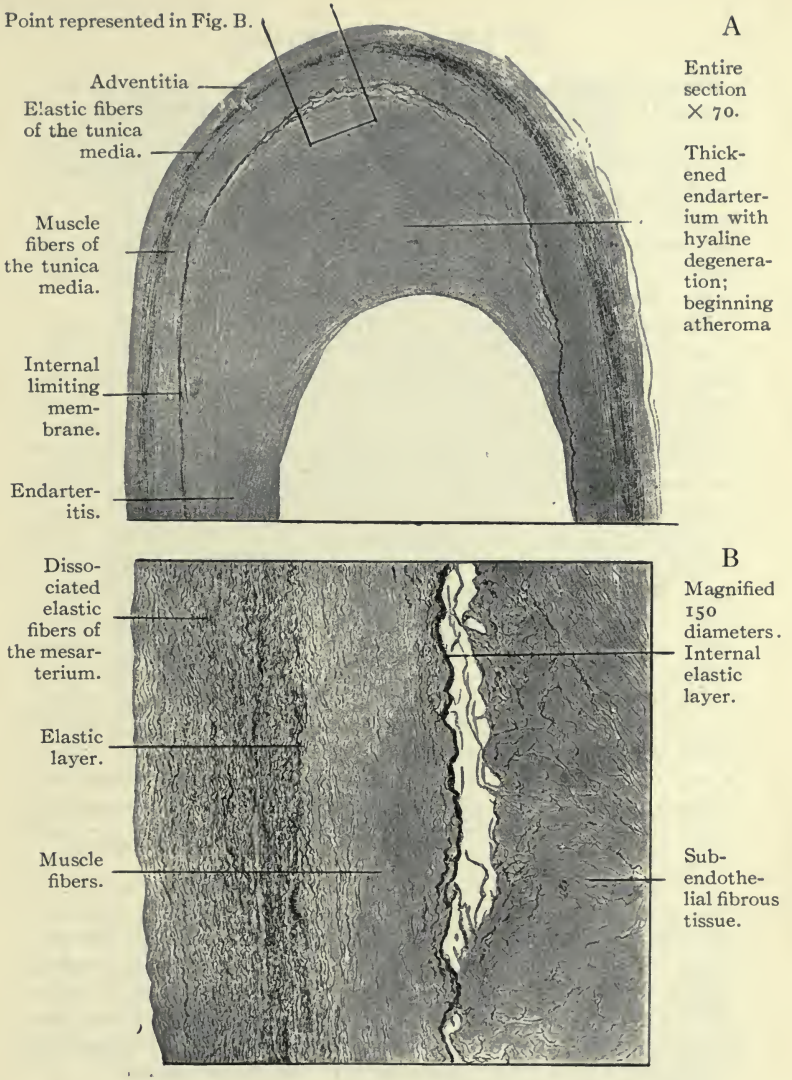


Fig. 48.—Endarteritis obliterans.

Stained with orcein.

Partly obliterated superior mesenteric artery of a woman aged seventy years.

Diagnosis of the Organ.—One can recognize the organ as a fragment of the wall of a large vessel of which the middle tunic is formed of muscle and elastic fibers (the elastic fibers are not visible in this case because the specimen has not been a appropriately stained) without a distinct internal limiting membrane. Such a structure is characteristic of the aorta or pulmonary artery. The external tunic is composed of a loose connective tissue containing a number of vessels, though the middle and internal tunics contain none.

Diagnosis of the Lesion.—In Fig. 49, A, the lower drawing, if one follows the section from left to right, he finds a certain point at which the inner tunic seems to separate from the middle one, and the endarteritis assumes greater and greater importance. From inside out, that is to say, from below upward, one notes the presence of an unaltered endothelium, an inner tunic slightly thickened, but of a colorless necrotic appearance, passing into the principal lesion—the area of arteriosclerosis—which is subjacent.

This area is composed of a pale zone of friable appearance in which there are elongated spindle-shaped crystals of fatty acids, and perhaps some lozenge-shaped crystals of cholesterin. These crystals have been subjected to the action of various reagents—alcohol, xylol, etc., in the course of the preparation of the section, and nothing is now left but the spaces in which the crystals were originally contained. Besides the crystals which prove the presence of fatty degeneration of the deeper layers of the intima, some much-altered leukocytes (macrophages), some globules of fat and above all some bluish masses which indicate the beginning of calcareous infiltration are still to be found in the area.

The internal tunic separating the area from the lumen of the vessel is very much thinned, and almost ready to rupture and liberate the contents of atheromatous swelling into the torrent of the circulation. Outside of the atheromatous area (above in the drawing) one notes the integrity of the middle coat of the artery. It is with difficulty that one sees the disappearance of some of the smooth muscular fibers separated by hyaline tissue (tiger appearance of the mesarterium).

Finally, the adventitia (not visible here) is intact and the vasa vasorum are normal.

Résumé.—*Chronic arteritis* with atheromatous degeneration such as one often sees at the source of one of the larger branches of the aorta—*arterial atheroma.*

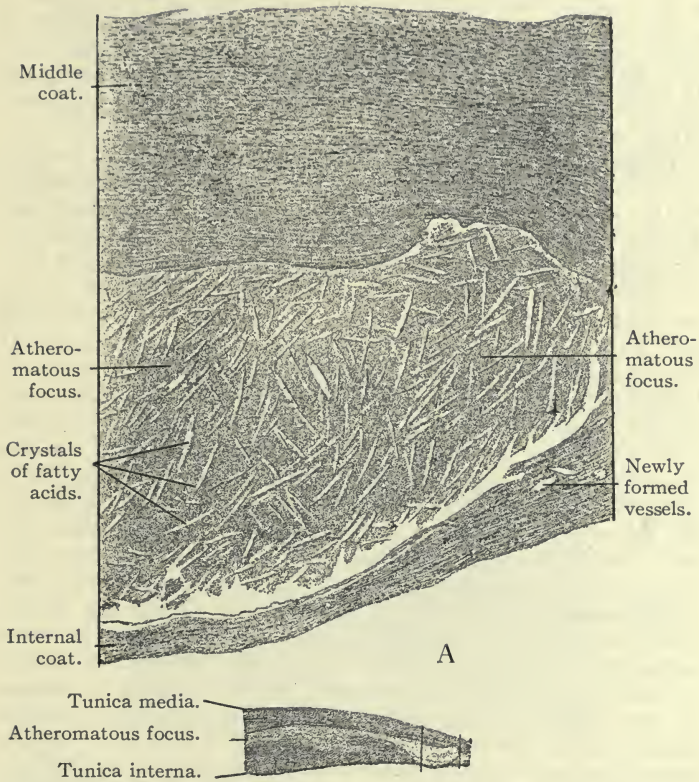


Fig. 49.—Atheroma of an artery.

Section of the wall of an atheromatous abdominal aorta of an old man.

A.—*General view of the specimen twice natural size. The portion between the vertical lines on the right side, is that selected for higher magnification in* B.

B.—*This shows an atheromatous focus with crystals of fatty acids and plates of cholesterin. It is limited above by the middle tunic, below by the internal tunic. The external tunic does not show, having been torn off in removal of the tissue at the autopsy.*

CALCIFIED ARTERY.

This is a common affection of the peripheral arteries of elderly people and may occur independently of endarteritis or in association with it. It is most common in the arteries of the extremities, but this particular section is from the cancerous breast of an old woman.

Diagnosis of the Organ.—The greater part of the section consists of a tissue whose architecture bears no correspondence to that of any normal structure of the body and therefore may not be within the knowledge of the student. It is cancer or carcinoma, and with it we have nothing to do at present.

That which concerns us now is the striking, dark-blue structure that occupies the greater part of the center of the drawing and forms a circle with an irregular central opening. It impresses one as a section of some tubular structure. It is bounded externally by concentrically arranged parallel connective-tissue fibers, which as one advances toward the center, here and there, in the better-preserved parts, abut against unstriated muscle cells. The central opening is limited by a thin, flattened cellular structure—endothelium. A brief reflection enables the student to recognize the adventitia, the media and the intima of a bloodvessel, and taking into consideration the thickness of the middle coat to diagnose an *artery*.

Diagnosis of the Lesion.—In the upper part of the sketch, when the wall of the artery is least affected and when the lesion is probably youngest—it will be seen that the middle coat is the chief seat of disturbance, and is partly replaced by masses of dark blue, at certain points in which there are colorless deposits of a highly refracting, crystalline substance. This is of calcific nature and constitutes *calcification* of the middle coat of the vessel. The calcareous material when crystalline remains uncolored; when amorphous, absorbs the hematoxylon, and as it increases the alkalinity of the adjacent muscular tissue causes it also to absorb the hematoxylon so that all about the mineral deposits the tissue becomes intensely dark blue in color.

In the lower part of the section of the vessel a much greater deposit occurs, distending the tissue so as to make it encroach upon the lumen which is diminished in consequence. At this point it is impossible to say that there may not have been endarteritis in association with the medium calcification, and, indeed, the two processes not infrequently occur in the same vessels, though they are independent of one another.

Such changes in the arterial walls makes them inelastic, brittle and subject to traumatic injury and rupture, as well as diminishing their conducting powers. The parts supplied by such arteries are, therefore, apt to fall into a state of malnutrition, and in the case of the extremities of the body into senile gangrene. Naturally the danger is greater when the calcification of the middle coat is accompanied by endarteritis by which the the lumen is further obstructed and the conducting power of the vessel further diminished.

Résumé.—Calcification of the middle coat of the artery—a condition which, when extreme and widespread, gives rise to the condition often described as "pipe-stem" arteries.

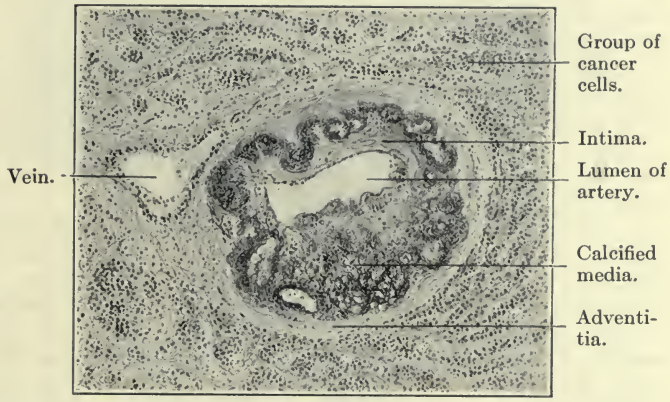


Fig. 50.—Calcified artery. The artery occurs in a mammary gland almost completely destroyed by carcinoma. The disease of the vessel wall, however, is independent of the tumor and probably antedates it.

Stained with hematoxylin and eosin. Magnified 50 diameters.

OBLITERATIVE PHLEBITIS.

Phlegmasia Alba Dolens.

Diagnosis of the Organs.—The section is of a tube with its wall and contents (Fig. 51, A). The smooth muscular and elastic fibers in the wall form a ring of considerable density, lined on the inside with a pale edging and on the outside by a cellular layer, showing that in all probability we have to do with a vessel. The thinness of the wall, the absence of an internal elastic limiting membrane, make us suspect that the vessel is a vein. Compare it with the section of the artery shown in drawing (Fig. 45).

Diagnosis of the Lesion.—The lumen of the vessel is obstructed by a clot—thrombosis (Fig. 51, B).

In following the wall of the vein from outside inward we encounter the following:

1. The adventitia, or external tunic, a loose cellular tissue with numerous vessels. There are no alterations here apart from a mild inflammatory infiltration suggesting a deeper lesion.

2. The middle tunic, musculo-elastic, of comparative thinness also seems to be intact. It does not show the mottled appearance of chronic arteritis.

3. The internal tunic, on the contrary, shows important alterations in all points comparable to those of chronic endarteritis (thickening of the connective tissue layers). However, the inflammatory process is a great deal more acute and terminates in the formation of a clot that obstructs the lumen of the vessel. The lesion of the wall of the vessel has produced the clot (thrombosis). The venous endothelium resting upon stratified subendothelial connective tissue has disappeared and the internal tunic is continuous with the thrombus.

The latter is formed by red blood corpuscles still distinct, and by bands of fibrin containing inflammatory cells in the meshes.

The center of the thrombus has become fragmented in the course of treatment with the reagents and the form of the rent, the distinct lines of the openings, and the absence of red blood corpuscles show their artificial nature.

Résumé.—*Obliterating* or *thrombosing phlebitis*, commonly observed in phlebitis of the limbs—*phlegmasia alba dolens*.

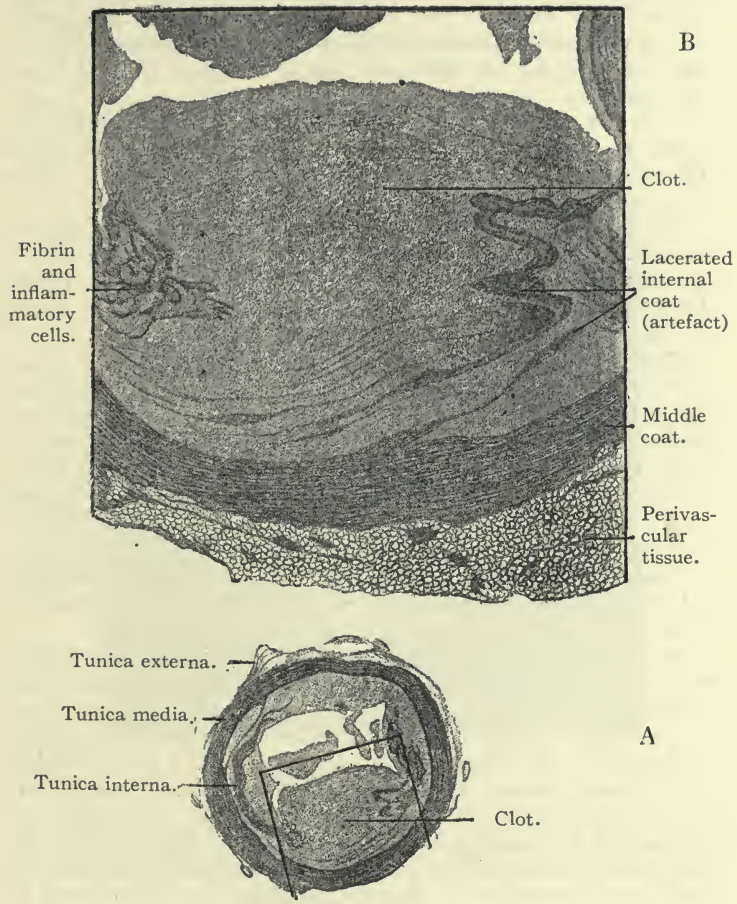


Fig. 51.—Obliterative phlebitis.

Stained with hematoxylon and eosin.

A.—*Transverse section of the femoral vein of a case of phlegmasia alba dolens, twice natural size.*

B.—*The portion of the tissue shown in the square, magnified* 20 *diameters. A large thrombus is attached to the diseased internal coat of the vessel.*

NORMAL BLOOD.[1]

The examination of a drop of blood spread upon a slide and stained with hematoxylon and eosin shows two kinds of cells:

1. Small circular masses colored in a homogeneous manner by the eosin and entirely without a nucleus—the red blood corpuscles.

2. Other protoplasmic masses, a little larger than the red blood corpuscles and containing a nucleus staining blue with the hematoxylon and having finely granular cytoplasm—white blood corpuscles, or leukocytes.

(A third cellular component of the blood is the *platelets*, but to demonstrate them it is necessary to use a special stain—Ehrlich's, Wright's, Jenner's or Leishmann's stains. These, therefore, do not show in this slide, and do not appear in the drawing.)

The Red Corpuscles.—These have the form of small biconcave-biconvex disks whose shape can be most easily recognized by gently varying the focus. Certain of the corpuscles are badly fixed or have been injured in the process of spreading upon the slide, and some of them may show no definite form. The size of the corpuscles is very regular (diameter, 7 to 8 mm.) and knowledge of this may be of use in roughly estimating the size of other objects with which they may be associated.

The White Corpuscles.—These at once divide themselves into two classes according to the presence or absence of granules in their cytoplasm:

(*a*) The granular leukocytes have multilobulated nuclei, hence are often spoken of as polynuclear, but are more correctly called *polymorphonuclear leukocytes*. Their cytoplasm contains fine granules whose staining affinities are somewhat variable according to the elements studied. Some have granules that are almost colorless—neutrophiles. Others have granules that are strongly stained with the red of the eosin—eosinophiles.

In order to recognize a third variety of the polynuclears, the basophils, it is necessary to employ a special method of staining with polychrome blue. But the basophils are exceptional in the normal blood, and only become numerous in certain inflammatory reactions and the leukemias.

(*b*) Non-granular leukocytes have homogeneous protoplasm and spherical or incurved nuclei without the definite constrictions of the polymorphonuclears. Some are about the

[1] In this country it is not customary to make examinations of blood corpuscles except in spreads stained by Wright's method, by which all of the elements, including the platelets are brought out. We suppose the author knew this, but introduced the hematoxylin and eosin preparation in order that the beginner might have a marked comparison between the corpuscles as they occur in the blood, and as he may find them in the tissues. (TRANS.)

size of the red blood corpuscles. The spherical nucleus occupies almost the entire cell, the cytoplasm itself scarcely appearing, being reduced to a narrow peripheral coronet. These are the *lymphocytes* (small lymphocytes).

Others, eight or ten times larger, with abundant protoplasm and slightly indented nuclei are the middle-sized or large mononuclears (large lymphocytes). Between the two are numerous transition forms.

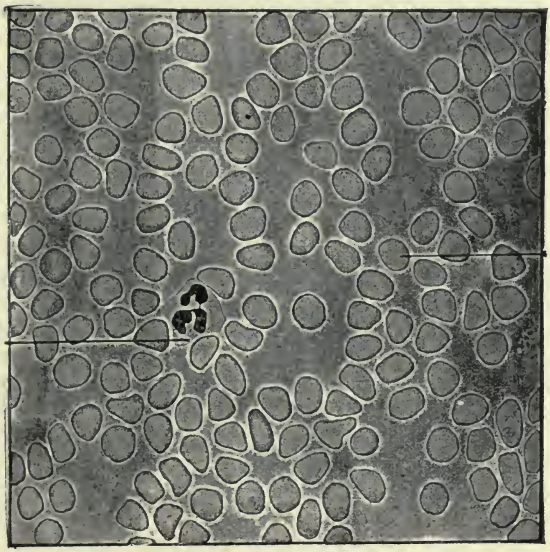


Fig. 52.—Normal blood.

A drop of fresh blood is thinly spread upon a clean slide, dried and fixed with alcohol-ether, and stained with hematoxylon and eosin, and examined under the oil-immersion lens. Magnified 570 diameters.

A single polymorphonuclear leukocyte and many red blood corpuscles are seen. The blood platelets are not visible in this preparation, requiring special stains to bring them out. Of the 6000 *leukocytes found in* 1 *c.mm. of blood the different varieties occur normally in the following proportions:*

Polynuclear neutrophiles	65 per cent
Lymphocytes	15 "
Mononuclear and transition forms	20 "
Eosinophiles	1 or 2 "

LEUKOCYTOSIS.

Polynuclears.

The specimen is a spread drop of blood, dried and stained with hematoxylon and eosin. In it are found the same elements as were seen in the preceding figure—red blood corpuscles, polymorphonuclears, lymphocytes, large and middle-sized mononuclears.

But that which distinguishes this preparation from the preceding and gives it a quite different appearance is the much larger proportion of white blood cells. The increase is so considerable as to make it possible to appreciate the leukocytes without having recourse to methods of enumeration. As the increase consists almost entirely of the polymorphonuclear neutrophilic cells it is clear that we have to do with a polynucleosis or *leukocytosis*. Such a condition betrays a general reaction of defense against an acute inflammatory process.

The discovery of leukocytosis is often of clinical and diagnostic importance. In the course of an acute appendicitis, for example, it can serve to reveal transformation from the latent state to peri-appendicular abscess and to indicate necessity for operation.

If, instead of concerning the polymorphonuclear neutrophiles the increase in number affects the:

1. Eosinophils, it is called *eosinophilia*. This is observed parasitic affections (hydatid cysts, intestinal parasites).

2. Mononuclears—if the large or middle-sized mononuclears are increased—*mononucleosis*—it usually indicates the presence of some special form of infection such as variola or vaccinia.

Differential Diagnosis.—By the examination of stained blood films one should be able to differentiate between leukemia and leukocytosis:

(*a*) Through the great number of lymphocytes in leukemia of the lymphatic type.

(*b*) Through the presence of new elements of the myeloid series (myelocytes) in the myeloid variety.

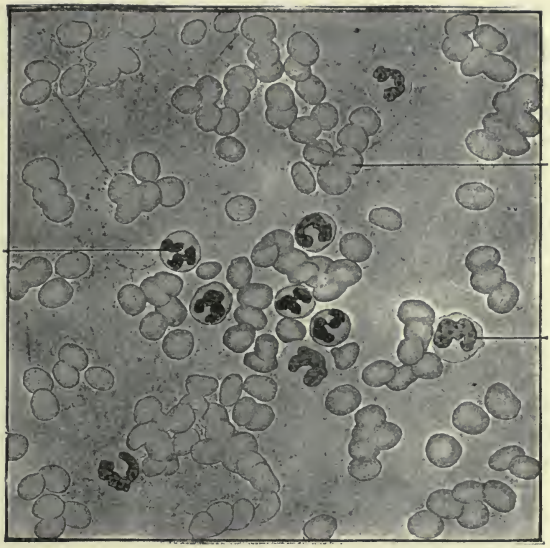


Fig. 53.—Leukocytosis.

A spread of blood taken from a pneumonic patient at the period of acme. Fixation with alcohol-ether, staining with hematoxylon and eosin. Magnified 570 diameters. There are eight polymorphonuclears in the field.

A count of the blood corpuscles made at the same time showed 24,000 leukocytes of which 85 per cent were polymorphonuclears.

MYELOGENIC LEUKEMIA.

The drawing, like the preceding, shows a spread of dry blood as it appears under the oil-immersion objective. The enormous number of white blood cells as compared with the red blood cells, as well as the varying types of leukocytes, give the specimen a very characteristic appearance which should at once make one think of leukemia. This can be confirmed by a blood count, which will show that the number of the red blood corpuscles is not increased, while that of the white blood corpuscles is.

The leukocytes are of different types: (*a*) Leukocytes with polylobed nuclei and finely granular cytoplasm—polymorphonuclear neutrophiles. (*b*) Mononuclears with pale nuclei, some showing fine protoplasmic granulations. These are called *myelocytes* because under normal conditions they are only found in the marrow of the bones. (*c*) Some lymphocytes or small mononuclears with very little protoplasm and nuclei rich in chromatin. (*d*) Eosinophils, more numerous than in the normal state, as they are easily found. (*e*) White blood cells with atypical karyokinetic figures in the nuclei.

Finally, there are cells of an entirely abnormal type, the *normoblasts* or nucleated red blood corpuscles. These are cells not found in the normal blood, belonging solely in the bone marrow from which the adult red blood cells are derived.

The morphological alterations of the red blood corpuscles should also be pointed out. They consist of deformity—elongation, oval or rectangular shape—and constitute what is described as *poikilocytosis*. There are also anomalies referable to artefacts in making the preparation, and indicate no more than fragility of the red blood corpuscles. (*Crenation*, or chestnut-burr appearance, not shown in the drawings, usually uniformly affects all of the red blood corpuscles in a field.)

Résumé.—The augmentation in the number of white blood corpuscles (which sometimes gives the fluid blood a truly milky appearance) beyond the limits occurring in infection, and the preservation of the red corpuscles, suggest the diagnosis of *leukemia*. The presence of the cells of the bone marrow series—granular myelocytes and normoblasts—permit one to differentiate between the myelogenic leukemia and lymphatic leukemia in which the augmentation in number is in the lymphocytes.

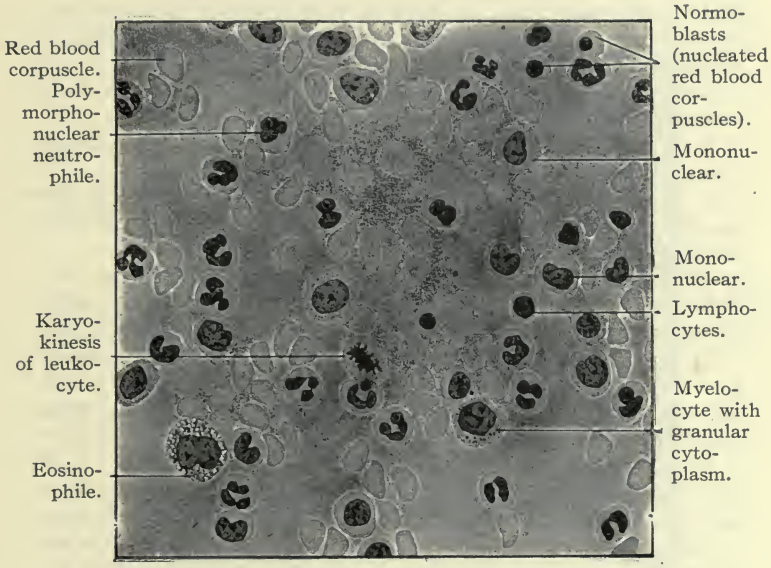


Fig. 54.—Blood of myelogenic leukemia.

Spread fixed with alcohol-ether, stained with hematoxylon and eosin, and examined under a magnification of 570 diameters.

Note the great number of white as compared with red cells; the various types of white corpuscles—polymorphonuclear neutrophiles, eosinophiles, middle-sized mononuclears, lymphocytes, granular myelocytes, leukocytes with karyokinetic figures, and lastly the nucleated red corpuscles or normoblasts.

ACUTE LYMPHATIC LEUKEMIA.

As in the preparation of myelogenic leukemia, one is struck with the enormous proportion of white relatively to the red cells. Besides this, a preliminary blood count of both red and white cells shows that the number of leukocytes has increased in considerable proportions (from 20 to 200,000, according to the case).

But the white corpuscles are all lymphocytes, of which there are two types:

1. The *small lymphocytes*, with very little cytoplasm forming a narrow coronet about an ovoid nucleus.

2. The *large lymphocytes*, or macrolymphocytes, which are much larger cells with larger and often irregular nuclei and relatively abundant protoplasm.

These two different forms of leukocytes result from two different reactions in the lymphatic tissues. The small lymphocytes express a chronic disturbance—*chronic lymphatic leukemia.*

The large lymphocytes represent a younger type of element, less differentiated than that which circulates in the blood, indicating, as in the present case, an acute reaction—*acute lymphatic leukemia.*

There are intermediates between these extreme types, but in this case the large lymphocytes being a great deal more numerous than the others, we have to do with a case of acute leukemia.

In leukemia both the red corpuscles and the leukocytes are very fragile, so that as the blood is spread for staining, they are easily deformed and crushed.

In the preceding drawing there are numerous fragments of cells that must not be mistaken for blood platelets, which, as has been said, do not show in smears stained with hematoxylon and eosin, but require special staining (Wright's stain).

Some normoblasts and plasmocytes can also be found in the preparation.

Résumé.—The formidable increase in the number of white blood corpuscles and the relative preservation in the number of the red corpuscles is sufficient to suggest the diagnosis of leukemia. The occurrence of lymphoid cells (lymphocytes and above all large lymphocytes) is sufficient to enable the diagnosis of *acute lymphatic leukemia* to be made.

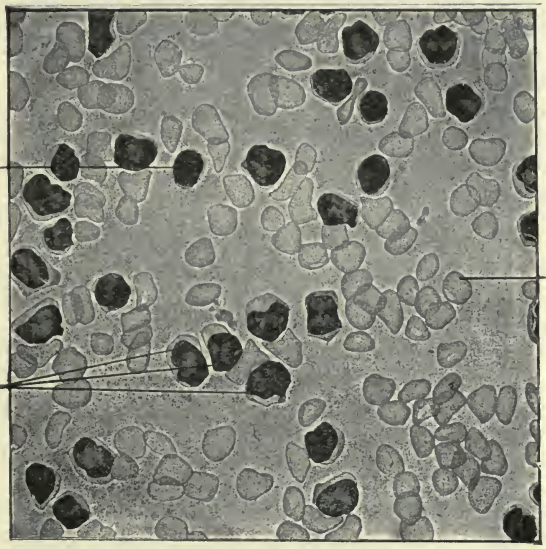


Fig. 55.—Acute lymphatic leukemia.

Fixed with alcohol-ether, stained with hematoxylon and eosin. Magnified 600 diameters.

The great number of lymphocytes, especially large lymphocytes is to be observed as characteristic of acute lymphatic leukemia.

NORMAL KIDNEY.

Kidney of an Executed Criminal.

Diagnosis of the Organ.—The section of the kidney, including both cortex and medulla, appears to be divided into two distinct portions. The one, darker, and at the periphery, contains in its interior a number of small rounded masses. These are the characteristic elements of kidney structure, the *glomerules*, or Malpighian bodies, which should always be looked for with care in order to make the diagnosis of the organ, and to recognize its cortical substance.

The other paler portion consists of tiny tubules, sometimes cut transversely, sometimes longitudinally and arranged in a radiating fashion: this is the medulla, much less characteristic than the cortex for making the diagnosis of the organ.

1. *In the cortical substance* the glomerules, or Malpighian bodies, are of much the same size in the normal kidney; some, however, being cut tangentially, appear smaller. The Malpighian bodies consist of two parts: one central, the vascular tuft; the other, peripheral, the capsule of Bowman.

The vascular tuft is a sort of undifferentiated plasmodium, that is to say, a protoplasmic mass not divided into cells, in the substance of which one perceives a great number of nuclei and numerous capillaries containing red blood corpuscles. About it there is a narrow space limited on the outside by the capsule of Bowman.

It has a delicate endothelial (epithelial?) lining. Here and there in the section it may be possible to find glomeruli that show the *vascular pole*, formed of two vessels, the afferent artery and efferent vein, or the *urinary pole*, at which the uriniferous tubule begins.

The glomerules are surrounded by a large number of tubules of unequal diameter sometimes cut transversely, sometimes longitudinally.

Examination under the low power enables one to recognize two principal types: Secretory tubes (convoluted and irregular tubes) and excretory tubes, ascending and descending loops of Henle.

(*a*) *The secretory tubes:* These, known as the *convoluted tubules*, are recognized by a lining of granular epithelium, more or less acidophilic and peculiarly fragile. It is very common for kidney tissue taken from autopsy cases to show cadaveric alterations in a variety of forms such as desquamation and protoplasmic

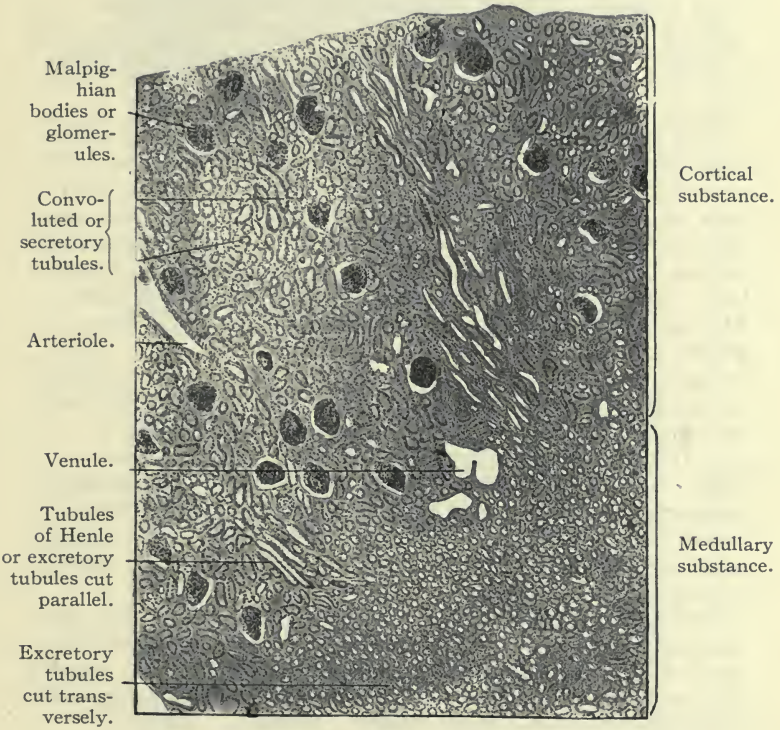


Fig. 56.—Normal kidney.

Stained with hematoxylon and eosin. Magnified 40 diameters.

The greater part of the drawing shows the renal cortex in which a great many Malpighian bodies or glomerules can be seen among the convoluted tubules. The capsule has been torn off and does not appear in the section. The lower right-hand corner shows the medullary substance with its excretory tubules cut transversely

fragmentation; one must be careful not to mistake them for pathological lesions. They can usually be recognized through uniform occurrence in all parts of the section. Such cadaveric changes begin to make their appearance a few hours after death.

The cells of the secretory tubules are mostly cubical, possess a nucleus situated basally and show in well-fixed specimens, even with the ordinary stains, a fine fringe upon the centrally directed surface—the so-called *rodded epithelium.*

(*b*) *The excretory tubules:* These are of two varieties. The first differ from the convoluted tubules by an epithelium with more distinctly basophilic staining reactions, in a much better state of preservation, as they are much less fragile. The cells have a bluish cast and darker nuclei than those of the secretory tubules. They comprise the larger or *ascending limbs of Henle's* loop. The others are fine tubules lined with an extremely flattened epithelium resembling endothelium, and have a general appearance not unlike capillaries, but are easily differentiated from them through the complete absence of red blood corpuscles from their interiors. *They correspond to the descending limb of Henle's loop* or to the loop itself.

2. *In the medullary substance* are found nothing but the transverse and longitudinal sections of tubules of various kinds —excretory tubules, ascending and descending limbs of Henle's loops just studied in the cortical portion, and much larger collecting tubes lined with tall cubical epithelium—the *collecting tubes of Bellini.*

3. Besides these epithelial components one sees the fine vascular and connective tissue of the organ. The connective tissue consists sometimes of a young tissue rich in cells—more frequently of collagenous fibers. The vessels, always large and abundant, are of the adult type.

Such is the picture presented by a histological section of the normal kidney, and such are the landmarks that one must know to recognize the parenchyma with which one chiefly has to do in recognizing the pathological alterations.

With regard to the renal lobule, represented by the unity of the uriniferous tubule, it is impossible to gain information through study of the different parts of a section. It is a conception acquired through the study of tissues specially prepared by injection methods.

In the pathological-histological study of the kidney, that which is of most importance is the recognition of the excretory and the secretory structures.

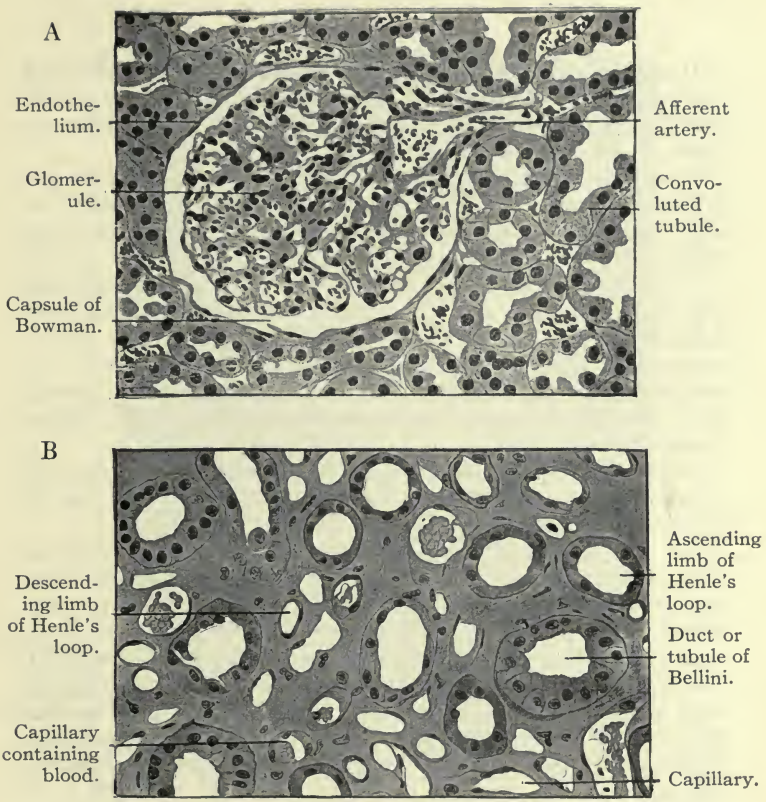


Fig. 57.—Normal kidney.

Stained with hematoxylon and eosin. Magnified 250 diameters.

Above A, *the cortical substance is shown. In it are a Malpighian body, convoluted tubules and some excretory tubules.*

Below B, *the medullary substance is shown with its various excretory tubules cut transversely.*

SUBACUTE NEPHRITIS.

Variolous Nephritis.

Diagnosis of the Organ.—Upon examining the section with a low-power lens it is easy to recognize the Malpighian bodies whose capillary tufts are characteristic and at once enable the organ to be diagnosed.

Diagnosis of the Lesion.—The lesions presented in the section are very varied. To understand them it will be necessary to study in detail the glandular parenchyma (glomerules and convoluted tubule) and the stroma or interstitial tissue.

At the upper part of the section, shown in the drawing (Fig. 58), there is a thick layer of connective tissue containing some fat cells. It is the capsule of the organ which, in this case, is abnormally thick and contains a few small lymphocytic collections (inflammatory cells). This thickening of the capsule with inflammatory infiltration denotes a long-standing inflammatory process.

Below the capsule the cortical substance shows extremely complex alterations affecting both the glomerules and tubules (glomerulo-nephritis).

(*a*) The *glomerules* have a very variable size and structure. The next drawing (Fig. 59) shows two different portions from the section, taken at random, and shown under a higher magnification. One (A) shows a glomerule whose capsule of Bowman is greatly thickened through stratified layers of connective tissue composed of collagen fibers, among which are numerous long bluish nuclei. In the center of the capsule the vascular elements of the glomerulus show with some exaggeration because of the large number of red blood corpuscles they contain, and by which the nuclei of the plasmodium are obscured (congestion). On the left-hand side of Fig. 59, A, there is a glomerular lesion of an entirely different kind. The sclerosis of the capsule has invaded the entire glomerule and the capillary structure can no longer be seen. The vascular strophy and the thickening of the capsule of Bowman have terminated in a glomerulo-capsular symphysis, and the formation of a rounded mass of fibrous substance to which the term "wafer" is sometimes applied. This is another indication that the lesion is old. Throughout the section there are all stages between the two types of lesion described.

(*b*) In the intervals between the glomerules the secretory

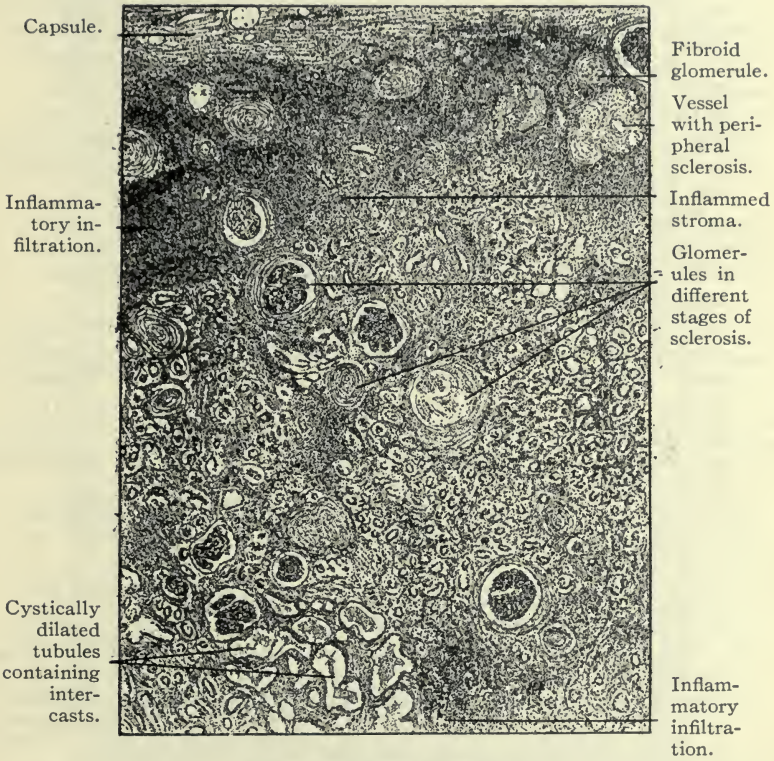


Fig. 58.—Subacute nephritis.

Stained with hematoxylon and eosin. Magnified 40 diameters.

Below the thickened capsule shown at the top of the drawing, the kidney substance shows a variety of glomerular and tubular lesions (glomerulo-nephritis). Between the glomerules and the tubules there is considerable infiltration of inflammatory cells.

tubes show lesions more or less important. In Fig. 59, B, on the next page, the cylindrico-cubical epithelium is disposed around an opening sometimes potential, sometimes completely disappeared. The lumen is found stuffed with desquamated cells with pycnotic nuclei crowded pell-mell into the center of a cavity more or less sinuous. Here and there, as in the right side of the Fig. 59, B, the desquamation of the epithelium is less marked, but the tubes tend to dilatation and cystic transformation. The lumen becomes a kind of cavity that is filled with hyaline fluid that stains distinctly with the eosin dye and is lined by flattened epithelium.

These lesions of the tubule comprise *desquamative* and *exudative tubulitis* and are certainly not *postmortem* alterations or artefacts due to bad fixation of the tissue. Such cystic appearances are never found under such circumstances.

(*c*) Besides the lesions of the parenchyma there are less marked alterations of the stroma characterized by an enormous infiltration of small round cells (bluish) placed immediately beneath the capsule (Fig. 58). These cells infiltrate more or less everywhere between the glomerules and about the tubules, accumulating here and there in masses more or less distinct and clear cut.

Finally are to be noted small interstitial hemorrhages, easily recognized by their brownish color with occasional traces of pigmentary change.

In addition to all this, the walls of the bloodvessels are thickened through stratifications of young connective tissue.

The medullary substances, not shown in the drawing, is not distinctly affected. In the excretory tubules, however, collections of desquamated cells indicate lesions further up the tubules. In some of these cells the details of nuclear structure can still be seen; others have undergone hyaline change.

Résumé.—Nephritis of the subacute variety, affecting at the same time the glomerules and the tubules (glomerulonephritis in different stages) and the stroma. In consequence it is a *mixed nephritis*, as is usually the case if of sufficient duration to effect changes of the interstitial tissue which always requires more time than the injury to the epithelium. Hence *the old division into interstitial and paranchymatous nephritis is too artificial to be valid.*

This type of subacute nephritis is common after scarlatina and variola.

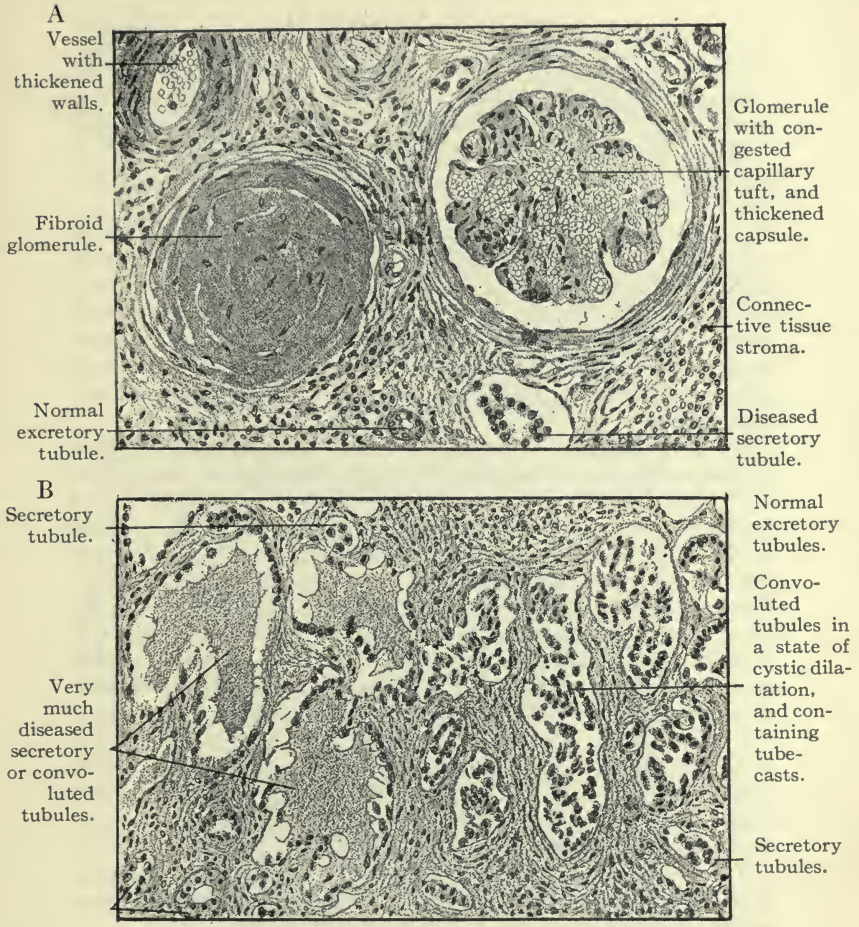


Fig. 59.—Subacute nephritis.

Stained with hematoxylon and eosin. Magnified 250 diameters.

Nephritis from a case of smallpox.
A.—*Two inflammed glomerules in different stages of disease.*
B.—*Diseased convoluted tubules with desquamated epithelium, cystic dilatation and tube casts.*

CHRONIC NEPHRITIS.

Bright's Disease.

Diagnosis of the Organ.—The diagnosis of the organ is easily made, thanks to the characteristic aspect of the glomerules.

Diagnosis of the Lesion.—As in the preceding case it is necessary to study the changes in both epithelial and connective tissue elements.

A. The *Malpighian bodies*, or *glomerules*, present alterations much like those of the subacute form of the disease, but more distinct. The progressive transformation of the glomeruli into fibrous masses (wafers) is marked. At first the capillary tuft retracts toward one pole, only occupying a part of the capsular cavity, then it unites itself with the capsule of Bowman and finally degenerates altogether and becomes a mass of collagenous material.

B. The *convoluted tubules* do not show any disturbance that can be attributed to cadaveric change, but under the capsule of the kidney they undergo a dilatation that is quite marked and explains the little bosselations that appear upon the surface of the kidneys of cases of Bright's disease, and remain as small pale spots when the capsule of the organ is torn off. The drawing shows two of these granulations separated by a slight groove, at the bottom of which an infiltration of blue cells (lymphocytes) can be seen. The ectasia of the convoluted tubules in the neighborhood of these granulations is referable to functional activity of the organ (compensatory hypertrophy).

C. The *stroma* also shows important changes. The masses of bluish cells between the glomerules and the tubules sometimes indicate an inflammatory reaction of chronic nature, sometimes a terminal process—an addition of a subacute nephritis to a chronic sclerotic one.

The vessels have extremely thick walls; their lumen is correspondingly diminished, and almost obstructed by the enormous proliferation of the middle and internal coats.

In the medullary substance, not shown in the drawing, the lumina of the collecting tubes is obstructed by rounded masses of homogeneous substance—*tube casts*.

Résumé.—*Nephritis*, whose lesions affect chiefly the glomerules and stroma, and relatively spare the convoluted tubules. The stroma and parenchyma are both affected, again showing the artificial character of the old division into interstitial and parenchymatous nephritis.

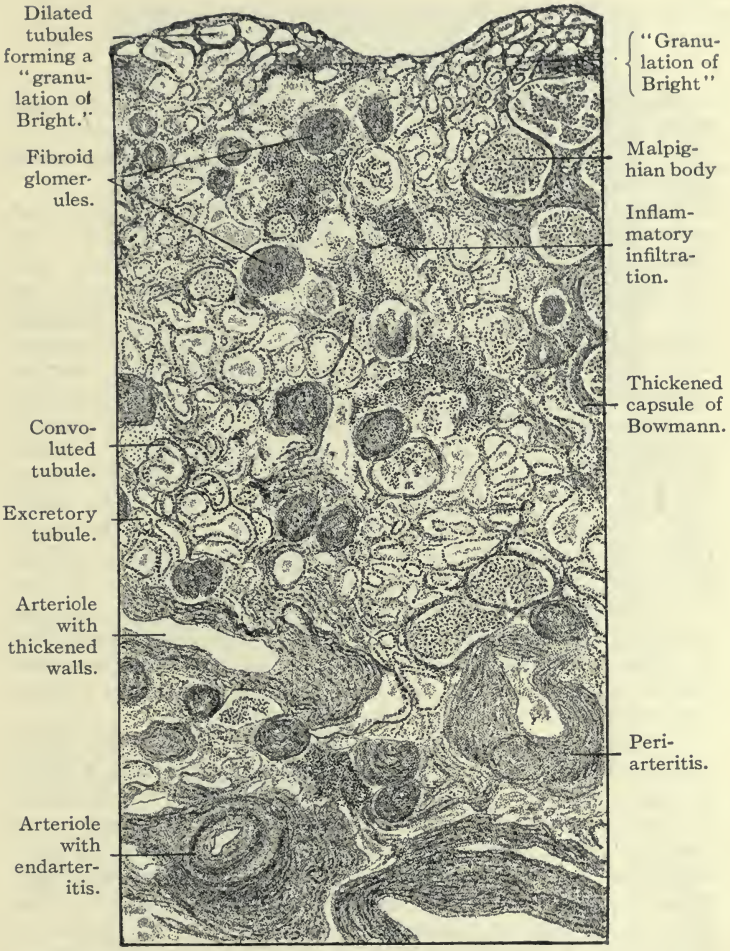


Fig. 60.—Chronic nephritis.

Stained with hematoxylon and eosin. Magnified 45 diameters.

Section of a small sclerotic kidney of Bright's disease. At the upper edge two of the so-called granulations of Bright project upon the surface beneath the capsule. The glomerular and perivascular sclerosis is striking.

PYEMIC NEPHRITIS.

Embolic Nephritis.

Diagnosis of the Organ.—This is relatively difficult because of the extent of the lesions. At certain points, however, as in the lower part of the drawing, it is possible to discover some glomerules and convoluted tubules.

Diagnosis of the Lesion.—Under a low-power lens one is at once struck by the pale color of the renal elements. The cellular limits are indistinct, both those of the tubules and the glomerules. The nuclei have often disappeared from the cells. The tubules are often filled with amorphous eosinophilic masses. This necrotic aspect of the parenchyma is in accord with the vascular alterations. The preparation is mottled with dark bluish patches which are even visible to the naked eye.

These are abscesses and can be seen in the upper part of the drawing. With a higher magnification they are seen to be made up of acidophilic cells with oval or multilobed nuclei (mononuclear and polymorphonuclear leukocytes). The acidophilic quality of the protoplasm and the pycnosis of the nuclei indicate a marked cellular degeneration—pus. At the peripheral limit of the abscess the necrosis is particularly marked by a zone of hyaline amorphous substance in which one can recognize tubules and glomerules. The abscesses are formed by a diffuse infiltration of inflammatory cells, mononuclear and polymorphonuclear cells, some of which lie between the tubules and some in the thickness of their walls.

In addition to these microscopic abscesses there are much smaller dark spots extremely irregular in form having a finely granular appearance and distributed without any order throughout the specimen. These are masses of bacteria mostly composed of great numbers of cocci that can be rendered more distinctly visible by special methods of staining, especially Gram's stain. They are microbic emboli brought by the blood from sources outside of the kidney. In the center of the drawing is a glomerule containing such a microbic embolus.

Thus is explained the origin of the abscesses. The parenchymatous necrosis is due to the presence of the areas of suppuration and to the vascular thrombosis.

Résumé.—*Pyemic nephritis*, with numerous abscesses and microbic emboli, such as occur in septicemia, and result from embolism.

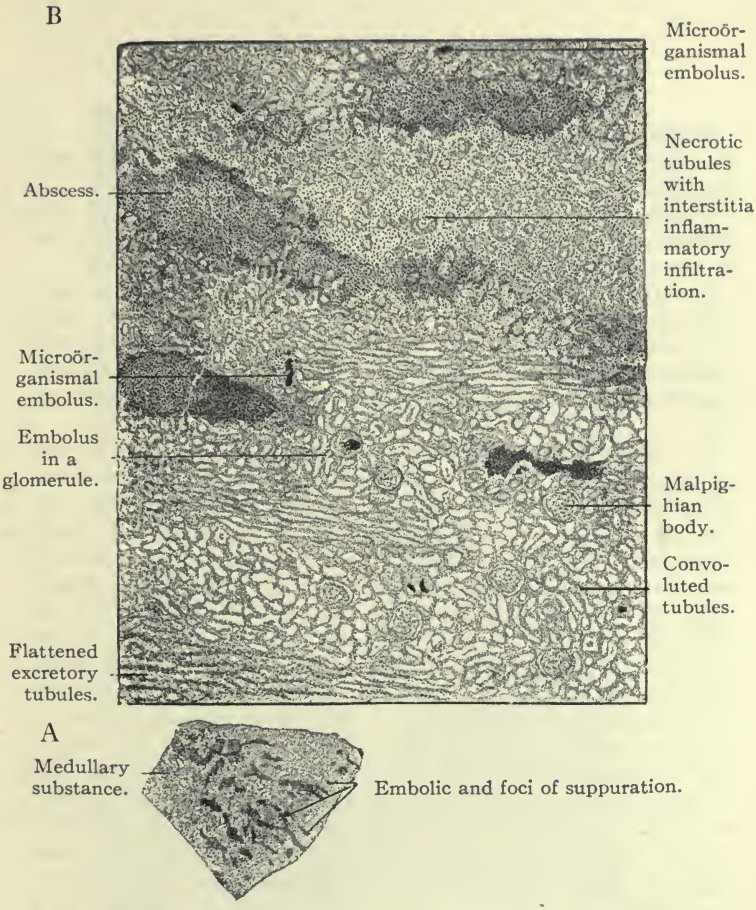


Fig. 61.—Pyemic nephritis.

Stained with hematoxylon and eosin.

Embolic nephritis in a boy, aged fourteen years, dying from septico-pyemia following acute osteomyelitis of the tibia.

A.—*The fragment of the kidney as it appears when twice magnified.*

B.—*Numerous abscesses and microörganismal emboli are seen in the upper part of the drawing, with necrotic renal tissue below. Magnification* 30 *diameters.*

ASCENDING PYELONEPHRITIS.

Urinary Nephritis.

Diagnosis of the Organs.—Under the low power it is easy to recognize the Malpighian bodies, the convoluted tubules and the collecting tubes of the kidney.

Diagnosis of the Lesion.—One is at once struck by the dissociation of the histological elements and by the diminution of the staining affinity of the cellular elements.

A.—In the *cortex* (Fig. 62, C) the convoluted tubules present alterations analogous with those described in connection with the subacute nephritis. In the interior of more or less irregular cavities desquamated epithelial cells are mixed with many smaller cells: mononuclears and more rarely polymorphonuclear cells.

The glomerules are less numerous, being crowded out by the inflammatory infiltration which dissociates all of the structures. Those that persist show varying congestion and capsular proliferation. An enormous number of blue cells diffusely infiltrate the entire stroma; in addition to which there are numerous dilated capillaries and small discrete interstitial hemorrhages.

B.—In the *medulla* (Fig 62, B) the parallel excretory tubules with their lining of cubical cells are relatively intact. Inside of them are two kinds of elements: *pus cells*, *i. e.*, polymorphonuclear and mononuclear leukocytes more or less degenerated with acidophilic protoplasm and pycnotic nuclei; and *desquamated epithelial cells*. The radiating appearance of the collecting tubules filled with pus and degenerated epithelium is characteristic of a nephritis of ascending origin (radiating nephritis of cystitis, prostatitis and urinary obstruction). In the interspaces between the tubules the stroma assumes a hyaline aspect: fine connective-tissue fibrillæ infiltrated with edematous fluid, and here and there, with numerous inflammatory cells sometimes difficult to distinguish from the nuclei of the fixed connective-tissue cells. In the medulla, as in the cortex, there are numerous capillary vessels, dilated and sometimes ruptured (interstitial hemorrhages).

Résumé.—*Ascending radiating nephritis* with parenchymatous changes (desquamation of the cells) as well as important interstitial changes.

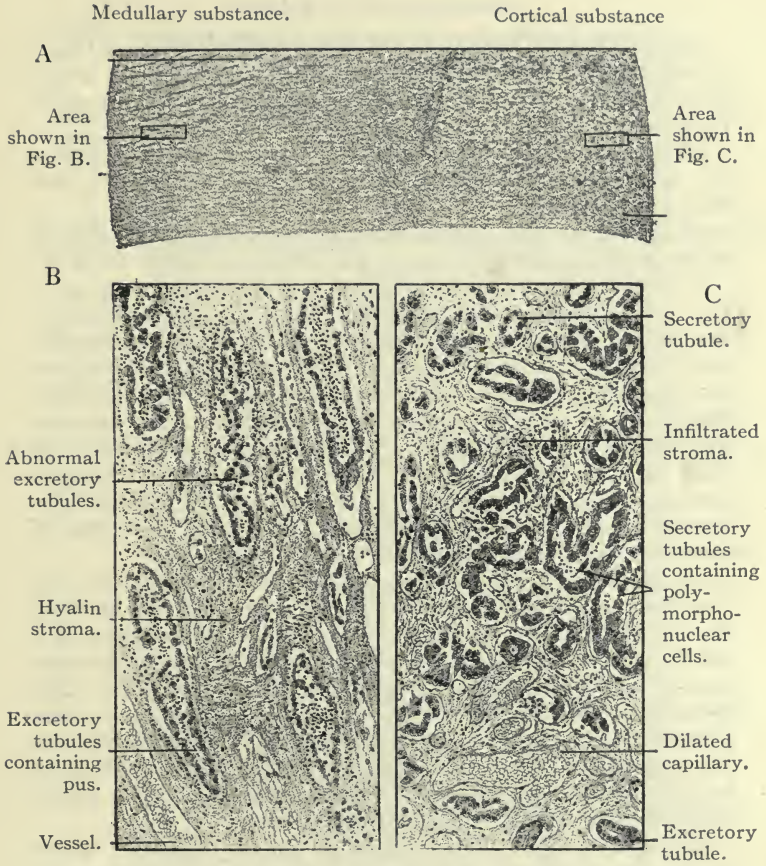


Fig. 62.—Ascending pyelonephritis.

Stained with hematoxylon and eosin.

Pyelonephritis following a gunshot wound of the dorsal spinal cord with paraplegia and retention of urine. The infection following the repeated catheterizations was the cause of death.

A.—*Appearance of a fragment of the kidney magnified* 5 *diameters.*

B.—*Medullary substance. Magnified* 100 *diameters.*

C.—*Cortical substance. Magnified* 100 *diameters.*

TUBERCULOUS PYELONEPHRITIS.

Tuberculosis of the Kidney.

The section has been made in the neighborhood of a tuberculous cavity or excavation. It is divisible into three zones; an upper which is the edge of the excavation, a middle in which the kidney tissue is relatively undisturbed, and a lower.

Diagnosis of the Organs.—This can easily be made by noting the presence in the middle zone of Malpighian bodies and convoluted tubules.

Diagnosis of the Lesion.—To accomplish this it will be necessary to separately examine the upper and lower thirds.

I. *Upper Third.*—This is the wall of the tuberculous excavation. It is composed of a caseous mass of a blue-violet color that is quite characteristic and has an undifferentiated appearance in which remnants of nuclei can be seen. It also shows numerous fractures or cracks that are caused by retraction effected by the reagents used in the preparation of the specimen for histological examination. At the periphery of the caseous mass some epithelioid cells are seen with stretched-out nuclei and pale and abundant protoplasm, and, above all, lymphocytes forming a dense bluish layer at the extreme edge of the wall of the excavation, and extending into the parenchyma.

II. *Middle Third.*—This shows the parenchyma variously disturbed by disease. Above, near the edge of the excavation, the tubules are deformed and compressed: lower down they are normal in appearance. In the secretory tubules desquamation of the epithelium is quite pronounced (tubulitis). The glomerules are but little altered (congestion) but the stroma presents an important lymphocytic infiltration with edema. In the lumen of some of the excretory tubules there are reddish hyaline masses (tube casts). The diminished staining power of all of the elements is to be noted.

III. *Lower Third.*—This contains miliary tubercles which can be recognized by their rounded form, by the presence of giant cells with nuclei arranged in horseshoe form, by their caseous centers and by the epithelioid and lymphoid cells at their peripheries.

It is easy to understand that with the occurrence of added caseation evacuation into a calyx might occur and thus begin a new open excavation.

Résumé.—*Pyelonephritis*, not unlike the preceding case in the epithelial desquamation, the infiltration of the stroma and the marked cellular necrosis but differing from it in the presence of the miliary tubercles and the excavation.

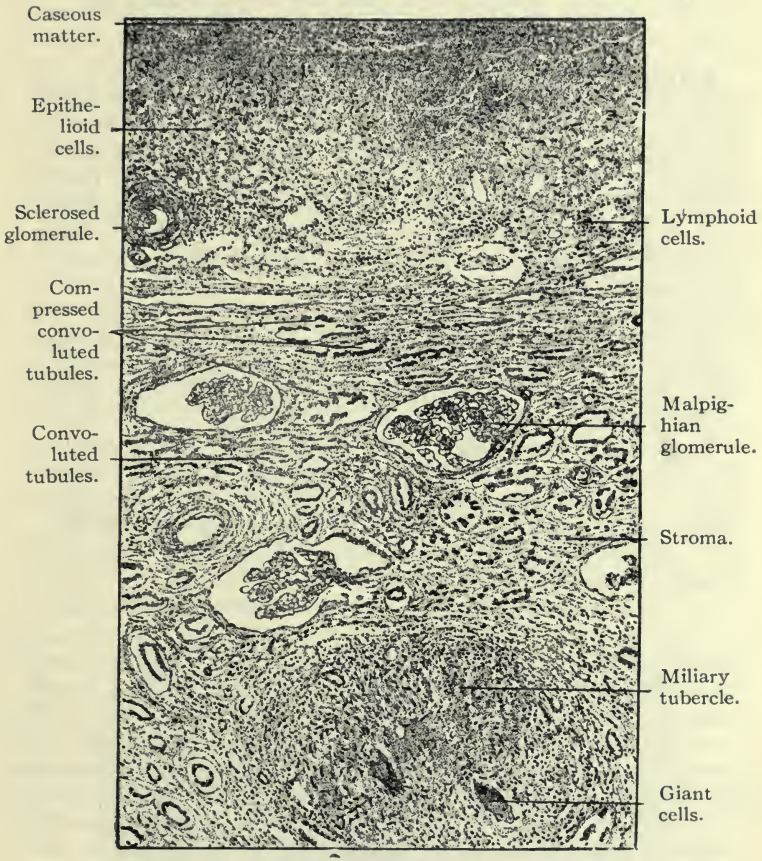


Fig. 63.—Tuberculous pyelonephritis.

Stained with hematoxylon and eosin. Magnified 100 diameters.

The upper third of the section shows a part of the wall of a tuberculous cavity of which the liquefied center cannot be seen. The middle part is composed of diseased renal tissue. The lower part contains a miliary tubercle with two giant cells.

AMYLOID INFILTRATION OF THE KIDNEY.

From a Case of Chronic Pulmonary Tuberculosis.

Diagnosis of the Organ.—This is very easy to make by a more extended study of the section than the limited field shown in the drawing permits. Under a low power the structure of the organ is found to be tubular, divisible into a cortical portion in which the tubules twist and turn among themselves, and a medullary part in which they occur in parallel formations—pyramids. Regularly distributed in the portions of the cortex lying between narrow, fairly equidistant, radiating, parallel, linear formations composed of excretory tubules and vessels—the medullary rays or pyramids of Ferrein—are rounded structures, which though so changed by disease that they no longer have the strawberry appearance, are recognizable of the glomerular or Malpighian bodies. We thus arrive at the diagnosis of kidney.

Diagnosis of the Lesion.—The examination just completed has shown the absence of gross abnormalities; so for future study the higher-power lenses must be used. With such magnification, changes, such as are represented in the drawing, are readily found. They embrace abnormalities of both glomerules and tubules.

1. *The Glomerular Disturbance.*—A diseased glomerule occupies the greater part of the center of the drawing. Instead of appearing as a nucleated plasmodium, as is normal, it is found to be largely composed of structureless, pink-colored, waxy substance in which a few cells and nuclei are caught, and between the masses of which some of the original structure survives. This is amyloid substance as can easily be determined by the application of the microchemic tests already described. Attention to the general arrangement of the amyloid material shows it to be deposited in a distribution corresponding to the letter S. This suggests that its seat of primary infiltration has been about the little vessels of the glomerules. This is in complete correspondence with its usual method of infiltration. Beginning its appearance about the small vessels, it gradually infiltrates the surrounding tissue, crowding its proper cells and causing them to atrophy.

2. *The Tubular Disturbance.*—These occur in association with the amyloid disease but are in no sense a part of it. Though it is rare for a kidney affected with amyloid disease to be otherwise normal, it may be possible. The amyloid infiltra-

tion is the result of certain chronic nutritive, or toxic, disturbance which may result in numerous and diversified associated changes. It is common, for example, to find fibrosis associated with amyloid. In this particular case the toxic disturbance of the patient's blood has manifested itself in tubular changes which assume various appearances that may be looked upon as indicating differing degrees of cell destruction. At the lower right-hand portion of the drawing are two transverse sections of convoluted uriniferous tubules (secretory tubules) that are fairly normal in appearance. In the upper left-hand portion there is a section of a similar tubule whose epithelial lining is transformed into an nuclear granular mass—complete distruction, or *necrosis* of the epithelium. Below it is a section of a slightly dilated tubule whose cells contain an excessive number of granules (cloudy swelling) among which are some very large granules and small spheres of translucent homogeneous substance much like the amyloid, but failing to give the microchemic reaction with iodine and gentian violet. These are *hyaline.* In some of the other tubules cells may be observed to lie free in the lumina of the tubules (desquamation). These cellular and tubular changes are not the result of post-mortem autolysis for they lack uniformity. They are the results of disease—*tubular nephritis.*

Résumé.—Kidney whose glomerules show homogeneous, waxy, perivascular deposits (*amyloid*), and whose tubules show destruction and desquamation of the epithelium in varying intensity—*tubular nephritis.*

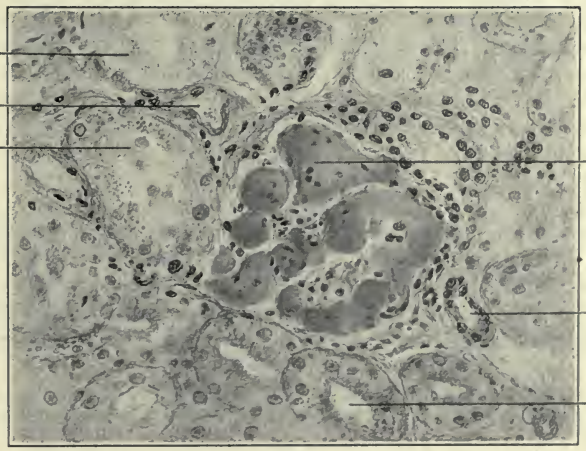


Fig. 64.—Amyloid infiltration of a renal glomerula. From a patient dead of chronic pulmonary tuberculosis. Magnified 250 diameters. Stained with hematoxylin and eosin.

BENIGN HYPERNEPHROMA.

Diagnosis of the Organ.—The section shown in the drawing divides itself into two distinct portions, which have different staining affinities. In the lower, Mapighian bodies and tubules leave no doubt as to the organ concerned. This portion is separated from that above by a thick band of vascular connective tissue which is the capsule of the kidney.

Diagnosis of the Lesion.—This constitutes the upper part of the drawing and is a tumor. When looked at closely it consists of nests of pale cells separated from one another by strands of connective tissue or by capillaries.

The arrangement is irregular and the absence of parallel columns is particularly noticeable. The cells when examined under a higher power are found to have a transparent protoplasm, and slightly excentric nucleus and a slightly reticulated or vacuolated protoplasm recalling that of the spongiocytes of the zona fascicularis of the adrenal body. Like them these cells are crowded with fine fatty granules (lipoid, neutral fats).

Between the cell nests is a fine trellis work of collagen fibers. Newly formed capillaries are extremely numerous and are in intimate contact with the cells of the tumor, as in the adrenal. The structure of these capillaries is normal: the endothelium reposes upon a thin layer of connective tissue. In the part of the drawing representing the kidney, attention must again be called to the fibrous capsule, which separates it from the tumor, and the compression of the tubules in its immediate vicinity.

We have here to do with a well-circumscribed definitely limited tumor of glandular origin, that is to say, with an *adenoma*—a benign tumor. But the appearance of the cells recalls the spongiocytes of the adrenal, and on this account it has been supposed that the tumor arises from débris of an embryonal vestige of that organ included in the kidney substance, from which it derives the name *hypernephroma.*

Résumé.—It is an epithelial tumor starting from the tubules of the kidney and in which the cells, in part or altogether, take the pale appearance. It is possible sometimes to follow the transition of the kidney cells to the transparent cells.

Sometimes in this case we have to do with a benign tumor, localized and encapsulated and not giving metastasis: adenoma with pale cells—*benign hypernephroma.*

Sometimes, one finds the characteristics of malignant tumors of the kidney—some with dark cells (epithelioma with dark cells), others with pale cells—*hypernephroma malignum.*

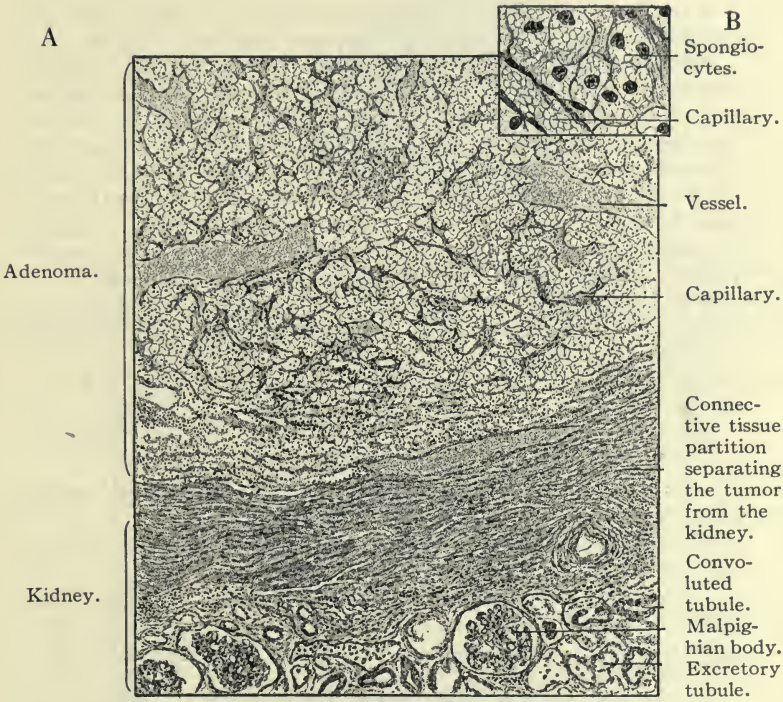


Fig. 65.—Benign hypernephroma.

Stained with hematoxylon and eosin.

A small sulphur yellow encapsulated benign tumor unexpectedly found at autopsy.

A.—*Separation between the tumor and the renal parenchyma, magnified* 80 *diameters.*

B.—*Spongiocytic cells of the neoplasm magnified* 450 *diameters.*

NORMAL TESTICLE.

Testis of a Dog.

A section perpendicular to the long axis of the testis with its epididymis and surrounded by the tunica vaginalis (Fig. 66, A).

The Testicle.—1. The *seminiferous tubules* (shown in the lower part of drawing, Fig. 66, B) are limited by a basement membrane upon which are placed two principal types of cells arranged in several layers. Some stain deeply and show a distinct contour and very distinct nuclei. They are the *cells of Sertoli*, very well shown here (dog's testis), but a great deal less distinct in human tissue. They are recognized by their somewhat peculiar nuclei flanked by a nucleolus and juxta-nuclear bodies. These are the so-called supporting cells.

The other cells, varying according to the layer examined, belong to the seminal line and include several strata passing from the periphery to the lumen of the tubule.

(*a*) The *spermatogonia*, rounded voluminous cells with large nuclei, in direct contact with the basement membrane.

(*b*) The *spermatocytes*, cells whose nuclei show numerous mitotic figures indicating cellular activity.

(*c*) The *spermatids*, a great deal smaller, with large nuclei and very dense protoplasm.

(*d*) The *spermatozoa*, elongated cells with a swelling at one end (head) and a caudal membrane (tail).

2. Between the seminiferous tubules a mass of large cells with finely granular protoplasm can be seen. These are the interstitial cells which seem to play a role in the internal secretion of the organ.

3. The intermediate zone, which separates the seminiferous tubules from the tubules of the epididymis, contains the vessels of the organ and its ducts are lined with cubical epithelium.

The Epididymis.—The tubules of the epididymis are composed of a rather thick basement membrane, upon which is arranged a single layer of cylindrical epithelium with pale protoplasm, and vibratory cilia that show very well. In the center of the lumen are collections of the spermatic secretion in which spermatozoa can be seen.

The structure of the seminiferous tubules with their stratified epithelium and highly specialized cells easily enables them to be differentiated from those of the epididymis.

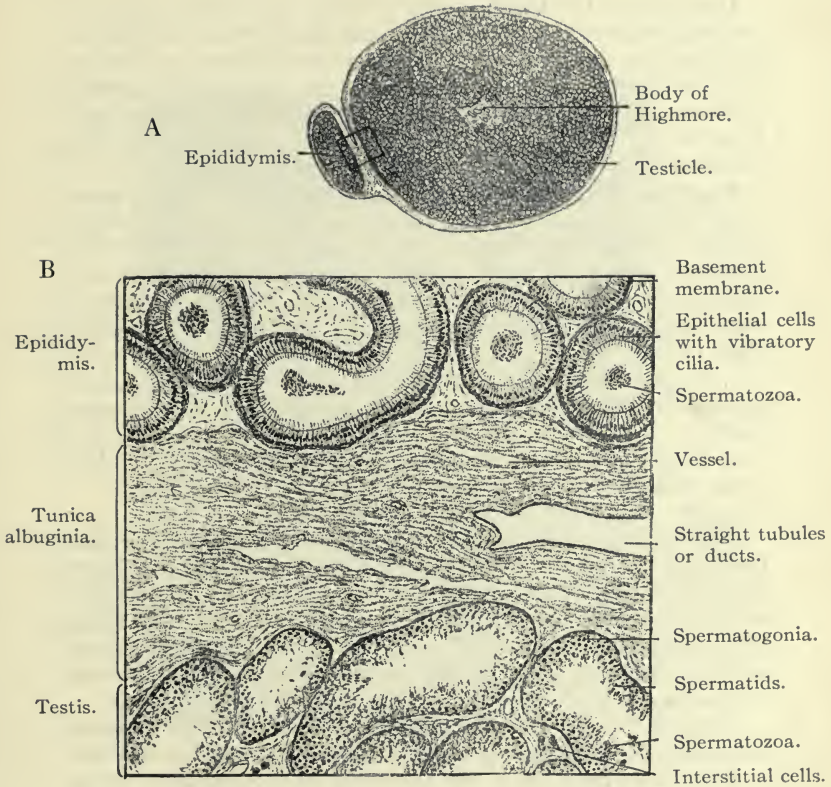


Fig. 66.—Normal testis of a dog.

Stained with hematoxylon and eosin.

A.—*Transverse section of the entire testis and epydidymis seen under a slight magnification.*

B.—*Part of* A *included in the square, magnified* 200 *diameters, and showing the epididymis above and the testis below.*

TUBERCULOSIS OF THE TESTIS.

Diagnosis of the Organ.—The drawing represents a group of tubules limited by a fairly thick lamina of connective tissue and lined on the inside by a stratified epithelium in a number of layers, which a high power shows to be composed of elements characteristic of the testis, and of its seminiferous tubules. None of the tubes has the structure characteristic of the epididymis. The tissue then includes only the testis.

Diagnosis of the Lesion.—The tubules are more widely separated and less numerous than normal. At certain points (upper left-hand portion of the drawing) the glandular elements of the organ have almost completely disappeared and their place is taken by a new combination which upon careful examination can be recognized as that of the miliary tubercle. That is to say:

1. A giant cell centrally situated and recognizable by its acidophilic cytoplasm and the coronet of peripherally arranged nuclei.

2. The epithelioid cells surrounding the giant cell with their usual transparent protoplasm and elongated nuclei.

3. The lymphoid cells more deeply colored.

Elsewhere—in the interiors of the seminiferous tubules themselves—miliary tubercles may be found with similar giant cells in the centers, epithelioid cells around them and seemingly derived from the cells of the seminiferous series by metaplasia. There is no caseation. It is, therefore, an early tuberculosis in which the cheesy change has not had time to develop.

Between the seminiferous tubules the inflammatory elements are mostly of the lymphoid type; some are, however, epithelioid.

As a contingent lesion the thickness of the basement membrane is to be noted. In this case it is very distinct and the modification of the seminal cells, which lose their differentiation, tend to give it an undifferentiated aspect.

Résumé.—An inflammatory lesion of the testis of tuberculous type—*tuberculosis of the testis.* Most frequently these lesions are associated with similar ones in the epididymis—*orchi-epididymitis.*

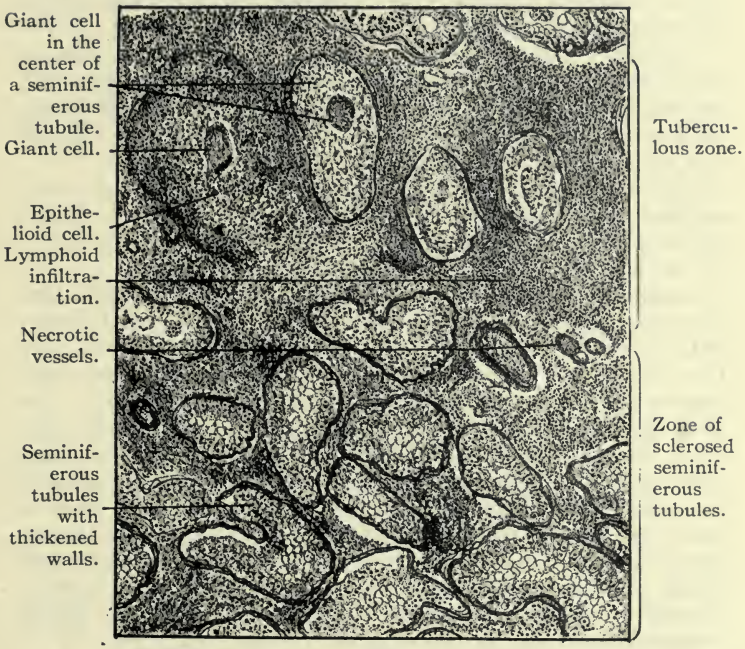


Fig. 67.—Tuberculosis of the testis.

Stained with hematoxylon and eosin. Magnified 200 diameters.

Tuberculous testis of an adult, removed at operation. The seminiferous tubules still show distinctly in the lower part of the drawing; miliary tubercles are seen above.

CANCER OF THE TESTICLE.

Seminal Epithelioma: Seminoma.

Diagnosis of the Organ.—When the drawing is examined with a low power it is found to be polymorphic and requires to be separately studied in its various parts. From above downward three different portions can be noted:

The *zone A* can easily be recognized as the testicle with its seminiferous tubules, showing their usual stratification and cellular elements of the seminal series—spermatogonia, spermatocytes in division and spermatozoa. There is no trace of the epididymis.

The *zone B* contains an enormous mass of bluish cells compressed one upon another. At first view these recall the appearance of lymphocytes and seem to be of inflammatory nature and more or less conjunctivo-vascular.

Diagnosis of the Lesion.—Under a higher magnification, and provided that the fixation of the tissue was good to begin with, these cells show, through their peripheral layer of pale protoplasm and large nuclei, their probable derivation from those of the seminal line. Elsewhere (left-hand side of the drawing) the transformation of the seminiferous tubules into these masses of pseudolymphoid cells can be followed: the tubes seem to melt, the basement membrane disappears and the epithelial cells mix with the neighboring stroma. Thus is conceived to take place the transformation of the seminiferous tubule and the origin of a tumor which bears the name *seminoma*. Elsewhere, between the seminiferous or cancerous tubules, there are extensive hemorrhagic areas such as are of frequent occurrence in these tumors.

The *zone C* is separated from the preceding by a thick band of connective tissue.

It is formed of very fine fibrillæ with scattered nuclei, or may be formed of a layer of homogeneous tissue recalling edematous fluid. In the substance of this mucous (myxoid) stroma there are elongated nuclei and cystic spaces, sometimes empty, sometimes filled with edematous fluid, lined with epithelial cells comparable to those of the cell nests described above. This appearance of the tumor with its hyaline stroma and cystic spaces is entirely atypical.

Résumé.—Malignant tumor or cancer of the testicle. In the least modified parts one recognizes a tumor of seminiferous origin—*seminoma*.

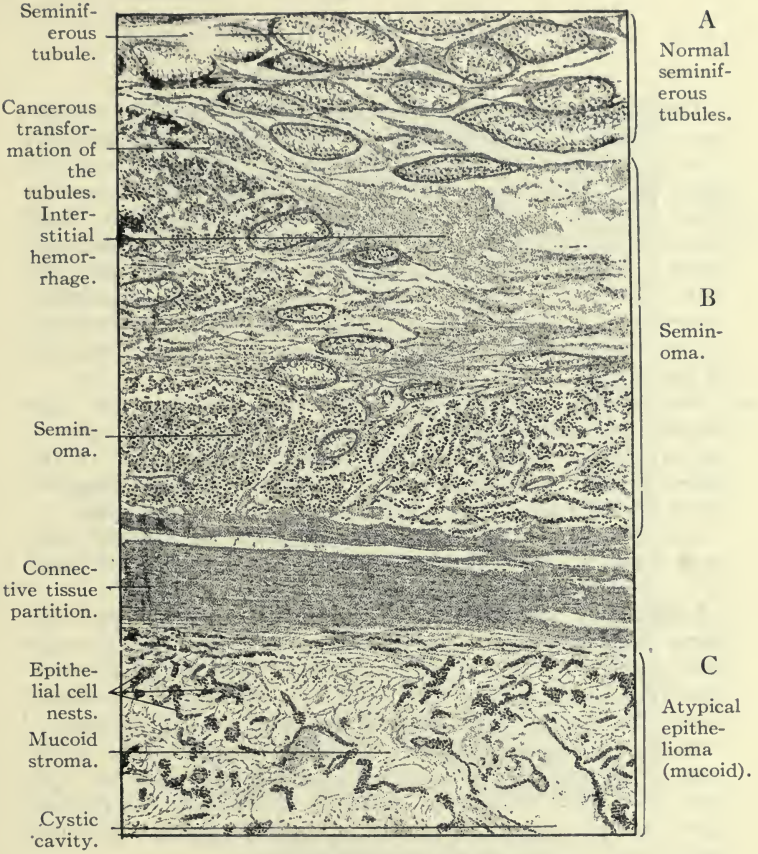


Fig. 68.—Seminoma of the testis.

Stained with hematoxylon and eosin. Magnified 50 diameters.

A rapidly growing tumor surgically removed from a man, aged fifty years. The drawing shows two different appearances of cancer of the testis. At the upper part the "seminoma" is shown with still recognizable seminiferous tubules; below the tumor has become atypical and myxoid through degeneration of the stroma.

HYPERTROPHY OF THE PROSTATE.

Adenoma of the Prostate.

Diagnosis of the Organ.—The tissue has a glandular appearance. The acini limited on the outside by a delicate basement membrane (condensation of the connective-tissue stroma) are lined by a single layer of cubical epithelium. The lumen is filled with a finely granular substance: the prostatic fluid coagulated by the reagents. In the interior of some of the acini there are peculiar formations of an ovoid form, and apparently made up of concentric stratifications of some amorphous material—protein concretions, corpora amylocia, or *sympexions*, of the prostate. Some of the narrow spaces are excretory ducts of the gland.

The stroma, which is very important, is composed of pale connective tissue with numerous smooth muscle fibers, appearing as reddish stripes upon the rose-pink background of the connective tissue. These fibers also differ from the connective tissue through their elongated nuclei swollen at the ends.

The glandular acini, the sympexions and the vascular connective tissue stroma enable the diagnosis of the prostate gland to be made.

Differential Diagnosis.—The mammary gland is the only organ with which the prostate can be confused, and is to be differentiated through its acini in which there is a double row of epithelial cells (myoepithelial cells), its stroma rich in adipose vesicles and the absence of muscular fibers in the stroma.

Diagnosis of the Lesions.—The chief characteristic is the great irregularity of the acini. In many places there are veritable microcysts lined with flattened epithelium. In proportion as the cavities are distended the epithelial lining is flattened until finally it may resemble endothelium.

In certain of the acini, as in the center of the drawing, the epithelium becomes stratified, and even sends little vegetations into the interior of the cavity. Such epithelial proliferation, limited to the tubes, belong to the variety of benign glandular tumors known as *adenoma.*

The stroma, equally hyperplastic, includes numerous smooth muscular fibers and connective-tissue fibers.

Résumé.—An *adenoma*, or benign tumor, of the prostate gland, a condition called in the clinic *hypertrophy of the prostate.*

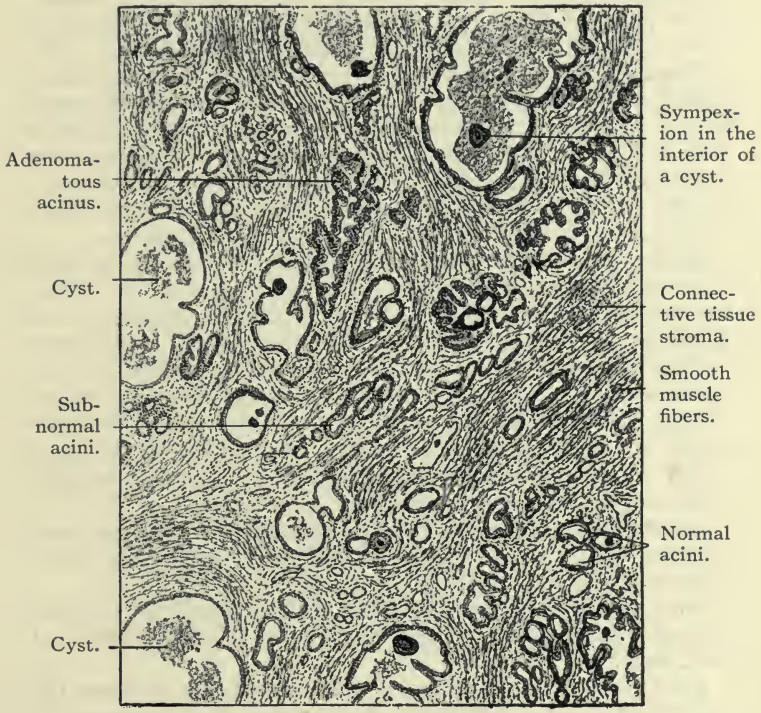


Fig. 69.—Hypertrophy of the prostate gland.

Stained with hematoxylon and eosin. Magnified 30 diameters.

A portion of the hypertrophied prostate surgically removed from a man aged fifty-five years. Numerous microscopic cysts are formed from the dilatation of the prostatic glandular acini. In some the epithelium is proliferating. Few or no ducts are seen. Smooth muscular fibers can be seen in the stroma.

EPITHELIOMA OF THE PROSTATE.

Diagnosis of the Organ.—This is scarcely possible to make unless there are, in some part of the section, prostatic acini with sympexions and smooth muscle fibers in the stroma.

Diagnosis of the Lesion.—The greater part of the drawing (lower part of the drawing, Fig. 70) has a very different appearance from that of the prostate gland. Everywhere are groups of dark staining epithelial cells arranged more or less regularly in strands that lose themselves in the depths of a dense connective tissue. Some of the groups vaguely recall the appearance of acini, but the architectural confusion is marked.

In the intermediate zone, that part of the drawing between the more healthy part and the cancer, one can see the transformation of the glandular into the neoplasmic formation. At certain points the glandular epithelium proliferates and finishes by rupturing the basement membrane of the acinus and disseminating its cells in the stroma. Even in the part of the section described as more healthy, one can see at various points the neoplasmic transformation of the glandular acini.

The muscular and connective tissue of the gland shows very distinctly between the tubules.

Schematically the section can be divided into three portions or zones which correspond to three different stages in the development of the tumor.

Zone A, where the gland is nearly healthy, some of its tubules beginning to proliferate; the beginning of the development of the tumor.

Zone B, in which the cancer is developed. It assumes the form of a typical epithelioma, that is to say, the arrangement of the glandular elements in acini is preserved for the most part.

Zone C, in which the tumor is infiltrating. Here it has become entirely atypical because of its degree of malignancy. It is impossible here to determine from what type of epithelium the tumor is derived.

Résumé.—An epithelioma developed from the prostate gland, comparable to what is observed in the breast—typical epithelioma in parts, atypical epithelioma elsewhere.

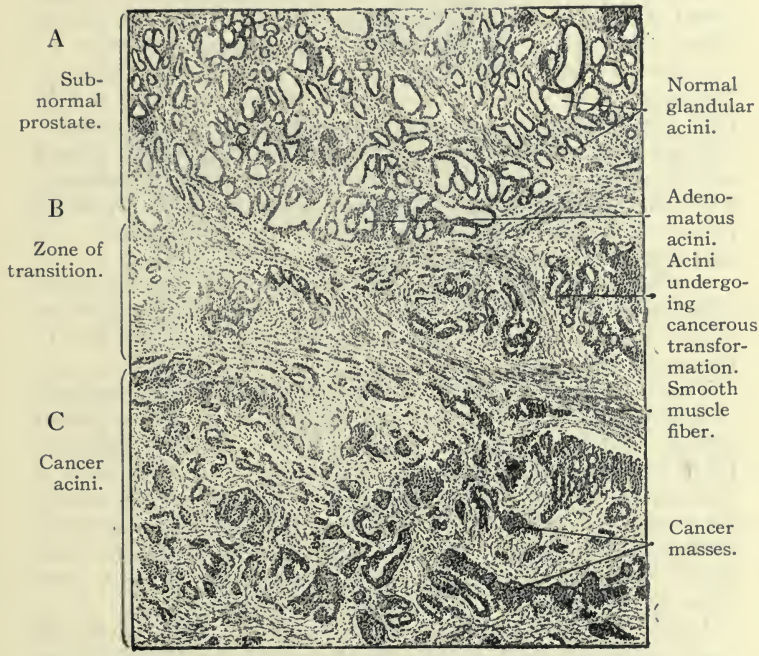


Fig. 70.—Cancer of the prostate.

Staining with hematoxylon and eosin. Magnified 50 diameters.

The tissue was operatively removed from a man aged seventy years. In the upper part A, *the structure of the prostate is still recognizable. In the middle part* B, *the neoplasmic development is beginning. In the lower part C, the cancer is well developed and is recognized either as atypical acini with thickened epithelial linings or as atypical epithelial cell infiltration.*

NORMAL OVARY.

Ovary of a Cat.

The section embraces almost the entire organ and is composed of a rather uniform tissue, paler at the center and darker about the borders. Each portion requires separate study.

1. *In the central zone*—the medullary portion—the matrix is composed of an abundant connective tissue, peculiarly rich in cells and, therefore, of an embryonal type—fibroblastic—through which pass, in serpentine fashion, numerous blood-vessels—some of which are cut transversely, some longitudinally. The veins among them can be recognized by their flattened condition, the arteries by their rounded sections. There are also a great number of capillaries.

2. *The peripheral layer*—cortical zone—includes an epithelial covering composed of cells resting upon a dense stroma in which appear numerous clear dots—enormous cells almost visible to the naked eye—the *ovules* characteristic of the ovary.

The surface epithelium, or *germinal epithelium*, is composed of cells of cuboidal form and rests directly upon the subjacent stroma. At various points it grows down into the depths of the tissue in the form of peculiar invaginations, the *cell cords of Valentine-Pflueger*, which give origin to the *primordial follicles*. Each of these follicles is formed of a protoplasmic mass with a central nucleus and is limited externally by an intercellular layer. The primordial follicles are distributed in the zone immediately beneath the germinal epithelium.

More deeply the *Graafian follicles*, or ovisacs, are developed from the primordial follicles. Each appears as a cavity filled with a finely granular substance — *liquor folliculi;* at the periphery there is a thick membrane—the *zona pellucida;* in the center, according to the thickness of the section, a very large nucleus, the *germinal vesicle*, provided with a very large nucleolus—the *germinal spot.* At the periphery of the ovisac there are cells more or less polygonal in shape, forming a thick investiture of concentric formation—the *membrana granulosa.*

The ripening of the ovules in the ovisacs, or Graafian follicles, takes place from the time of puberty to the menopause (*ovogenesis*). At the time of each menstrual period an ovule, arrived at maturity, ruptures its protecting membrane, escapes from the follicle and is caught in the infundibuliform extremity of a Fallopian tube where it is either fertilized by a spermatozoön, or eliminated externally with the menstrual blood. That which remains of the ovisac after its rupture forms the corpus luteum.

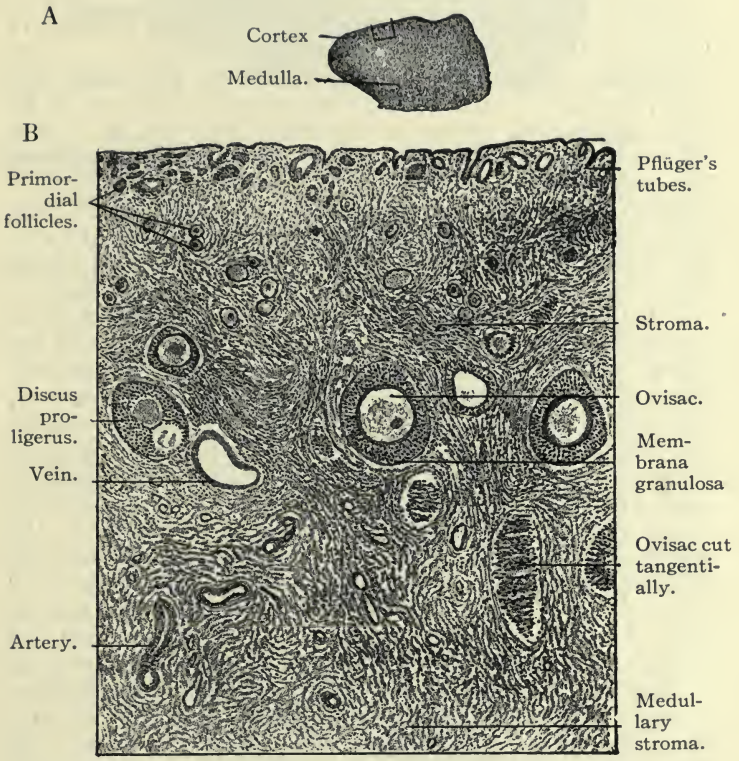


Fig. 71.—Normal ovary.

Stained with hematoxylon and eosin.

Ovary of an adult cat. A *shows the entire organ magnified* 3 *diameters.* B *shows the fragment of the cortical substance within the square in* A, *magnified* 100 *diameters. It shows the details of cortical structure above and of medullary structure below.*

FIBROUS CORPUS LUTEUM.

Senile Ovary.

The section is made perpendicularly to the long diameter of the ovary (A).

Diagnosis of the Organ.—This is attended with some difficulty, but can be arrived at by observing the division of the structure into the central or medullary zone rich in vessels, continuous with the pedicle of the organ and the peripheral zone, or cortex.

In the cortex there are few or no Graafian follicles, but there are numerous larger structures visible even to the naked eye; the *corpora lutea*, with an undulating outline; specific formations of the ovary which enable the organ to be recognized.

If the section be examined under a higher magnification the germinal epithelium, which usually covers the surface of the ovary, will be found to have almost entirely disappeared. This atrophied epithelium no longer dips down into the stroma, and there is an entire absence of primordial follicles or ovisacs. The cortical substance below is no longer composed of fibroblastic connective tissue. A little lower down the homogeneous masses of the corpora lutea are found. Each is formed of an undifferentiated material, a veritable cicatricial mass in the depths of which are some fine strands of connective tissue with nucleated cells. These are the *corpora albicantes*, resulting from the sclerosis and hyaline transformation of the corpora lutea of menstruation. In consequence of their retraction and atrophy these elements undergo characteristic transformations.

Elsewhere (Fig. 72, C) a different type of the corpus luteum, younger, much more rare in senile ovaries, is formed of polyhedral cells with pale granular protoplasm (lutein cells), with large nuclei arranged about the bloodvessels—an arrangement that recalls the structure of the glands of internal secretion, especially the adrenal.

The cortical stroma is composed of spindle-shaped connective-tissue cells (fibroblasts) arranged in whorls.

In the most vascular part of the organ (medullary substance) there are many bloodvessels in a state of hyaline degeneration.

Résumé.—The disappearance of the germinal epithelium, the ovules and the follicles and the presence of cicatricial corpora lutea and vessels with hyaline walls, in the absence of any signs of pathological change, lead to the conclusion that the diagnosis of senile ovary is justified.

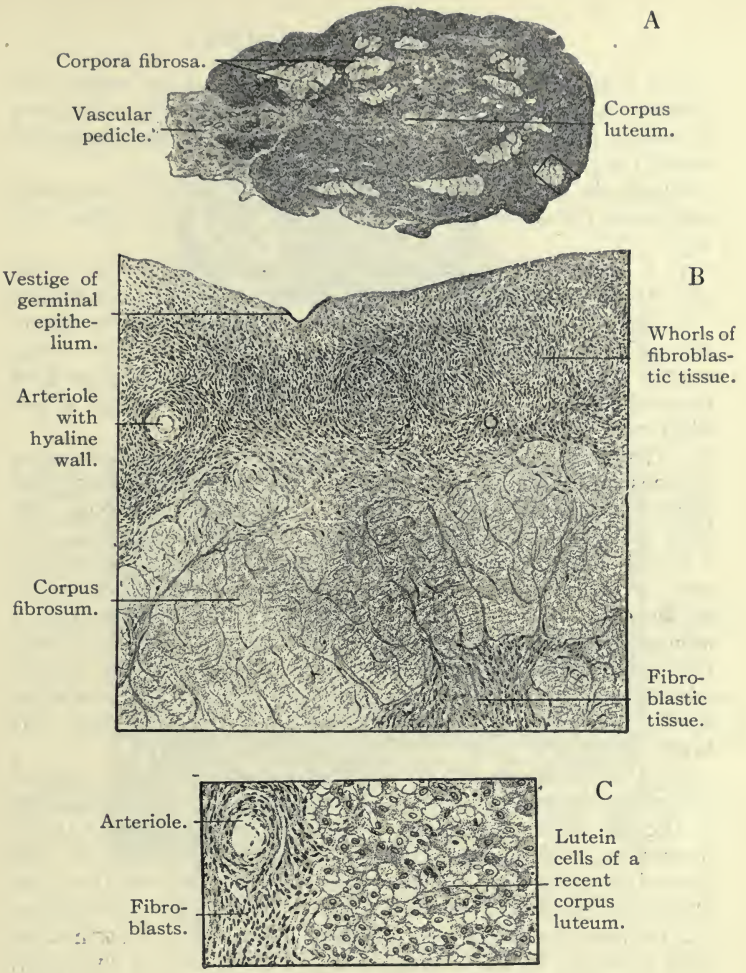


Fig. 72.—Ovary with corpora fibrosa.

Stained with hematoxylon and eosin.

Longitudinal section through the entire ovary of a woman, aged seventy years. A, *entire section magnified* 3 *diameters.* B, *part of the cortex magnified* 100 *diameters, corresponding to the part included in the little square in* A. *It shows the structural details of a corpus luteum—corpus fibrosum.* C, *magnified* 150 *diameters, the details of structure of a fresh corpus luteum.*

The section passes through the long axis of an ovary and consists of a swollen part and a pedicle. With the naked eye or with a hand lens a series of cavities can be seen arranged about the periphery of the organ.

Diagnosis of the Organ.—Examination with a low-power lens shows the characteristic elements of the ovary. That is to say:

1. A connective tissue rich in fibroblasts which surrounds each of the cystic cavities and separates them one from another.

2. Here and there, in the thickness of this connective tissue, are primordial ovules or Graafian follicles with their large central germinal vesicles, the zona pellucida, colored rose with the eosin dye and their granular membrane. These are somewhat rare and may be absent altogether.

3. The corpora lutea of oval shape. Some have undulating outlines and homogeneous structure and are old, hyaline and sclerotic. Others, more rare, are composed of large pale cells filled with fatty granules and are more recent corpora lutea.

Under a higher-power magnification one notes the disappearance of the germinal epithelium which can only occasionally be found. The cysts, variable in size and number, contain a homogeneous mucilaginous substance that colors rose red with the eosin dye. It sometimes entirely, sometimes only partly, fills the space on account of retraction or fragmentation effected by the reagents or manipulations to which the specimen has been subjected.

Fig. 73 (B) shows the details of the structure of the walls of the cysts, as well as the mode of their formation. Below and to the left there is an entire small cyst, arising through transformation of an ovisac with its granular center, and its wall formed of polyhedral cells in many layers, derived from the membrana granulosa of the ovisac. To the right, and above, is a portion of a larger cyst of which the wall is still formed by cells arranged in numerous layers. Below, and to the right, in consequence of further distention with fluid, the epithelial lining of a cyst is reduced to a single layer of flattened cells.

Between these different cysts the stroma is represented by collaginous fibers with a small number of young connective-tissue cells and numerous capillary vessels of which the walls are composed of a single layer of endothelial cells.

Résumé.—*Cystic transformation of the ovary*, or *sclerocystic ovary*, supposed to result from chronic inflammation.

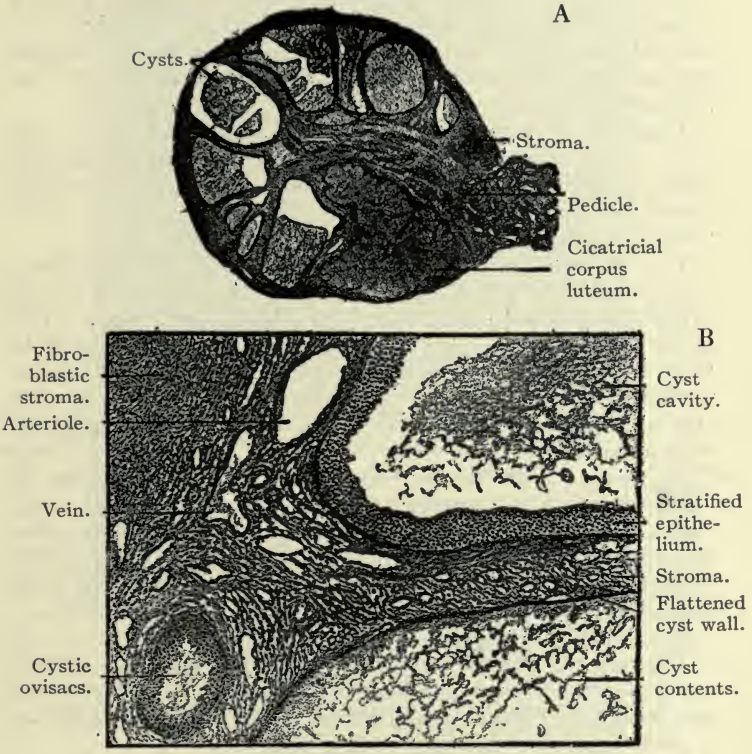


Fig. 73.—Sclerocystic ovary.

Stained with hematoxylon and eosin.

Sclerocystic ovary of a woman aged seventy years.

A.—*Entire section, cut longitudinally and magnified 3 diameters.*

B.—*Showing the structure and formation of the cysts, separated from one another by a richly vascular connective tissue. Magnified 80 diameters.*

NORMAL UTERUS.

A histological section of the body of the uterus, passing through the entire thickness of the organ, and including two distinct zones: the one quite thick—the *muscularis*, or muscular wall; the other much thinner, the mucous membrane, or *endometrium*.

Diagnosis of the Organ.—Examined under a low-power lens (Fig. 71, A), the muscularis is seen to be composed of a very thick layer of smooth fibers—the greater part cut transversely, others longitudinally or obliquely. This gives the wall of the uterus its characteristically plexiform appearance.

The mucosa, very thick, is formed by a simple epithelium, lining the whole interior as a narrow band composed of tall cylindrical cells with clear slightly acidophilic protoplasm. The nuclei stained deep blue, the long diameters corresponding to those of the cells, are somewhat close together at the basal portions. By the ordinary method of preparation it is difficult to distinguish the vibratory cilia with which the epithelial cells are provided.

At many points the epithelium dips down in the form of "glove fingers" and penetrates into the depth of the subjacent tissue. The cells lining these prolongations are of the same character as those of the primitive epithelial cells (Fig. 74, B). They are not active glandular cells with dense and finely granular protoplasm, but simple invaginations of the mucosa—glanduliform invaginations.

The mucous corium, which is very abundant, is formed almost entirely of young connective-tissue cells (fixed cells and leukocytes) which must not be taken as an indication of a pathological state.

The nature of the epithelium, the glandibuliform depressions of the mucosa and the thick plexiform subjacent muscular layer, are sufficient to enable the diagnosis of the body of the uterus to be made (the neck is covered with a stratified squamous epithelium in its vaginal part).

Differential Diagnosis.—Sections of the alimentary canal—stomach, small intestine and colon—ought not be confused with what has just been described, for in them all besides the difference in the epithelium there is always a thick layer of connective tissue—the submucosa, which is missing here.

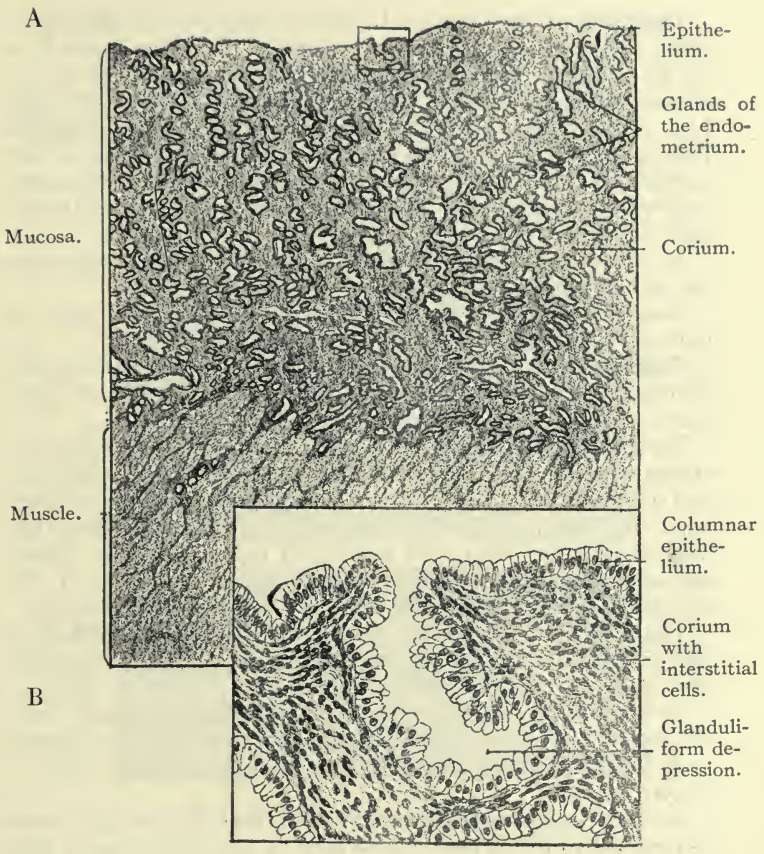


Fig. 74.—Normal uterine mucosa.

A portion of normal uterus removed at surgical operation from a woman, forty years of age.

A.—*The entire thickness of the mucosa and part of the muscularis magnified 20 diameters.*

B.—*The part included in the little square in* A *magnified 200 diameters, and showing the structural details of the glanduliform depressions.*

Diagnosis of the Organ.—In actual practice it is difficult to make the diagnosis of both the organ and the lesion if one is to do so from the examination of the sections alone. He should always have information from the clinic or autopsy to guide him. Nevertheless it is possible to arrive at a reasonable degree of accuracy without it. In the section there is a part in which it is possible to recognize the uterine mucosa elsewhere and much changed, and in which scarcely any of the glanduliform invaginations exist.

In the corium young connective-tissue cells and leukocytes are to be found as usual.

Immediately below the mucosa there is a narrow band of pale connective tissue.

Diagnosis of the Lesion.—The greater part of the section, as shown in the drawing (Fig. 75, A), is formed by a large mass of dark staining elements arranged in whorls.

Under a higher power lens these are found to be composed of elongated cells grouped in bundles cut transversely, obliquely and longitudinally. Their dense protoplasm is strongly colored with the eosin, and each shows in the center an elongated nucleus of a rod shape, not pointed at the extremities. These are unstriped muscle fibers such as are encountered in the thickness of the uterine wall.

That which differentiates this muscular tissue from that of the normal uterine wall is the marked disposition to occur in whorls, with disarrangement of the fibers.

In some areas, in the substance of the muscular mass, rose-red patches are formed by connective tissue rich in collagen, with fusiform nuclei a little shorter than the muscle nuclei—*fibrous fasciculi.*

Such an appearance corresponds with that of a benign tumor—a *myoma* or *fibromyoma*—according to the proportion of connective to muscular tissue present.

With greater precision, the tumor is a submucous intraparietal myoma, easily enucleable.

Résumé.—A benign tumor—a *uterine fibromyoma*—developed in the wall of the uterus and formed chiefly of unstriated muscular fibers.

Such common muscular tumors of the uterus frequently undergo a malignant degeneration and terminate in myosarcoma with frequent interstitial hemorrhage, monstrous nuclei, necrotic zones and metastases.

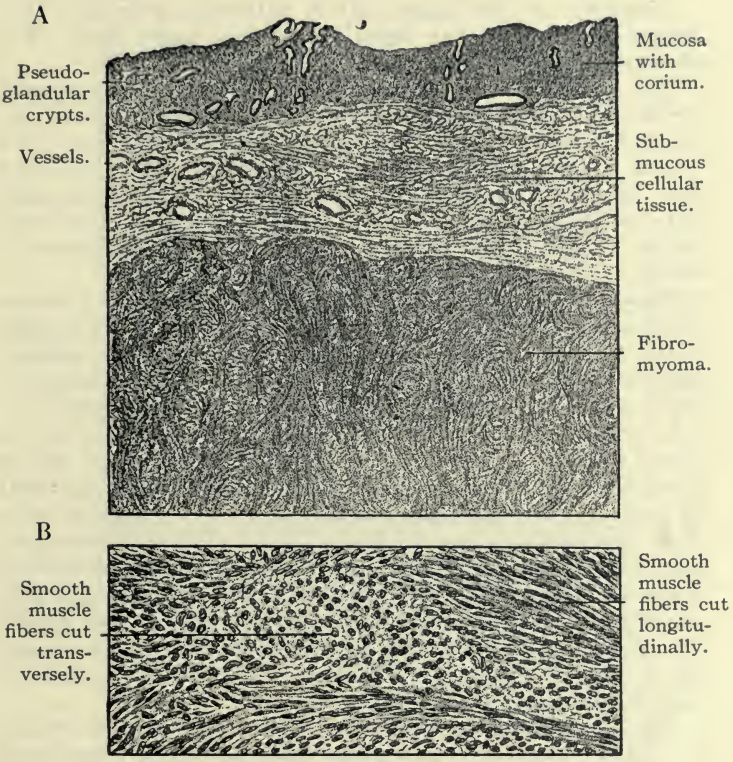


Fig. 75.—Fibromyoma of the uterus.

Stained with hematoxylon and eosin.

Intramural fibromyoma of a uterus which showed in addition an enormous submucous sloughing fibromyoma. Removed at operation.

A.—*The uterine wall with the enucleable intramural fibromyoma, magnified* 25 *diameters.*

B.—*A portion of the tumor magnified* 200 *diameters.*

CANCER OF THE BODY OF THE UTERUS.

Diagnosis of the Organ.—It is extremely difficult if not impossible to say what organ the section comes from. The diagnosis has to be presumptive.

The greater part of the tissue, upon careful examination, proves to consist of a musculo-connective-tissue matrix, particularly rich in smooth muscle fibers which makes us think of the uterus, the bladder or the prostate. The abundance and disorderly arrangement of the pseudoglandular formation with which the tissue abounds, some of which are united while others are separate, gives the impression of a neoplasm—a tumor of the type of columnar glandular epithelium.

Diagnosis of the Lesion.—The spaces, or epithelial cavities, are lined with tall cylindrical epithelial cells with abundant protoplasm, and nuclei also elongated and deeply stained. They are arranged parallel and in several layers, thus constituting a stratified epithelium. Under a higher power magnification (Fig. 76, B) the cells, which line the spaces are found to retain their tiny filaments—vibratory cilia. In a nest full of epithelial cells the cylindrical form may be lost, the arrangement in parallel rows has disappeared and the cells, side by side, sometimes contain nuclei of monstrous size with abnormal karyokinetic figures. Finally, the substance of the protoplasm frequently contains little dark chromatin granules (pseudococcidia). In the centers of the glandular tubules small masses of amorphous substance with more or less nuclear débris (cellular necrosis), sometimes less altered desquamated epithelial cells can be found.

The *stroma* is formed of connective tissue and smooth muscular fibers. The paler connective tissue is chiefly represented by fibroblasts with elongated protoplasm and fusiform nuclei and by some fixed connective-tissue cells.

The smooth muscular fibers (more deeply stained with the red) have nuclei that are not pointed at the ends. There are some masses of round cells especially formed about the blood-vessels—small areas of inflammatory infiltration.

Résumé.—It is a neoplasm of the columnar epithelial glandular type; a tumor because of the architectural confusion of the tissues and a malignant tumor because of the atypical character of the cells. This epithelial tumor, or *epithelioma*, is developed from the mucosa of the fundus of the uterus and penetrates the entire thickness of its wall. The lymphocytic infiltration is explained by the fact that the tumor was ulcerated.

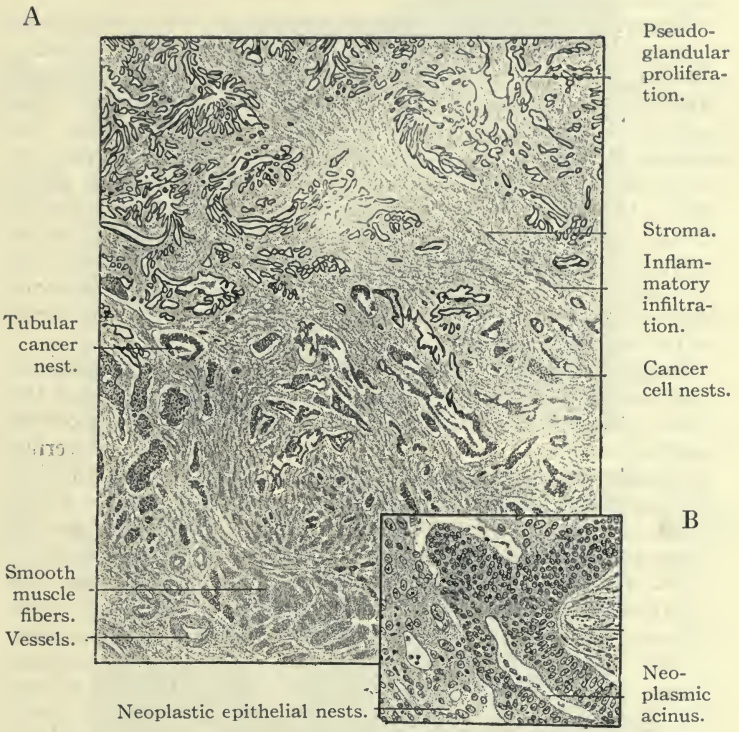


Fig. 76.—Cylindrical epithelioma of the body of the uterus.

Stained with hematoxylon and eosin.

A.—*Section of a fragment of the body of the uterus taken from a part of the muscular wall infiltrated with cancer nests. Magnified 20 diameters.*

B.—*The same showing the pseudoglandular appearance of the tumor formed of cylindrical cells containing nuclear monstrosities.*

CANCER OF THE NECK OF THE UTERUS.

Epithelioma Spinocellulare.

Diagnosis of the Organ.—An examination of the section under a low-power lens enables a presumptive diagnosis to be made. The left-hand part of the drawing shows a stratified squamous epithelium supported upon a musculo-connective tissue. The superficial layers are not cornified and the corium does not contain fat cells. It is then a Malpighian (squamous) mucous membrane. The arrangement of the smooth muscle fibers below the squamous epithelium makes one think of the neck of the uterus. This, however, refers to the *vaginal portion* only, for the neighboring portion of the isthmus is covered with a single layer of columnar epithelial cells. This opinion, however, should be confirmed by information from the clinic or the report of the autopsy.

Diagnosis of the Lesion.—If the epithelium be followed from one side to the other (Fig. 77, A) it will be seen that the basal layers become less undulating and thicken into a condition of *acanthosis*. Further to the right the epithelial covering disappears—an *ulceration*. In the corium there are epithelial prolongations that deeply invade the musculo-connective tissue of the organ. It is, therefore, a tumor and a *squamous-cell carcinoma* of the vaginal portion of the neck of the uterus.

The drawing B gives the histological details of the tumor. It is formed of cells more or less resembling those of the squamous mucous membranes—*epithelioma spinocellulare*. In the center of the drawing there is a bloodvessel—an arteriole—whose tunica musculo-elastica is much thickened. About it in the perivascular space is some protoplasmic débris, some of which is multinucleated. This is the débris of cancer cells which have invaded the perivascular lymph spaces and might have been transported to other parts of the body. In the upper right-hand part of drawing B there is another lymph vessel stuffed full of cancer cells. Such invasion of the lymph vessels is common in epitheliomas in general. In the neck of the uterus it explains the peculiar tendency of the tumor to extend widely and early reach the cellular tissue at the base of the broad ligament, especially the periurethral parametrium.

One should be particular to notice the presence of numerous monstrous nuclei and the frequent cellular divisions which evince the malignant nature of the tumor and the tendency of its tissues to proliferate and to degenerate.

Résumé.—*Epithelioma spinocellulare of the vaginal portion of the neck of the uterus.*

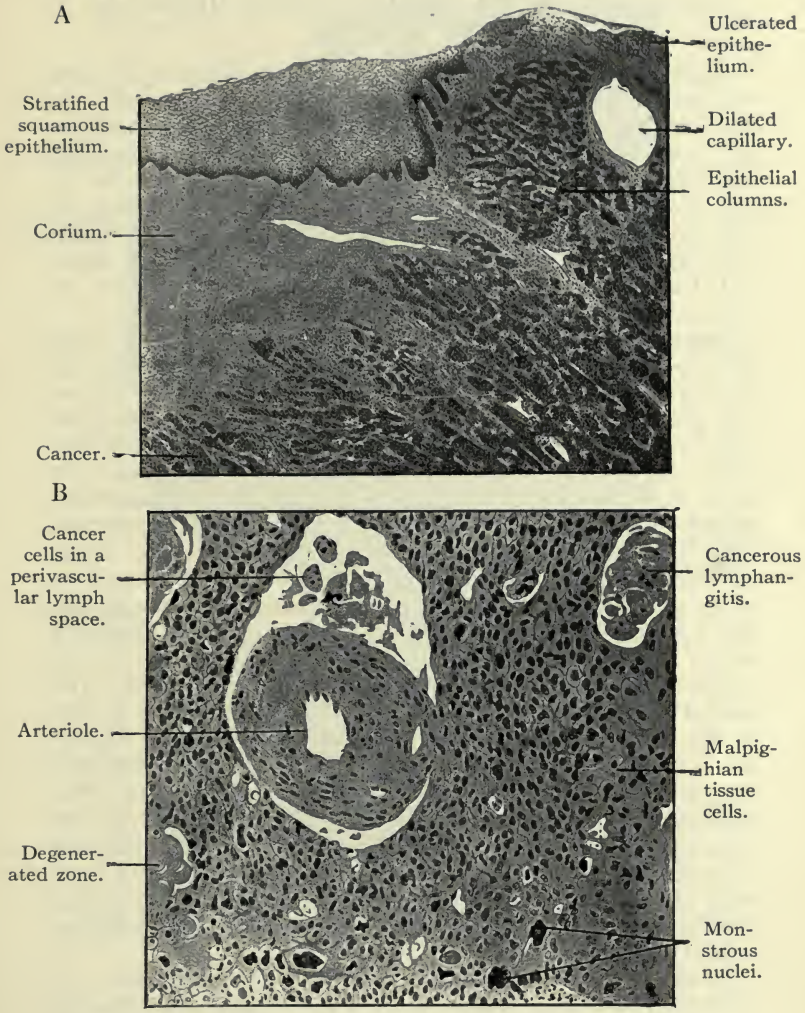


Fig. 77.—Squamous cell carcinoma of the neck of the uterus.

Stained with hematoxylon and eosin.

A.—*Vaginal portion of the neck, magnified 25 diameters.*
B.—*Cancer masses with nuclear monstrosities.*

ULCERATIVE METRITIS OF THE NECK OF THE UTERUS.

Diagnosis of the Organ.—This should be made by noting the simultaneous presence of a very thick mucosa covered by columnar cells and a muscularis separated from one another by a corium of a pseudolymphoid appearance. These together with the unstriated and plexiform character of the muscularis, and the fact that the mucosa sends extensions consisting of young cellular connective tissue deeply into a corium, make the diagnosis of uterus with certainty. The somewhat dissociated appearance of the muscular fibers makes one think of the neck of the uterus.

Diagnosis of the Lesion.—The section is drawn under a low-power magnification. Fig. 78, A, shows in the right-hand upper portion a thick mucosa, in the depths of which there are numerous glandular crypts. These are sometimes cut perpendicularly, sometimes parallel, and show as cavities with sinuous walls. At the left of the section the mucosa disappears; it is an ulceration. In the depths of the mucosa the glands are greatly dilated, forming cysts with mucous or mucopurulent contents; these are called the *cysts* or *follicles of Naboth.* They are formed through the inflammatory obliteration of the orifices of the glandular crypts and are extremely common in the uterus. But a diagnosis of metritis must not be made upon their presence alone. Under a higher magnification (Fig. 78, B) the details of the inflammatory lesion of the corium can be studied. The epithelium consists of tall cylindrical cells, covering the surface of the neck and descending deeply into the glandular depression. The mucous corium is formed, in the normal state, of a stroma full of young connective-tissue cells of a pseudolymphoid appearance. This infiltration is strongly emphasized in the present case and at two points the cells are approximated so as to form definite inflammatory masses. Going hand in hand with this lymphatic hyperplasia there is an unusual number of capillaries. The unstriated muscle shows no pathological alteration.

Résumé.—The hypertrophy of the mucous membrane, its ulceration at certain points, the cysts, the infiltration and the deformity of the glands make the diagnosis of ulcerative metritis of the neck of the uterus. *Hypertrophic subacute metritis* with diffuse glandular and periglandular lesions of the mucosa.

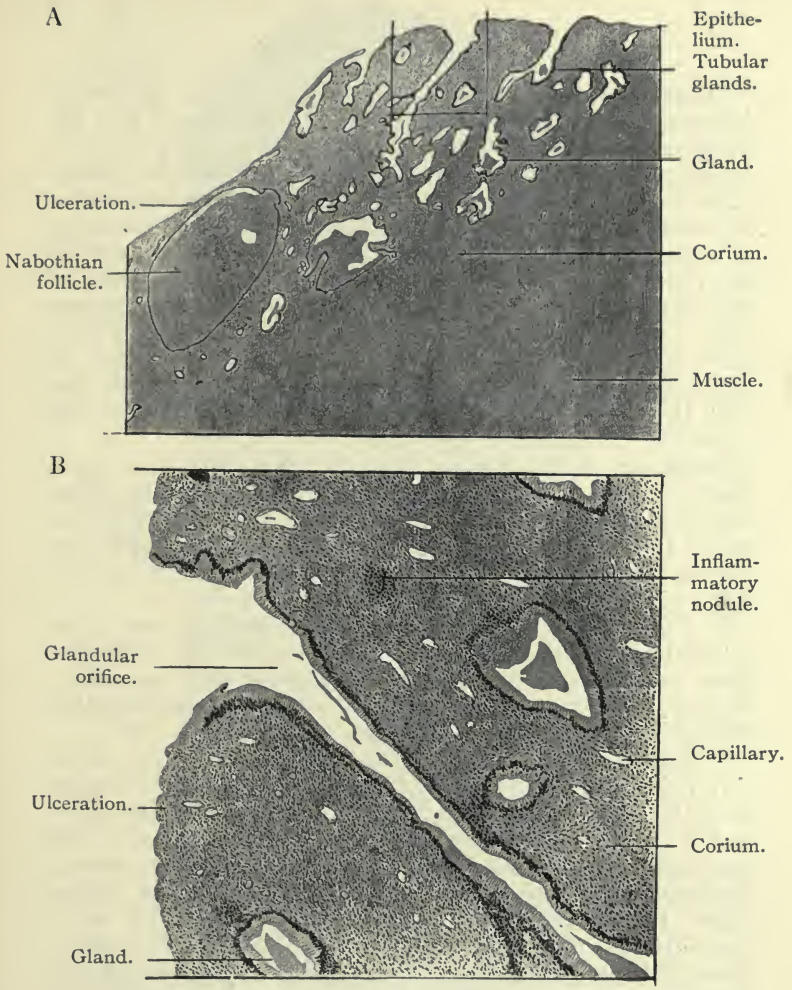


Fig. 78.—Ulcerative cervical metritis.

Stained with hematoxylon and eosin.

A.—*Portion of the section magnified* 10 *diameters, showing the general topography of the structure and the ulceration of the mucosa.*

B.—*A glanduliform depression with lesions of the ulcerated epithelium, of the corium, and the inflammatory infiltration, magnified* 150 *diameters.*

Diagnosis of the Organ.—A circular section (Fig. 79, A) with irregular spaces in the center. Under a low-power lens the peripheral part of the section is found to be made up of interlacing smooth muscle fibers cut longitudinally and transversely. Here and there are dark spots. Inside of the muscular coat is a mucosa with its multiple tubules deformed and ramifying in so peculiar a manner as to give the impression of a veritable labyrinth—an appearance that is only to be encountered in the infundibuliform Fallopian tube with its multiple mucous folds. In this case the secondary and even the tertiary folds have lost some of their epithelial covering as the result of inflammation, and have become soldered together. It is thus that the peculiar diminished and divided appearance of the interior of the tube is brought about.

Diagnosis of the Lesion (Fig. 79, B).—The muscularis, which is covered on the outside by a peritoneal endothelium which is imperfect, is composed of bundles of fibers indefinitely mixed together. The normal arrangement in two layers, one circular and one longitudinal, does not obtain here, or, at least, is not visible.

In the entire thickness of the walls, but especially near to the external surface, there are numerous dilated vessels, and about them an inflammatory infiltration composed of round cells—leukocytes. These same cells are separately disseminated throughout the smooth muscle tissue of the wall.

Further inside the mucosa is very much altered. The vibratory cilia have entirely disappeared. All that can be seen is that the epithelium on the mucosa occurs in a single layer and is frequently interrupted through desquamation. This appearance is particularly distinct in the spaces or pseudo-glandular cavities which result from the adhesion of the various folds. In the interior of these cavities degenerated polynucleated leukocytes are mixed with the desquamated epithelium, all bathed in a serous fluid which in case of obstruction can occasion the distention of the tube and the occurrence of the condition known as pyosalpinx.

Résumé.—Acute inflammation with preponderating lesions in the mucosa—*acute salpingitis.* By special methods of staining it may be possible to demonstrate the presence of microörganisms, the most frequent and specific being the gonococcus; less specific the more common microörganisms of suppuration, the staphylococcus or the streptococcus.

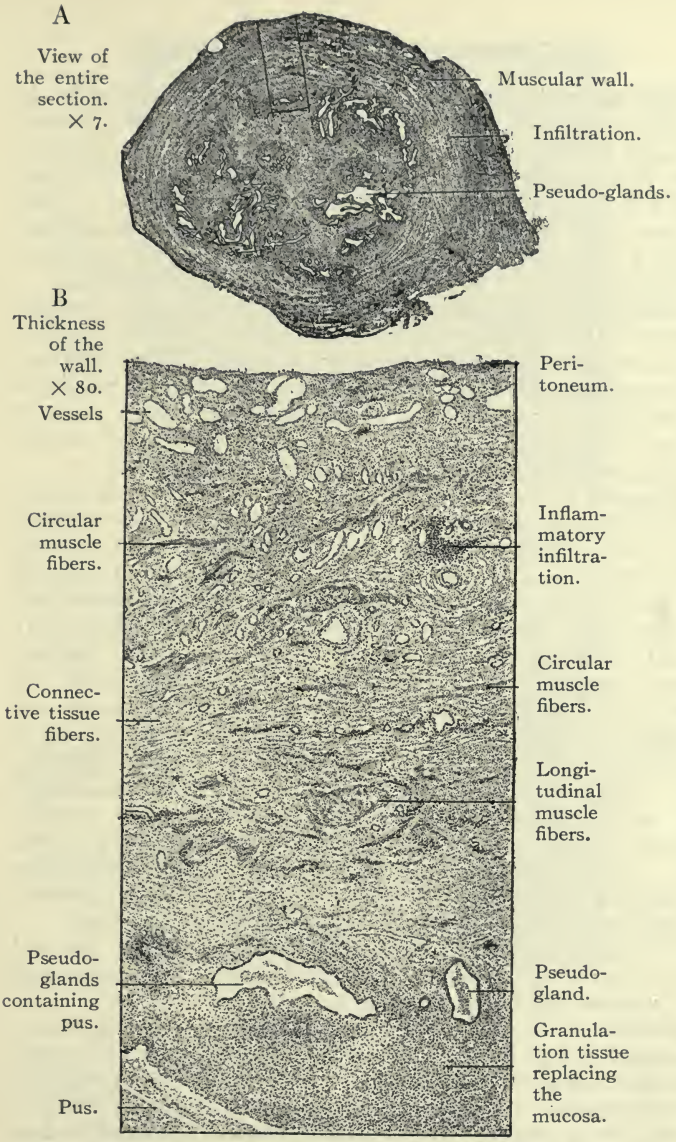


Fig. 79.—Acute gonococcic salpingitis.

FIBROADENOMA OF THE BREAST.

Diagnosis of the Organ.—At the right-hand part of Fig. 80, A, there is a connective tissue in which are a number of small duct-like structures, some of which are grouped as acini about little ducts (galactophorous ducts) which appear as small slits or crevices in the tissue, each lined with epithelium. There are also occasional groups of fatty vacuoles. This arrangement of acini in groups about galactophorous ducts, in a stroma fibrous and fatty, is characteristic of the mammary gland.

Differential Diagnosis.—One single other organ can be mistaken for the mammary gland—that is the prostate. But in its stroma there is no fatty substance, but instead an admixture of smooth muscle fibers and in the acini there are nitrogenous concrements or sympexions. Moreover, under a high power it is easy to recognize, in well-fixed tissue, two rows of nuclei, as there are both glandular cells and myoepithelial cells.

Diagnosis of the Lesion.—One cannot help being struck by the architectural confusion of the remaining half of the drawing (left-hand portion of Fig. 80, A). There are no acini; everywhere there is a starred appearance, formed by attenuated ductules, the extremities of which are variously evaginated and exvaginated. The lumina are lined by an epithelium that appears to be partly desquamated on account of bad fixation. These structures are derived from the proliferated acini. A matrix of a special variety of connective tissue surrounds and separates the glandular formations. The most internal part of this tissue, with a pale tint, has undergone mucoid degeneration. The proliferation and development of this tissue, which has crowded out the acini and compressed their walls, explains in large measure the peculiar appearance of its epithelial structures. At the periphery of the neoplastic nodule, and separating it from the mammary tissue proper, there is a delicate connective-tissue wall that definitely circumscribes the neoplasm.

It is to be noted that the mammary tissue proper does not have a normal appearance; the acini are small and compressed in a sclerosed matricial tissue.

Résumé.—Tumor of the breast following the abnormal development and proliferation of the connective-tissue stroma; a benign tumor, or *fibroadenoma:* (1) Because of its distinct circumscription and independence from the organ in which it develops; (2) because the basement membrane is not broken through so that processes of the epithelium can escape into the stroma; (3) because the connective tissue is of adult type, with few cells.

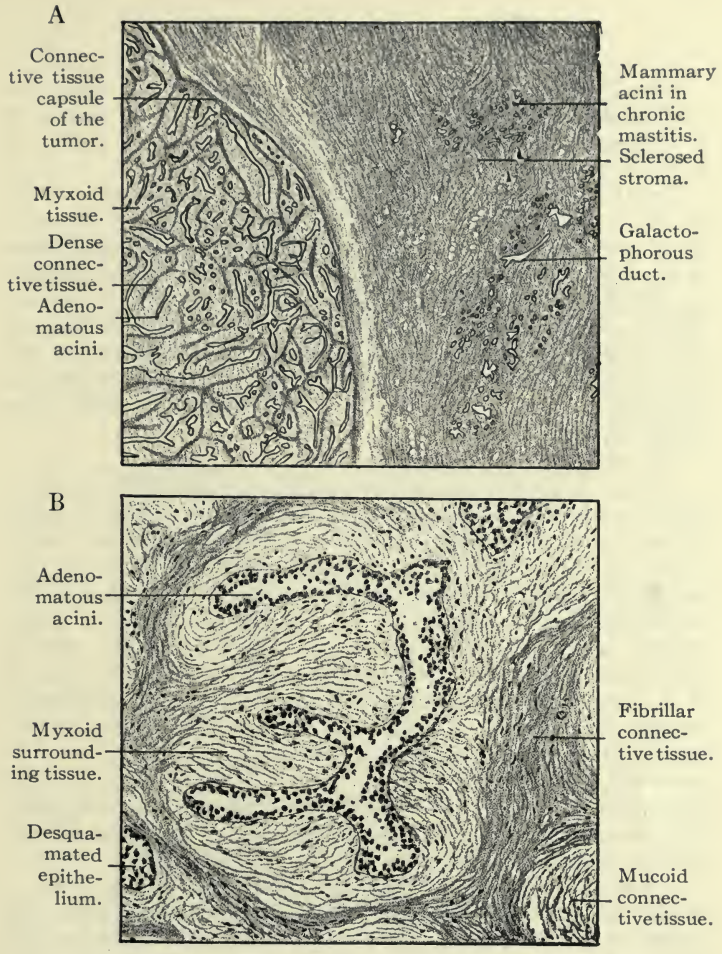


Fig. 80.—Pericanalicular fibro-adenoma of the breast.

Stained with hematoxylon and eosin.

A benign enucleable tumor, movable beneath the skin, removed from the breast of a woman aged thirty years.

A.—*Showing the line of separation between the tumor and the breast, magnified* 12 *diameters.*

B.—*A portion of the tumor, magnified* 150 *diameters.*

CANCER OF THE BREAST.

The drawing, which represents in its totality a section of a considerable extent of breast tissue, enables one to follow in a methodical fashion the mode of development of cancer of the breast.

Toward the upper right-hand corner of the drawing (Fig. 81, A) a few rare glandular acini are almost lost in the very dense fibrous tissue, but permit one to recognize the tissue of the breast, and from an organ affected with chronic mammitis (mastitis). In the lower right-hand portion of the section (Fig. 81, A) there are numerous cystic formations of varying size—beginning intracanalicular epithelioma. Finally, at the lower left-hand corner (Fig. 81, A)there is an extensive infiltrative mass of nests and processes, composed of cells that color deeply with the nuclear stains—atypical epithelioma.

Let the different portions be studied in detail:

1. Fig. 81, B, represents No. 1 of Fig. 81, A, drawn under a higher power. The glandular acini are lost in a stroma of dense connective tissue formed chiefly of collagen fibers with only occasional nuclei and few if any fatty vesicles. The acini are dissociated, isolated or extinguished by the proliferation of the connective tissue (sclerosis). In the center there are longitudinal sections of two galactophorous ducts. The use of the higher power shows distinctly the characteristic structure of a glandibular epithelium: cells resting upon a peripheral basement membrane, a simple condensation of the connective-tissue stroma, but whose topographical interest from the point of view of tumor study is great. If the structure of the mammary acini is still recognizable their scarcity coincides with the density of the stroma resulting from a diffuse inflammation—chronic mammitis.

2. The following figure (Fig. 82, C) shows the details of No. 2 of Fig. 81, A. Here are larger or smaller cysts, sometimes even visible to the naked eye. The contours are very irregular and the wall formed of epithelial cells in numerous layers limited on the outside by the basement membrane. The cells are of the cuboidal, sometimes cylindrical, form and have nuclei of various size, rich in chromatin; some of them are monstrous and show mitotic figures. The mucosa that lines the cysts grows into the interior, forming numerous prolongations (invaginations). Sometimes these are provided with a connective-tissue axis that enables them to project into the cavity of the

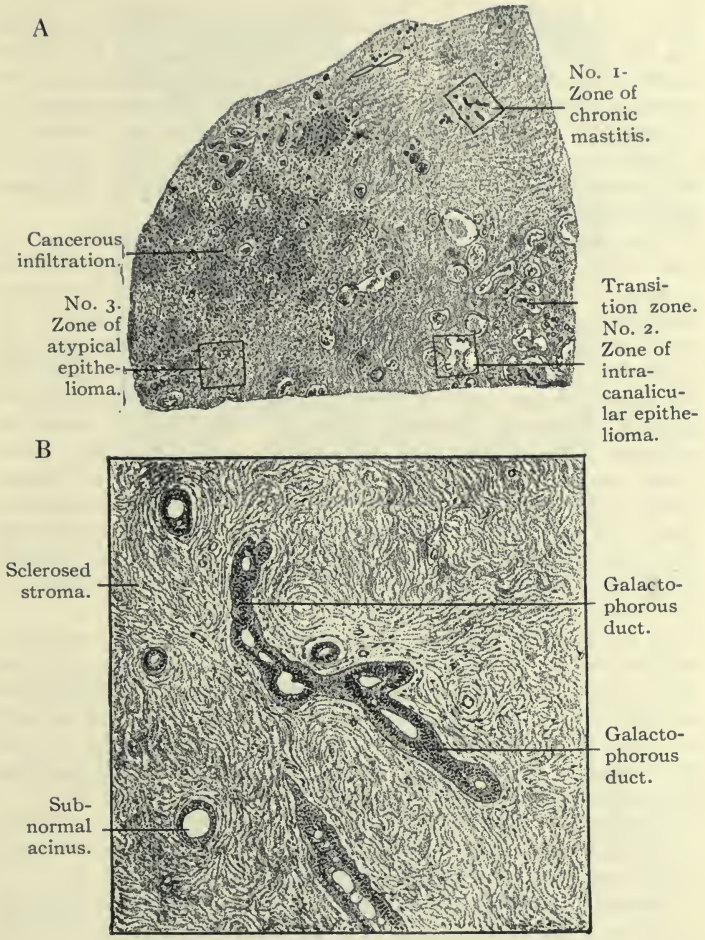


Fig. 81.—Epithelioma of the breast.

Stained with hematoxylon and eosin.

Cancer of the breast of a woman, aged forty-five years, removed at surgical operation.

A.—*The entire section magnified* 5 *diameters.*

B.—*Zone of chronic fibrous mastitis, magnified* 75 *diameters.*

cyst. These intracanilicular invaginations or processes can take on a considerable development. In the thickness of their walls there may be innumerable minute cysts—secondary intraparietal cysts. The cavities contain a structureless mass of coagulated material, usually of a finely granular nature, in which there are apt to be numerous desquamated epithelial cells from the alveolar walls, in an advanced state of degeneration, with nuclei in a state of pycnosis.

The presence of intracanalicular buds, the stratification of the epithelial bed and the numerous atypical cells make the aspect of the tumor very suspicious from the point of view of malignancy. It can be already affirmed that we have to do with an intracanalicular epithelioma or dendritic epithelioma. In order to confirm the diagnosis one studies with care the condition of the basement membrane, an important element not only from the diagnostic point of view, but also from the point of view of prognosis. Insomuch as the basement membrane appears to be intact, one has to do with a malignant tumor still limited, with little chance of lymphatic metastasis after ablation by the surgeon. Here, on the contrary, though the basement membrane appears to be intact, one already finds neoplasmic cells (cancerous emboli) outside of certain of the cysts in the interior of the vessels.

3. In Fig. 82, D (No. 5 of the drawing A), the cancerous infiltration is established. Only at rare points does one find cystic glandular formations; elsewhere there are little masses or fine strands of cells, with an occasional large nest of cells distributed, throughout the stroma. Only occasional circular groupings distinctly recall the glandular arrangement of the neoplasm—atypical or infiltrating epithelioma.

The stroma of the tumor is an adult connective tissue infiltrated with small round cells which indicate an infection added through ulceration of the tumor.

Résumé.—In this specimen all of the stages in the development of a glandular tumor can be followed from the precancerous stage (chronic mammitis) to the formation of an atypical epithelioma. It ought not be imagined that one easily finds, as in this case, all of these various stages in a single histological preparation of cancer of the breast. It is usually necessary and, therefore better, to prepare several fragments from the material removed at operation in order to make the diagnosis of the tumor.

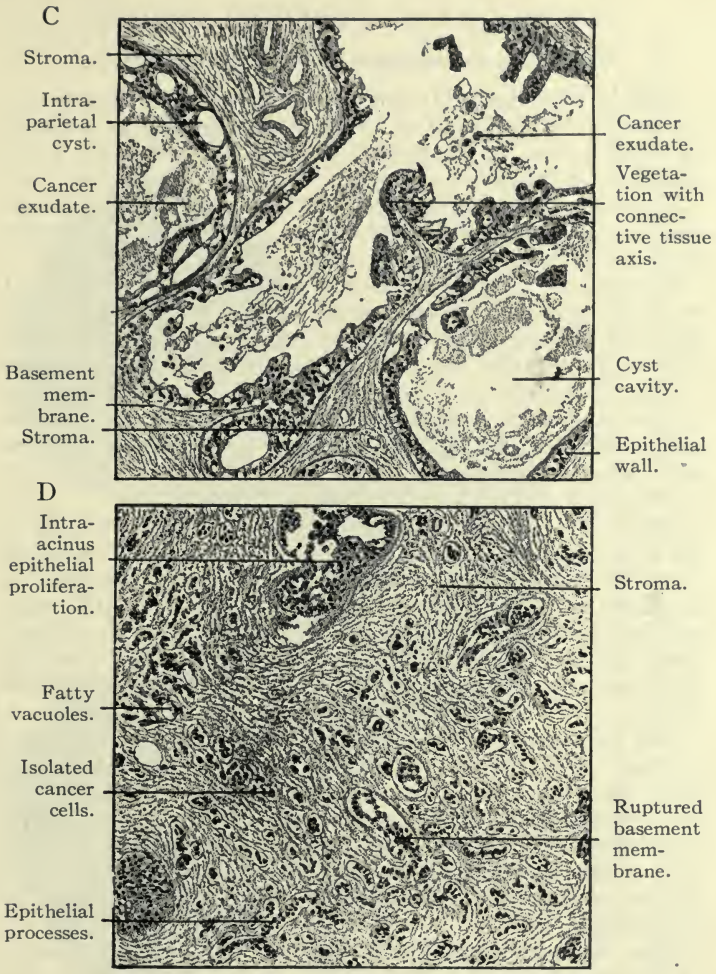


Fig. 82.—Epithelioma of the breast.

Stained with hematoxylon and eosin.

Same case as Fig. 81, *magnified* 75 *diameters.*

C.—*Zone of intracanalicular epithelioma with cystic formations and vegetations* (*point No.* 2, *Fig.* 81).

D.—*Zone of atypical infiltrating epithelioma* (*point No.* 3, *Fig.* 81).

HEMIPLEGIA OF CEREBRAL ORIGIN.

Descending Degeneration of the Pyramidal Tract.

In order to be able to interpret the sections which follow and to appreciate their lesions it is indispensable to have at least an elementary idea of the technic employed in the study of the pathology of the nervous system.

The tissues of the central nervous system are fixed in formaline (10:100) and after hardening are cut into sections either frozen or after embedding in celloidin or paraffine.

The staining of the sections is achieved through a variety of methods according to the particular information that it is desirable to gain. This may have reference to the nerve cells, the myelin sheaths, the neuroglia or the fibrovascular tissue.

The cellular elements visible in sections stained with hematoxylon and eosin are particularly well brought out by the method of Nissl (fixation in alcohol and staining in polychrome blue) which colors the protoplasmic granulations of the nerve cells blue.

When it is desirable to demonstrate the myelin sheaths of the nerve fibers and bring out fresh or old degeneration of the fibers the methods of Weigert, Weigert-Pal or Nageotte are appropriate. The myelin sheaths which surround the axis-cylinders are colored blue by the method of Nageotte; intense black by the methods of Weigert and Weigert-Pal. The cells stain badly by these methods and appear brown upon a yellowish field.

The tracts of nerve fibers stained intensely black, cut longitudinally or transversely in the sections and contrasting with the brown background are highly characteristic of sections of the central nervous system stained by the methods of Weigert or Weigert-Pal. But it only applies to healthy nerve fibers with intact myelin sheaths. The degenerated sheaths whose continuity has been interrupted (Wallerian degeneration) do not stain.

The employment of the Weigert method, therefore, result in the demonstration of dark areas—healthy nerve tracts—and pale areas—degenerated nerve tracts. These methods are, therefore, only adapted to the study of the white matter which is composed entirely of nerve fibers and should not be employed when it is desired to determine the condition of the gray matter and nuclei. But care must be taken not to confuse cell aggregations, which stain palely, with fiber degeneration, and the beginner will do well to begin by assuring himself of the absence of

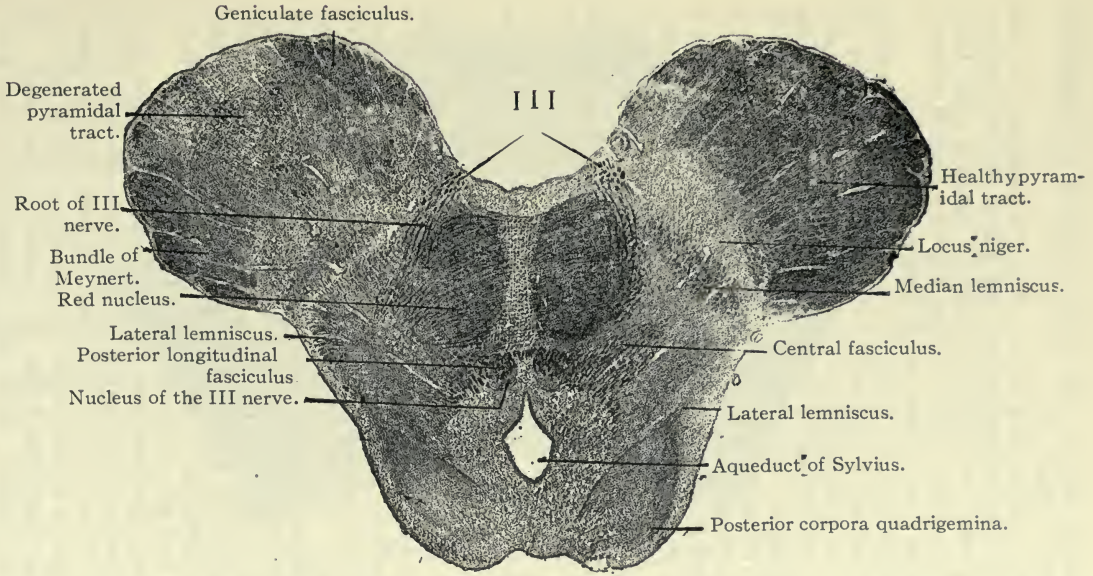


Fig. 83.—Cerebral peduncles.

Stained by the method of Weigert-Pal. Magnified 3½ diameters.

Right hemiplegia: degeneration of the pyramidal tract in the floor of the left peduncle. Above, the anterior part of the peduncles, the crusta; below, the posterior part, the tegmentum.

cells, and noting that the part under examination corresponds to some tract of fibers.

It is further indispensable to know the anatomy of the different motor and sensory tracts of the central nervous system.

We now proceed to examine a series of sections made from different levels of the central nervous system of a case of hemiplegia following upon a lesion in the left cerebral cortex.

The drawing (Fig. 83) represents a section passing through the cerebral peduncles, sufficiently characteristic to be easy to recognize. The general form of the section can be compared to a triangle with rounded corners, the summit corresponding to the "*tegmentum*" and the two angles to the two cerebral peduncles. The tegmentum is posterior and the crusta anterior in the microscopic sections.

In the tegmentum the central and median part contains a triangular canal—the *aqueduct of Sylvius*—which effects a communication between the third and fourth ventricles. On each side of the aqueduct, at the periphery of the section, is a pale oval mass, the posterior *corpus quadrigeminus*, in which the fibers of the auditory nerve terminate, and which bounds the section in front of the corpus.

In front of the aqueduct of Sylvius, a pale mass of cells marks the position of the nucleus of the third pair of cranial nerves (oculomotor), of which one sees the fibers directed forward, traversing a dark mass of large size, the *nucleus ruber*, and passing on to end in the *interpeduncular space*.

The tegmentum is separated from the crusta by a pale band (not to be confused with degeneration); it is the *locus* or *substantia niger*. Behind it is a dark band—the *median ribbon of Reil*, or *median fillet*. In the foot of the peduncle the motor tracts are arranged as follows: The internal fifth comprises the voluntary fasciculus from the face or *face genicule;* the external fifth, the *fasciculus of Meynert;* the middle part to the *pyramidal tract* which contains all of the motor fibers passing to the *pons*, the medulla and the spinal cord.

Thus far all of the described tracts and nuclei have presented a normal appearance, but in the middle part of the foot of the left peduncle there is a distinctly pale median zone of degeneration in which a higher power lens shows no normal myeline sheaths. This degenerated area is bounded on the inner and outer sides by healthy zones and corresponds to the space occupied by the fibers of the pyramidal tract on their way from the cortex to the medulla.

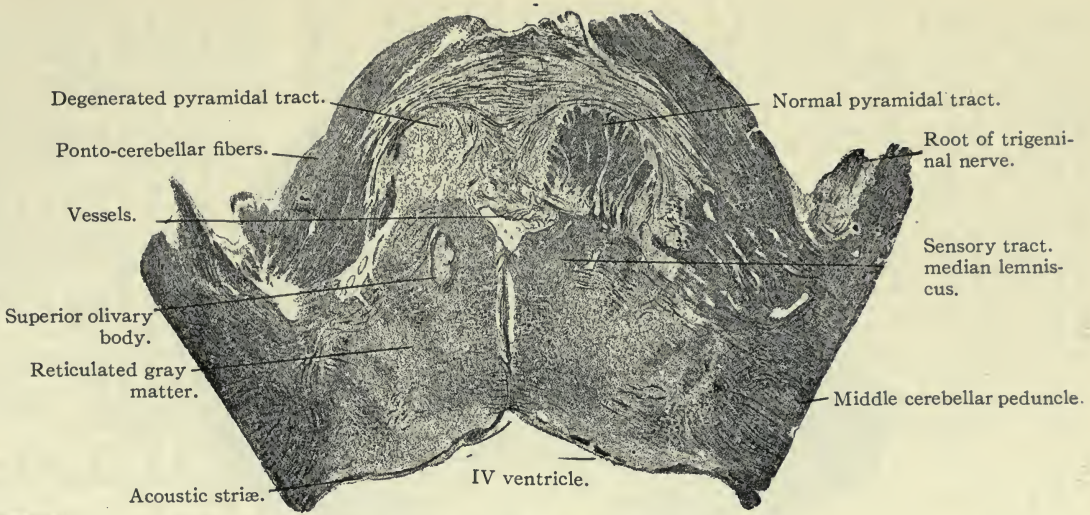


Fig. 84.—Annular protuberance. The Pons.

Stained by the method of Weigert-Pal. Magnified 3½ diameters.

The section passes through the middle portion of the pons, including, on the left side, the superior olivary body. Degeneration of the left pyramidal tract. The anterior part of the pons is above, the posterior part below.

The drawing (Fig. 84) is sharply limited on the right and left by two straight lines which correspond to cuts made by the knife in diminishing the extent of nervous tissue to be sectioned.

The tissue shown in the drawing includes the middle cerebellar peduncles which have been divided for the removal of the cerebellum. It thus forms an antero-posterior section of the *annular protuberance*, or *pons*, at its middle portion. The anterior rounded part corresponds to the foot, the posterior slightly flattened part to the floor of the fourth ventricle. In the foot are a number of thick fasciculi of fibers cut longitudinally, mixed up with little cells—the *pontine nuclei*. These fibers form a thick bundle on each side which are cut transversely: they are the *ponto-cerebellar fibers* and enter into the composition of the middle cerebellar peduncles and participate in the accessory motor paths. In the middle and a little behind these are two large transversely cut bundles of fibers—the *pyramidal tracts*, of which the left is degenerated.

Behind these, in the posterior part of the pons, there are various structures: fibers and masses of gray matter more or less rich in cells (nuclei of the cranial nerves). The principal of the structures are as follows: the *median ribbon of Reil* on each side of the median line; the *posterior longitudinal fasciculus;* the *acoustic striæ* and the *arciform fibers* in the white substances; the *pontine olive* also called the *superior olive*, a little mass of gray matter placed at the anterior part of the anterior portion of the pons. It only shows to the left of the median line; the section being a little oblique does not pass through it on the right side.

In fine, the only lesion that is to be found in the section is the *degeneration of the pyramidal tract* of the left side following closely upon that seen in the last section.

Fig. 85 represents a section of the medulla at its middle part where it passes through the *olivary bodies*, flattened layers of gray substance having an undulating arrangement and bending so as to make a kind of horse-shoe, the opening in which is directed toward the median line, and a little posteriorly. These bodies, which attract immediate attention, facilitate the diagnosis of the organ and approximately indicate the height at which the section was cut. Between the olives and extending backward almost to the floor of the fourth ventricle is a layer of transversely cut fibers, the *inter-olivary layer* or sensory tract (median tract of Reil). A little to the outer side of the sensory tract are the fibers of the *great hypoglossal* nerve, the XII

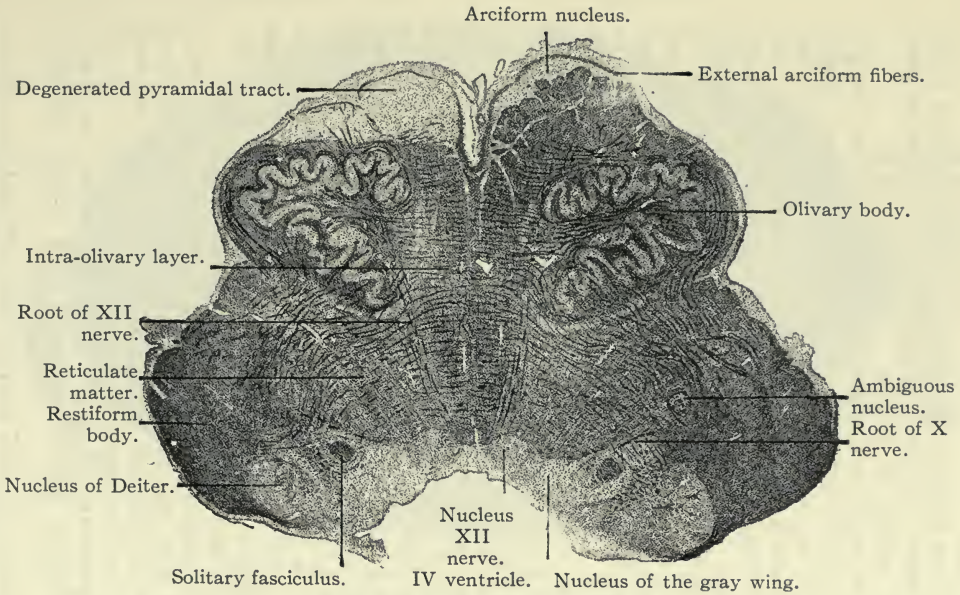


Fig. 85.—Section of the medulla.

Stained by the method of Weigert-Pal. Magnified 3½ diameters.

The section passes through the middle part of the medulla: olivary region. Degeneration of the left pyramidal tract. Above the anterior, below the posterior part.

cranial nerve, which arises from a nucleus situated immediately below the floor of the bulb, near the middle line, to pass out a little in front and outside of the pyramidal tract, which makes a slight projection in front of the section on each side of the median line.

At the inferior angle of the section is a thick layer of transversely cut fibers: the *restiform body*, with, at its internal part, the *vestibular nucleus of Deiters*.

Between the nucleus of Deiters and the hypoglossal nucleus there is an isolated bundle: the *solitary fasciculus*, a sensory root of mixed nerves, notably of the tenth pair, or pneumogastrics, of which the *posterior nucleus*, *nucleus of the gray wing* may be seen under the floor of the fourth ventricle, immediately outside of the nucleus of the twelfth nerve, and the *anterior nucleus*, or *ambiguous nucleus* at the middle of the reticulated structure of the bulb. Some oblique fibers directed forward and outward can be distinguished between the two nuclei of the tenth nerve: they are the *radicular fibers of the pneumogastric*, which are on their way to emerge at some distance outside of and behind the swelling of the olivary body.

Finally, in front and above in the drawing are the two pyramids containing the pyramidal tracts. On the left the pyramid is somewhat diminished in size, and is of a gray color; degeneration of the pyramidal tract on the left side, following upon those described above. In the right pyramid there is a fine band of gray matter bounded anteriorly and internally by the pyramidal tract, which should not be mistaken for degeneration. It is a special gray formation: the *arciform nucleus of the bulb*, in which the cells can be seen with a higher lens.

The three sections which follow are of the spinal cord and have as common characteristics an ovoid shape, central gray matter arranged in the form of a letter H, and surrounding white matter almost entirely made up of transversely cut fibers.

As representation of spinal-cord structure, the cervical spinal cord (Fig. 86) will first be considered. The section is divided into symmetrical halves, in front by a broad and deep fissure, reaching downward to the transverse branch of the H, into which penetrate the meninges and the vessels, and behind by an incomplete fissure continued by a narrow septum of neuroglia.

On each side of the cord the gray and white matter are clearly differentiated. The gray matter is expanded into large masses anteriorly, and contains large multipolar nerve cells easily visible under a low-power lens: the *radicular cells*. The posterior horn is slender and reaches to the periphery of the section where it

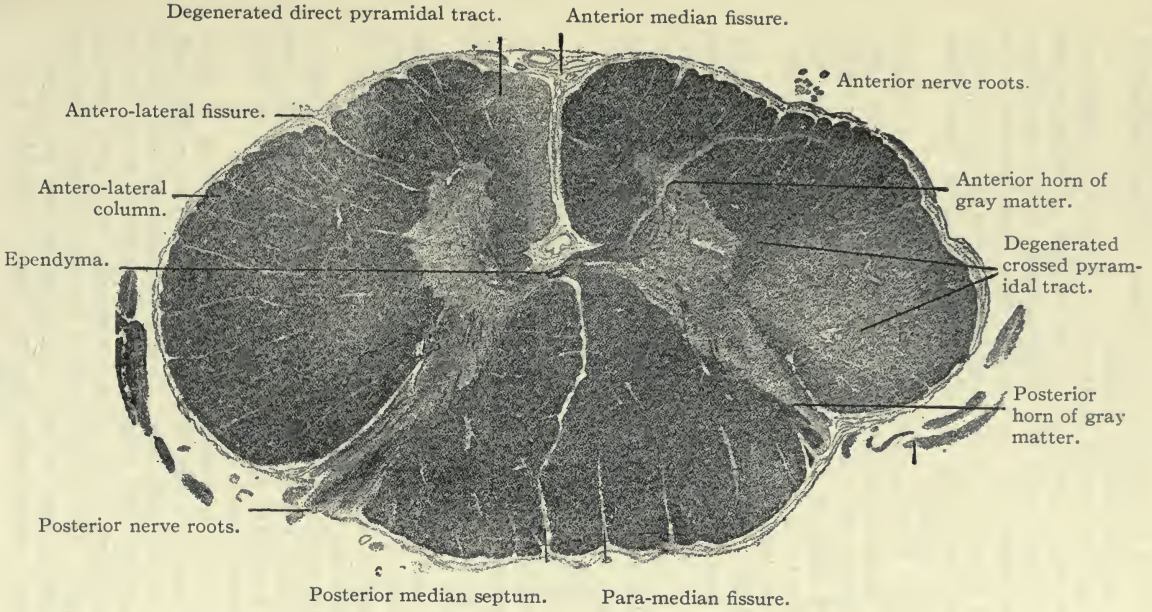


Fig. 86.—Cervical spinal cord.

Stained by the method of Weigert-Pal. Magnified 10 diameters.

Right hemiplegia. The section passes through the cervical enlargement—fifth cervical segment—and shows the degeneration of the direct pyramidal tract on the left, and of the crossed pyramidal tract on the right.

is continued into the posterior nerve root; at the extremity of these horns are the *zones of Lissauer.*

The two halves of gray matter are united by a transverse branch, the *gray commissure,* in the middle of which is the *central canal,* lined with the cuboidal cells of the *ependyma.* The peculiar shape of the anterior horn, the presence of a little lateral point at the base of each (lateral horn), together with the shape and large size of the section enable the cervical cord to be recognized.

On each side of the anterior surface, at some distance outside of the *deep* anterior median fissure, there is a slight and indistinct depression: the *anterior collateral fissure,* through which the anterior radicular fibers—anterior nerve roots—pass out. The white matter is thus divided into three columns: anterior, lateral and posterior.

The *posterior columns* are composed entirely of posterior roots: the anterior and lateral are combined under the name *antero-lateral* columns, and include all the remainder of the cord. The posterior column is further divided into two portions, indistinctly separated in sections of normal tissue, the differentiation being based chiefly upon the study of its degeneration: an *internal fasciculus,* the *column of Goll* and an *external fasciculus,* the *column of Burdach.*

In the *antero-lateral column,* in addition to the association fibers that connect at different levels, there are the following:

1. On each side of the anterior median fissure, a narrow band corresponding to the *direct pyramidal tract.*

2. In the remainder of the antero-lateral column there are three important fasciculi, the *crossed pyramidal tract,* directly against the gray matter, the *direct cerebellar tract,* and a *fasciculus of Gowers* thrust out toward the periphery.

The cord is surrounded by a layer of pia mater that contains vessels not only belonging to the membrane itself but also those that penetrate into the substance of the cord to form its fibro-vascular axes.

Alongside of and external to the posterior horn of gray matter, on the right side, is a large decolorized zone that does not appear on the other side. It is a degenerative lesion which evidently involves the entire *crossed pyramidal tract,* limited solely to the fibers of the crossed pyramidal tract and showing its topography. In the other half of the cord there is a narrow pale degenerated zone in front and along side of the anterior median fissure, representing the left *direct pyramidal tract.*

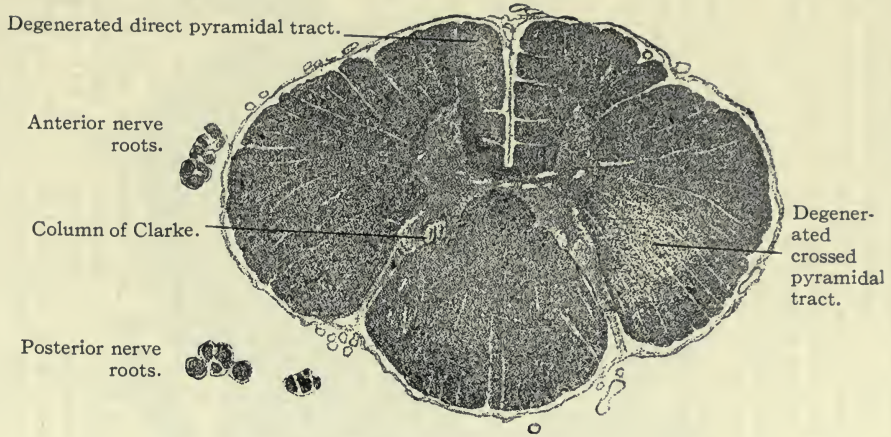


Fig. 87.—Dorsal spinal cord.

Stained by the method of Weigert-Pal. Magnified 10 diameters.

Right hemiplegia. The section passes through the fourth dorsal segment, and shows the degeneration of the direct pyramidal tract on the left, and of the crossed pyramidal tract on the right.

This degeneration, crossed on the right and direct on the left, is in accord with what we have observed at higher altitudes: peduncles, pons and bulb. It enables one to demonstrate the decussation of the fibers of the pyramidal tract which takes place at the bulb, a few fibers remaining in the spinal cord on the homolateral side (direct pyramidal tract), but the greater part passing to the other side (crossed pyramidal tract).

Fig. 87 shows a section of the *dorsal cord*, which can be recognized by its relatively small size, the narrow and attenuated anterior and posterior horns, and above all by the presence of an oval mass of gray matter: the *column of Clark*, characteristic of the dorsal cord, on the internal surface of the posterior horn, in the neighborhood of the gray commissure.

The same degenerated tracts are found here as in the cervical cord; to the left in the anterior column, the direct pyramidal tract: on the right, in the lateral column, the crossed pyramidal tract, the shape and size of which are a little different from those seen in the other sections.

Fig. 88 represents a section of the *lumbar cord* in its middle part. It is recognized by the swollen appearance of the anterior horns of the gray matter, rounded and a little projected externally, by the absence of the lateral horn, and the irregularly circular shape of the section

There is no longer degeneration of the left anterior column because the direct pyramidal tract disappears at the inferior part of the dorsal cord. But the degeneration in the lateral bundle can still be distinctly seen on the right side in the crossed pyramidal tract.

Résumé.—Descending degeneration of the motor nerves, affecting the pyramidal tract in its entire length, can be traced through different attitudes of the cerebrospinal axis. It is the only lesion observed in the sections. The case was one of softening in the motor area of Rolando in the left cerebral hemisphere with descending degeneration of the pyramidal fibers, which in the cord are found partly on the left side, but in greater part on the right side, because of the decussation of the greater part of the pyramidal tracts in the medulla. Thus is explained why lesions of the left hemisphere (region of Rolando) occasion motor symptoms (hemiplegia) of the right side of the body.

Résumé.—*Hemiplegia following a lesion of the left hemisphere.*

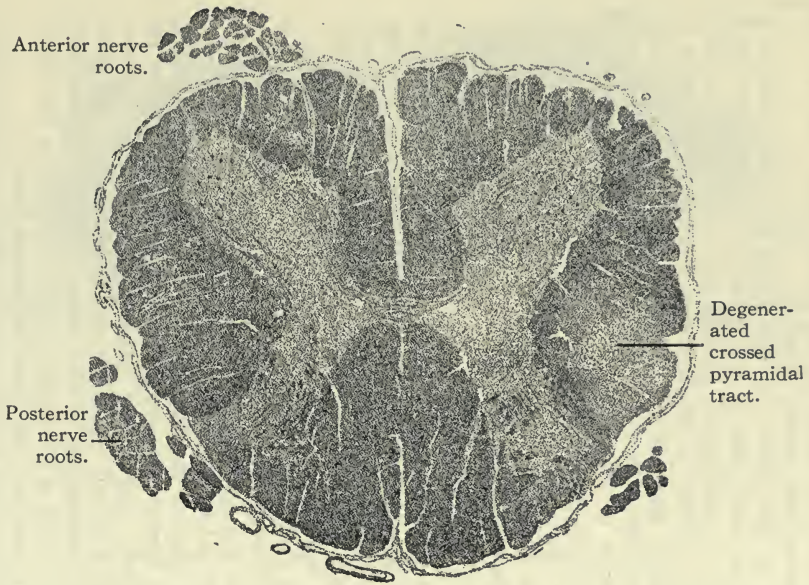


Fig. 88.—Lumbar spinal cord.

Stained by the method of Weigert-Pal. Magnified 10 diameters.

Right hemiplegia. The section passes through the fifth lumbar segment and shows degeneration of the crossed pyramidal tract on the right. There is no longer any direct pyramidal tract.

Diagnosis of the Organ.—The cervical spinal cord can be easily recognized by its oval and laterally extended shape, the size of the anterior cornua, their quadrilateral form which depends upon the presence of the lateral horn, and by the depth of the anterior median fissure.

Diagnosis of the Lesion.—That which at once strikes the observer is the small size of the posterior horns of the gray matter which are atrophied, though not degenerated in their entire extent. Areas of healthy dark-colored fibers separate the degenerated pale areas. The most degenerated portions on each side form a hand corresponding to the external part of the columns of Burdach. This little tract bifurcates at its postero-external part in the form of a fork whose two branches surround an almost normal zone, the external band of Pierret. The more interior part of the posterior column, or column of Goll, is a great deal less degenerated than the column of Burdoch. The posterior nerve roots, cut transversely or longitudinally are completely degenerated. Their entrance into the cord, the zone of Lissauer, is equally affected and appears bleached. The external fasciculus being an ascending prolongation of the posterior nerve roots, having penetrated lower down, the lesion passes through the posterior roots in their intramedullary as in their extramedullary course (*posterior radiculitis*).

The zones that remain intact correspond to the territory of endogenous fibers, i. e., to those fibers that have their cells of origin in the gray substance of the spinal cord. These endogenous zones consist at first of a kind of blackish arch situated immediately behind the gray commissure and extending along the posterior horns—the *cornu-commissural zone.* Between the branches of the fork of the external fasciculus the postero-external field is found: equally a territory of endogenous fibers.

Thus the distribution of the endogenous zones, relatively simple at this level of the cervical cord, is limited to the cornu-commissural zone and the postero-external fields.

The meninges in this case are slightly adherent to the sclerosed zones in the neighborhood of the posterior columns. Other methods of staining—hematoxylon and eosin—would show a slight infiltration of inflammatory cells in the meninges.

Résumé.—Tabes dorsalis: that is to say, of degeneration with sclerosis of the nerve roots and posterior columns. The disease is not very far advanced, as the degenerative process still respects the areas of the endogenous fibers.

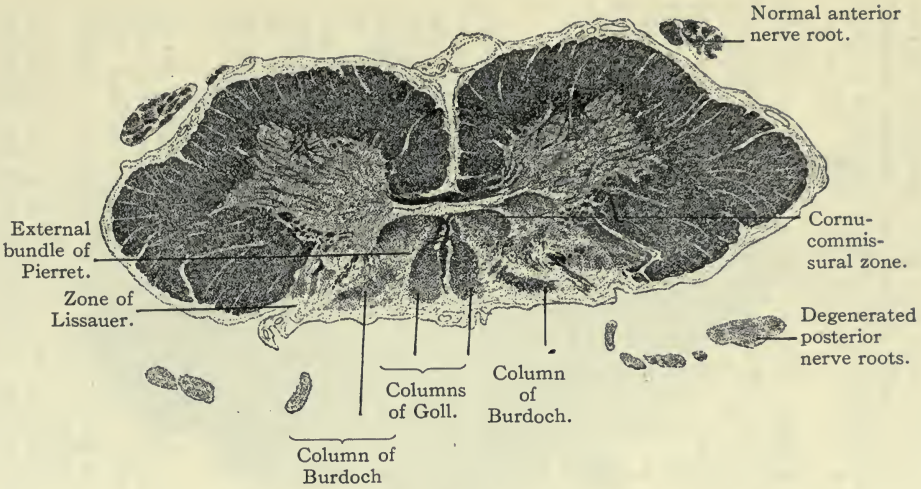


Fig. 89.—Tabes dorsalis.

Stained by the method of Weigert-Pal. Magnified 9 diameters.

Section of the cervical spinal cord of a case of tabes in the period of ataxia. The degeneration of the posterior columns is limited to the column of Pierret, the zone of Lissauer, and to the posterior nerve roots. The integrity of the columns of Goll, the postero-external zones and cornu-commissural zones is to be noted.

Diagnosis of the Organ.—The oval shape of the section, in which, in spite of the lesions, the gray medullary matter with its large triangular anterior horn and slender posterior horn, reaching to the periphery, can be seen, shows it to be a section of the spinal cord at the altitude of the cervical enlargement.

Diagnosis of the Lesion.—One is struck by the extent and asymmetry of the decolorized zones which are irregularly distributed throughout the section. These pale patches, of which three are situated in the heart of the antero-lateral and posterior columns, are shaped like wedges forcing themselves into the periphery of the medullary mass. Under a higher magnification, these pale areas do not show any traces of myeline sheaths, but are entirely degenerated. The distribution of the patches is devoid of system: the degenerated zones do not correspond with either tracts of nerve fibers (direct or crossed pyramidal) or even with the gray matter.

The patch to the right, for example, affects the entire antero-lateral column except its anterior angle and some few fibers of the direct pyramidal. It also equally affects the gray matter, but seems to spare the nerve cells which show with great distinctness as brown upon the white background. It is impossible any longer to recognize the network of fibers surrounding the nerve cells in the anterior horn. Toward the inner side and in front the patch of sclerosis encroaches a little at the bottom of the anterior median fissure, upon the anterior column of the opposite side of the cord. There is no invasion of the posterior column except the part immediately contiguous to the gray commissure.

It is an old lesion—*neurogliar sclerosis*—of which the details ought to be shown by elective stains. If the lesion were fresh sclerotic patches, when stained by the Marchi method with osmic acid, fatty vesicles enclosed in the interior of macrophages (compound granular cells should show).

Résumé.—The presence of the patches of sclerosed degenerated tissue, without system, occurring in both the white and gray matter, make the diagnosis of *disseminated sclerosis.*

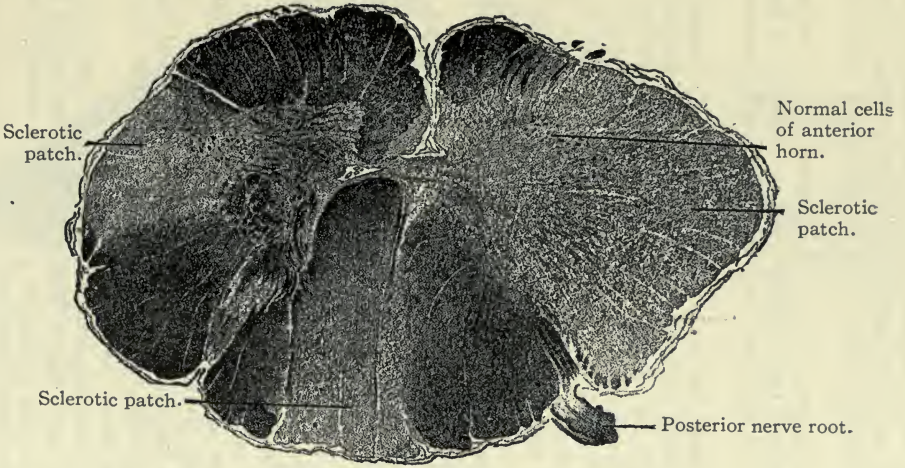


Fig. 90.—Disseminated sclerosis.

Stained by the method of Weigert-Pal.

Section through the cervical spinal cord of a case of disseminated sclerosis. The sclerotic areas are disseminated without system and affect both white and gray matter.

Diagnosis of the Organ.—It is possible to recognize the cervical cord because of the arrangement of the gray matter in the form of a letter H, with two large quadrilateral anterior horns, the deep anterior median fissure, and the elongated transverse diameter.

Diagnosis of the Lesion.—The cord flattened antero-posteriorly is more elongated than normal. In its center is a long transverse cavity which gives the section a pathognomonic appearance.

1. The central canal has an asymmetrical stretched appearance, the part toward the right side being the most disturbed. The cavity is empty and its walls are not lined with the cylindrico-cubical endothelium of the ependymal canal which so much resembles epithelium. The cavity is surrounded by a quite thick band of structureless tissue that has not taken the Weigert stain and which under a higher magnification presents a finely granular or a vaguely fibrillar appearance. It is a special tissue, the neuroglia, the demonstration of which requires special staining such as that of Lhermitte.

The condition is *glioma* or a *gliosis* of the spinal cord, of which the center has softened and given origin to a cavity. This gliosis has very precise limits: in front, the anterior white commissure composed of horizontal fibers, behind the posterior columns, laterally the internal substance of the gray matter where it penetrates a little into the posterior and sometimes also into the anterior horn.

In the clinic this condition may give rise to muscular atrophy.

2. Central gliosis of the lateral columns, with degeneration of the two crossed pyramidal tracts: a degeneration that presents itself in the form of a transversely elongated band following the flattening of the cord after collapse of its central cavity, may occur as an accessory lesion.

Such pyramidal tract degeneration is due to the interruption of the fibers at a point above that at which the section has been made, by a cavity analogous to but more extended than that which we have been studying.

Résumé.—The transverse slit, the gliosis which surrounds it and the absence of an ependymal epithelium lining the cavity permit the diagnosis of *syringomyelia.* The only condition that can be confused with it is hydromyelia which is a dilatation of the central ependymal canal with modified but recognizable ependyma, and without neuroglia new formation.

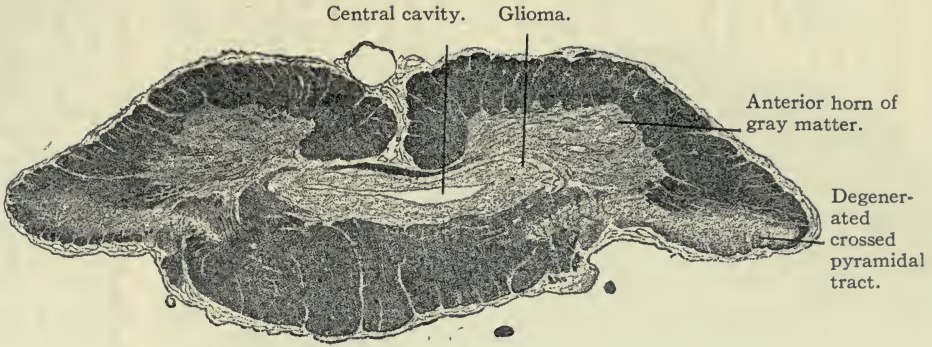


Fig. 91.—Syringomyelia.

Stained by the method of Weigert-Pal. Magnified 9 diameters.

Section of the cervical spinal cord in a case of syringomyelia. It shows: Central gliosis excavated to form a cavity; secondary degeneration of the crossed pyramidal tracts, explaining the clinical spasmodic paraplegia; the relative integrity of the other columns of white matter and anterior horns, and the extension of the lesion into the posterior horns.

Diagnosis of the Organ.—It is a section of the lumbar cord as can easily be recognized by the globular shape of the anterior horn and the absence of a lateral horn.

Diagnosis of the Lesion.—Under a low-power magnification a number of distinct small dark points can be seen in the gray matter of the anterior and posterior horns. These are the ganglionic nerve cells. In the white matter there is a fine stippling in the form of lines radiating from the periphery to the gray matter.

Under a higher power lens, small round cells—embryonal cells or lymphocytes—can be seen disseminated irregularly, or united to form small inflammatory nodules in the gray matter. The larger of these are not centered about any visible element, but the smaller can be seen to surround vessels or more or less altered ganglionic nerve cells. This infiltration, particularly abundant in the anterior horn, encroaches a little upon the base of the posterior also, and occurs in the form of fine lines in the vascular connective-tissue trabeculæ of the white matter.

The nerve cells of the anterior horn (Fig. 92, B) show atrophy which explains the palsy and muscular atrophy observed in the clinic. These cells, very much diminished in number, are not arranged in groups as in the normal condition. Some still show large nuclei with nucleoli and protoplasmic granules. But the greater number are much changed through the disappearance of their protoplasmic prolongations, the rounded shape of the cell bodies and the excentric position of the nuclei which may be strongly colored or have disappeared through fragmentation of the protoplasm.

Immediately about the nerve cells the lymphocytes seem to encroach upon the protoplasm and even to penetrate into the cell to devour it: a form of phagocytosis called *neuronophagia*, much discussed.

The vessels, apart from the perivascular infiltration, the connective tissue and the meninges show nothing in particular.

The triangular mass of cells in the center of the section is a proliferation of the ependyma (ependymitis).

Résumé.—It is an acute inflammatory lesion chiefly affecting the gray matter of the anterior horns of the lumbar cord, but extending equally into the white matter along the vascular connective tissue axes. It results in the destruction of the motor nerve cells: *poliomyelitis anterior acute.*

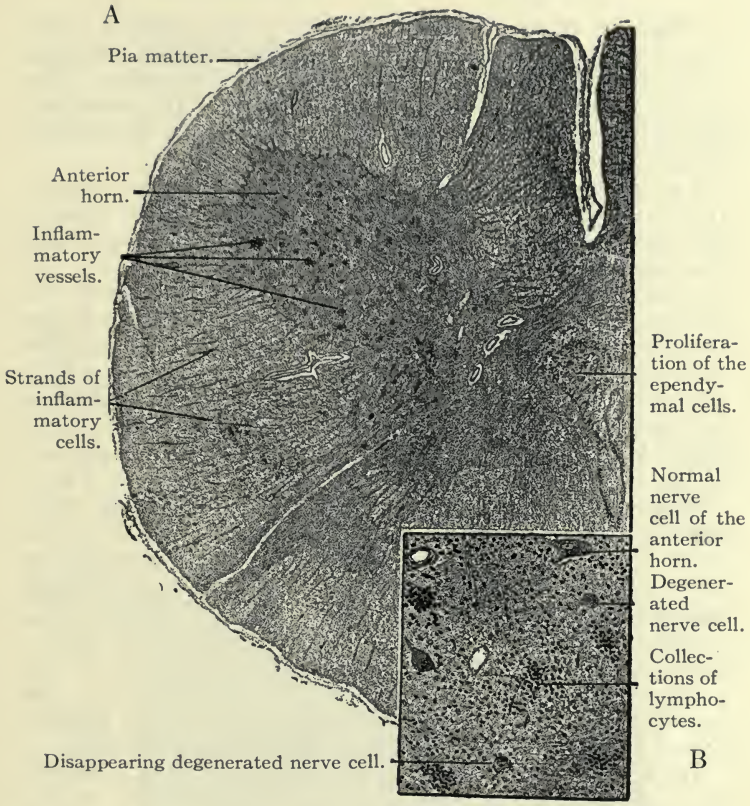


Fig. 92.—Acute anterior poliomyelitis. Section of the lumbar spinal cord.

Stained with hematoxylon and eosin.

From a young soldier dying of epidemic acute anterior poliomyelitis with bulbar lesions.

A.—*Shows numerous infiltrations in the anterior and posterior horns of the gray matter, and fine lines of inflammatory infiltration in the white matter, magnified* 15 *diameters.*

B.—*Shows the progressive disappearance of the nerve cells of the anterior horn, magnified* 100 *diameters.*

Diagnosis of the Organ.—A section of the cerebral cortex showing a characteristic festooned line which enables the organ to be recognized as brain. The size of the convolutions shows the section to be from the cerebrum, as those of the cerebellum are not only much smaller but branched in an arborescent fashion.

Fig. 93 shows one of the fissures or sulci separating two contiguous convolutions. The entire depth of the fissure is occupied by a dark-colored band representing the pia matter, in this case much thicker than normal.

Passing through the gray matter of the cortex from the surface downward, it is possible to recognize numerous layers of cells: (1) *The outer molecular layer*, composed of undifferentiated round or oval cells, with central nuclei; (2) *the middle pyramidal layer*, composed of triangular cells, with numerous prolongations (prolongations of Deiters) and a basal nucleus with a large nucleolus; (3) *large pyramidal cell layer*, composed of large cells (giant cells of Betz) and polymorphous cells.

Diagnosis of the Lesion.—The pia mater forms a thick membrane in which there is a fine meshwork of fibrin. In the interior of the meshes of the middle layer there are a great number of larger and smaller cells, polymorphonuclears and large and small mononuclears, betraying an acute inflammatory lesion.

Their protoplasm stains strongly with eosin (acidophilic). Their nuclei stain uniformly (pycnosis). In a word, it is a purulent exudate which covers the external surface of the convolutions and penetrates in the least folds of the cerebral fissure. The vessels are abundant, dilated and congested.

With the aid of a special selective stain (toluidin blue, Gram's etc.) the presence of the causative microörganism, in this case the pneumococcus, can be demonstrated.

In a section stained simply with hematoxylin and eosin it is difficult to see the changes in the cortical nerve cells (lesions of atrophy, which show blue by Nisl's method of staining).

Résumé.—Acute inflammation of the pia mater, *purulent leptomeningitis*, of which it is difficult to find the cause. The further study of the specimen by methods of staining designed to demonstrate bacteria, and information obtained from the autopsy are needed to complete the diagnosis, and permit one to say as here that it was caused by the pneumococcus.

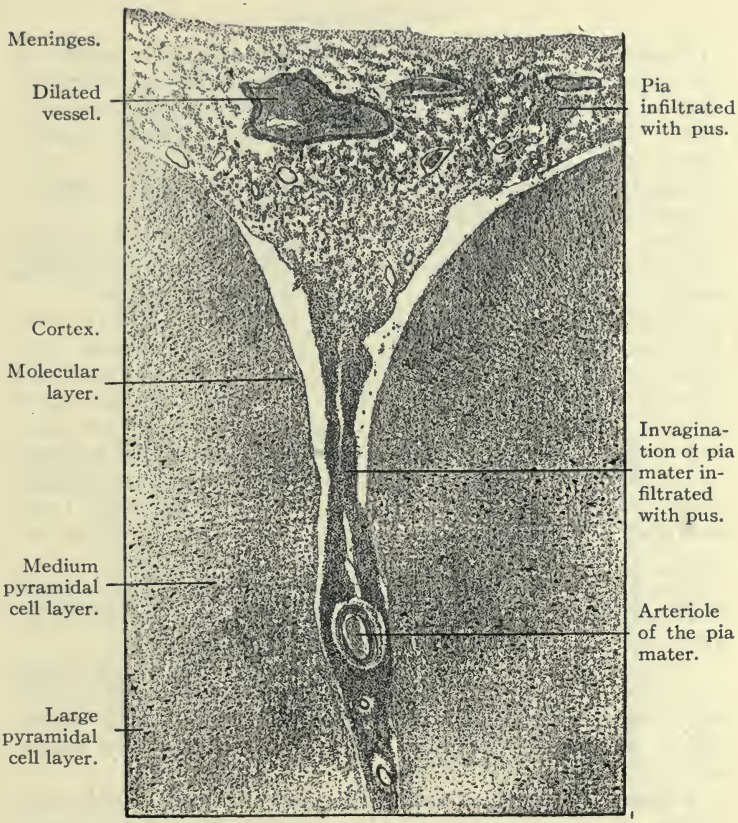


Fig. 93.—Purulent cerebral meningitis.

Stained with hematoxylon and eosin. Magnified 30 diameters.

Purulent leptomeningitis in an old man aged eighty years. The autopsy showed it to be secondary to pneumonia with empyema. The drawing shows a cortical cerebral sulcus into which the pia mater, infiltrated with pus dips down between the convolutions.

EPIDEMIC CEREBROSPINAL MENINGITIS.

Spinal Meningitis.

Diagnosis of the Organ.—It is easy to recognize a section of the spinal cord, in which the gray matter stands out distinctly upon a pale background. The anterior horn of gray matter is small, the posterior slender and the presence of Clark's column shows that it is of the dorsal cord.

Diagnosis of the Lesion.—The cord is surrounded by a dark-colored sheath, the pia mater greatly thickened.

Even with a low-power lens it is possible to see a fine dark-colored stippling, very dense and with numerous dilated vessels, which are sufficient to make the diagnosis of meningitis.

A higher power magnification (Fig. 94, B) shows an extensive infiltration of inflammatory cells; polymorphonuclears and mononuclears in a state of granular and fatty change, nuclei without chromatic details forming a homogeneous mass deeply staining with the hematoxylon (pycnosis), and protoplasm with fine fatty vacuoles. A little further advance of the process, and the nuclei disappear and the cells become homogeneous masses. Here and there little dark granules represent fragments of nuclei or of cell protoplasm (cell necrosis, globules of pus).

The inflammatory cells are disseminated without order and without special grouping in fine meshes of fibrin, similar to those seen in the lung.

In the remainder of the section, that is to say, in the spinal cord itself, nothing further abnormal is to be seen, or at most only fine lines of cellular infiltration along the connective-tissue septæ, which penetrate from the periphery toward the center as radii.

Résumé—One makes the diagnosis of purulent spinal meningitis, on account of the great number of degenerating polymorphonuclears. Selective bacterial stains (toluidin blue or Gram's method) should reveal the presence of encapsulated diplococci—*meningococci*—sometimes inclosed in the interior of the mononuclear cells.

It is a case of *epidemic cerebrospinal meningitis.*

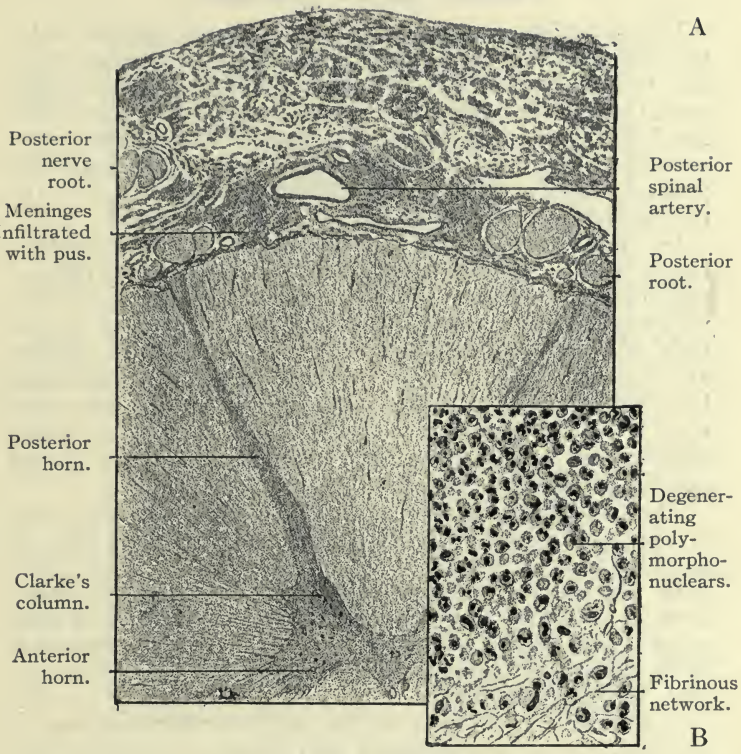


Fig. 94.—Cerebrospinal meningitis.

Stained with hematoxylon and eosin.

Epidemic cerebrospinal meningitis in a young soldier aged twenty-one years.

A.—*Shows the dorsal spinal cord with the posterior meninges infiltrated with pus, magnified* 12 *diameters.*

B.—*Shows a part of the meninges with polymorphonuclears and mononuclears in a state of degeneration.*

PSAMMOMA.

Calcified Fibroma of the Meninges.

Upon examining the section under a low-power magnification, the same characteristic appearance will be seen everywhere, due to the presence of a multitude of small, rounded, transparent, refracting bodies of variable size, separated one from another by a tissue which constitutes the stroma of the tumor. A medium-power magnification enables one to recognize this variety of tumor which neither resembles any other, nor any normal tissue of the body.

In studying it let attention be paid to the small rounded bodies, and to the vascular connective tissue between them.

I. The rounded masses are calcareous or hyaline and of a very peculiar appearance. The largest, structureless, without cells or nuclei, are formed of a series of concentric lamellæ, and show at the center or periphery bluish patches caused by the affinity of the calcareous matter for the hematoxylon stain. Connective-tissue cells gather about the bodies. Other smaller, but similar bodies are without calcification, though equally homogeneous and structureless: *hyaline.*

The very smallest of the bodies are formed of concentrically arranged connective-tissue cells compressed like the coats of an onion.

II. The connective-tissue stroma which separates the bodies from one another is young and is characterized by a great number of fibroblasts and relatively few fibers. The appearance is the same as is found in connective-tissue tumors—fibroma or sarcoma (fibrosarcoma).

The vessels of the tumor are not abundant, and are either of the adult type or are capillaries with a simple endothelial wall.

The concentric calcareous or hyaline bodies give the tissue of the tumor a certain degree of friability, which explains the rough and frayed appearance of a cut surface.

The bodies seem to be formed from the endothelial lining of the vessels whose cells proliferate either inside or outside, giving rise at first to buds, then to concentric bodies, and then charge themselves with calcareous salts. This origin can be completely verified in some of the tumors.

Hence the name calcareous fibroma or *psammoma* given to the tumor.

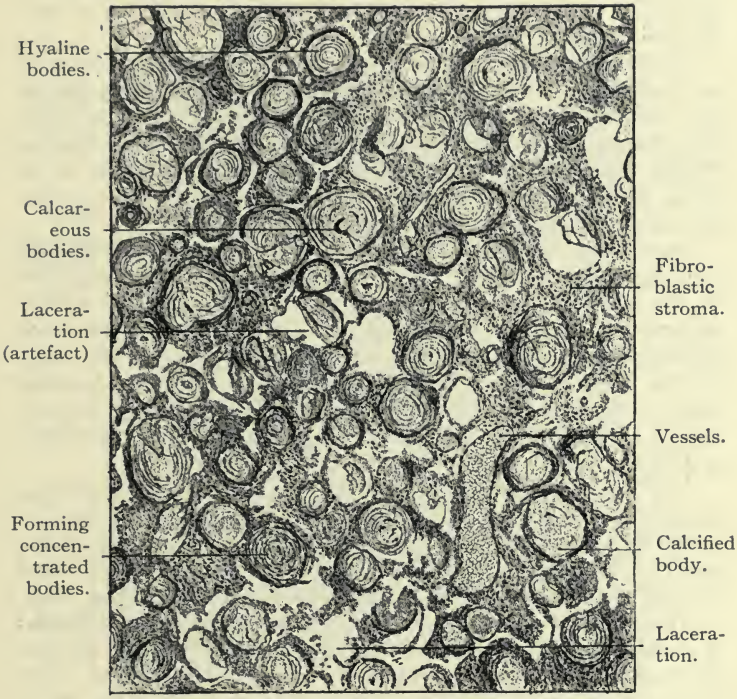


Fig. 95.—Psammoma.

Stained with hematoxylon and eosin. Magnified 80 diameters.

A tumor of characteristic appearance and sandy consistence not infrequently observed in the meninges either of the brain or spinal cord, essentially benign, and sometimes first discovered at autopsy, not having, as in this case, provoked any symptoms during life. It is easily enucleable.

Large, fairly regular rounded spaces, filled with a homogeneous material colored red with eosin, giving the appearance of a glandular organ formed of separate acini separated by a connective-tissue stroma.

Under a medium magnification each of the acini is found to be limited by a fine bluish stippling, the nuclei of epithelial cells with indistinct protoplasm. In fragments of tissue taken at autopsy it is difficult to distinguish the finer histological details (principal cells and colloidal cells). Both seem to be of the same type and composed of granular protoplasm containing in the center a deeply colored nucleus.

The content of the acini or vesicles is formed of an amorphous homogeneous substance called colloid, retracted at some points in the form of vacuoles (artefacts of fixation). The colloid substance, ordinarily red, and frankly acidophilic, at other times appears purple (amphophilic), or even blue (basophilic), these diverse tinctorial affinities corresponding to different chemical states. Sometimes the colloid has an appearance as if in palisades, or is marked by numerous parallel fissures (artefacts of preparation).

The slight variations in the size of the vesicles is due to tangential or central sectioning.

Between the acini is a connective tissue, fairly dense in the adults, containing numerous blood and lymph vessels, and masses of undifferentiated round cells: masses of young acini.

The characteristic appearance of the acini with their colloidal contents, and the absence of efferent ducts enables one at once to recognize a gland of internal secretion: the *thyroid*. The relative equality in the size of the vesicles and the slight development of the connective tissue indicate a normal thyroid and exclude all thought of a goiter.

Differential Diagnosis.—Certain of the histological appearances may lead to confusion, and it is possible to mistake the section for:

1. Edematous lung, with the capillaries between the alveoli dilated. The epithelial cells desquamated into the edematous fluid filling the alveoli and the broncho-vascular axes should be searched for throughout the section.

2. Cavernous angioma (of the liver, for example), formed of cavities filled with blood. Under a high-power magnification the red corpuscles, the endothelial cells of the walls and the hepatic tissue in the immediate vicinity ought be found.

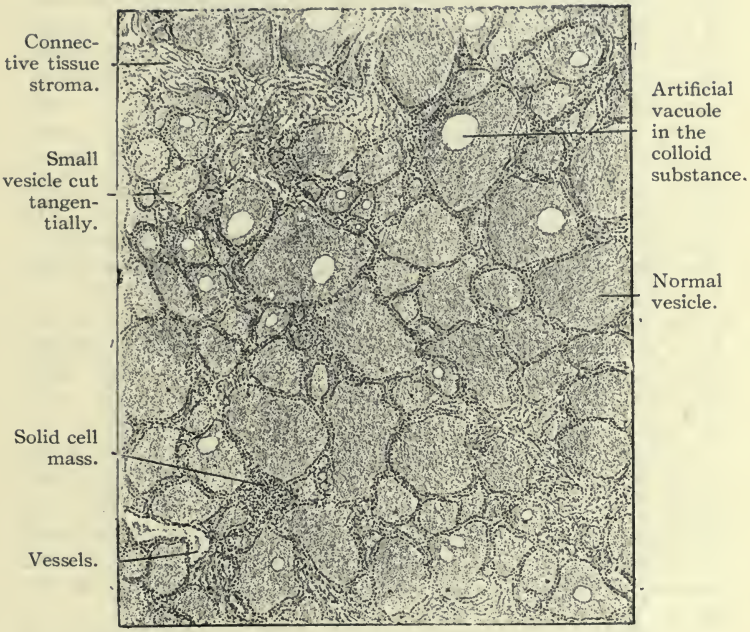


Fig. 96.—Normal thyroid body.

Stained with hematoxylon and eosin. Magnified 50 diameters.

The relatively equal size of the thyroid acini is to be noticed. Note also the occasional presence of solid masses of cells which are to be referred either to young, not yet fully formed acini, or to acini in a condition of retrogression.

GOITER WITH IRREGULAR VESICLES.

Colloid Goiter.

Diagnosis of the Organ.—It is easy to recognize the thyroid body through the characteristics already given. But that which strikes one as remarkable and may make him hesitate as to the nature of the organ is the astonishing disproportion in size between the different acini. If in the normal condition the acini are of uniform size, here, on the contrary, they are very different, some being enlarged to veritable cysts, even visible to the naked eye (cystic goiter). The more these morphological alterations affect the acini, the more their structure is modified. In proportion as they become distended, their epithelium becomes flattened—from cuboidal to flat—so great may be the distention. At some points the walls seem to give way so that neighboring vesicles become confluent and thus the cysts are formed.

The colloid contents of the acini are but slightly altered. They are a little paler and a little less acidophilic as regards their staining, than in the normal section that preceded; they are, however, a little more fluid and the palisade-like striæ are less distinct.

Between the larger cysts are masses of little vesicles, more or less normal in appearance, of which a certain number are shown in the central part of the drawing. Sometimes the acini are rounded or polyhedral, sometimes drawn out and narrowed by reciprocal pressure. Finally, here and there are rounded masses of cells, without any central cavity, suggesting the appearance of the embryonal thyroid.

In other parts of the section there are occasional areas of hemorrhage, in which red blood cells infiltrate into the thyroid acini. There are both old and fresh hemorrhages, the last recognized by the presence of crystals of hematoidin and the absence of fresh blood corpuscles.

The stroma consists of loose connective tissue, small in amount and showing a tendency to sclerosis.

Résumé.—A goiter characterized by the irregularity of the acini and the presence of colloid cysts: a tendency to interstitial hemorrhage, whose occurrence corresponds to the clinical periods of rapid growth.

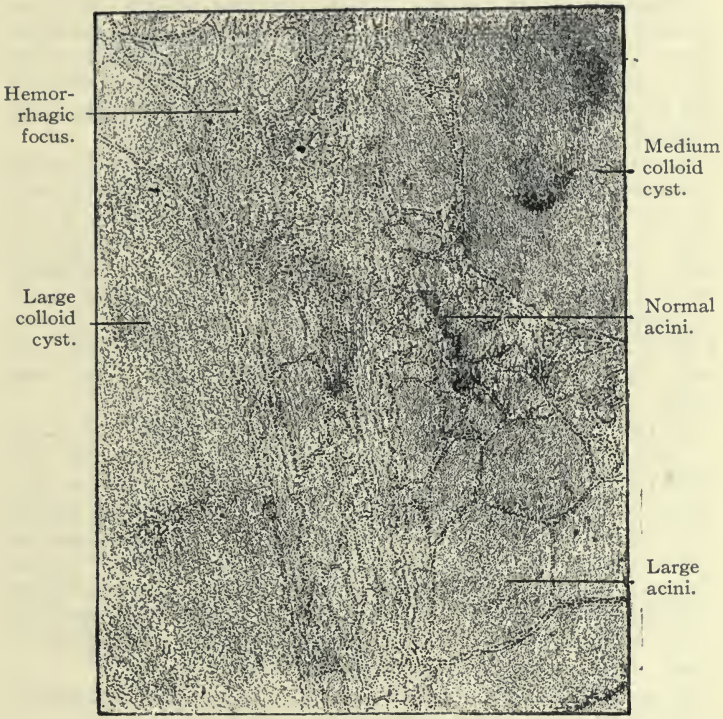


Fig. 97.—Colloid goiter.

Stained with hematoxylon and eosin. Magnified 50 diameters.

Unilateral colloid goiter of the size of a mandarin orange, taken from the neck of an old woman, at autopsy. Note the enormous disproportion in the size of the acini, the occasional large cysts and the occasional interstitial hemorrhages.

GOITER WITH SMALL ACINI.

Parenchymatous Goiter.

Diagnosis of the Organ.—This is somewhat difficult to make because the structure of the gland is so modified. However, in most cases it is easy to see that it is an organ of the glandular type with acini and without excretory ducts, which added to the fact that the acini contain colloid substance, enables the thyroid to be recognized.

Diagnosis of the Lesion.—In the upper part of the drawing the section shows a large number of little vesicles almost entirely of the same size, the greater number of which do not contain any of the colloid substance, and others of which contain very little. In other parts of the section they are closely pressed one against another. Between these glandular acini are dense cell masses or cords of a bluish color, and without a central lumen or cavity, which recall the appearance of the fetal thyroid, and which sometimes lead to the lesion being called *fetal goiter.*

In the lower part of the drawing the histological appearance is different. The acini become very few and more or less widely separated from one another by interstitial tissue which takes on a considerable development. The stroma, very palely stained, sometimes forms extensive areas, the structure of which can only be made out with a higher power lens. Sometimes it consists of a fibrillar connective tissue, with rare fixed cells, sometimes, on the contrary, of a homogeneous amorphous tissue of the hyaline type, or in still other cases of a field of pale rose color, suggesting edematous fluid.

Some of the destroyed acini seem to be no more than cells bunched together in the interior of the stroma.

Adult vessels and capillaries appear in the substance of the stroma, and sometimes there are foci of hemorrhage.

Résumé.—Goiter with tiny vesicles or tiny acini as contrasted with the form described just previously. This microscopic variety corresponds to the macroscopic type known as *parenchymatous goiter.* In this case the hypertrophy of the gland is due to the increase in the number and not to increase in the size of the acini.

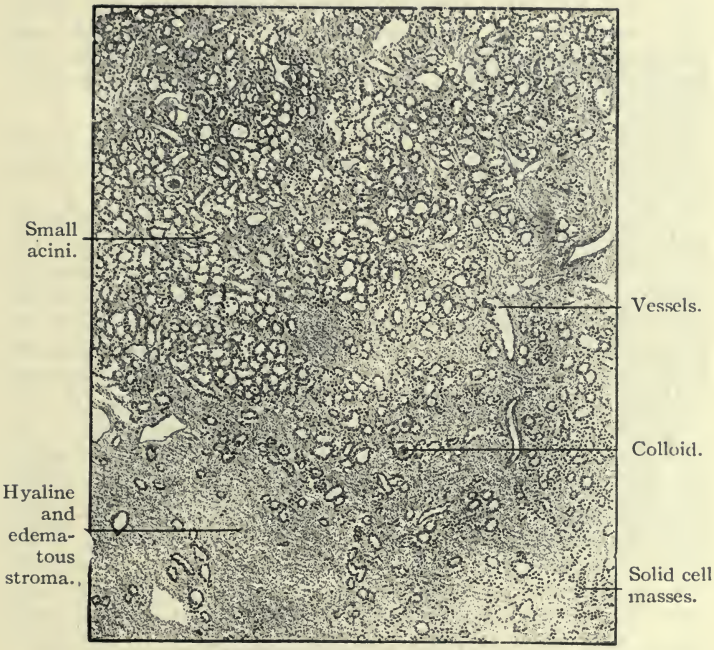


Fig. 98.—Parenchymatous goiter. (Goiter with small acini.)

Stained with hematoxylon and eosin. Magnified 50 diameters.

The tissue was removed at autopsy from the neck of an old woman. In the upper part of the drawing the goiter is characterized by the presence of a large number of small acini mostly empty of colloid; in the lower part the acini are dissociated by edema and hyaline degeneration of the stroma.

THE NORMAL ADRENAL BODY.

A histological section of the adrenal or suprarenal body made perpendicularly to the transverse axis, and presenting to the naked eye the characteristic elongated appearance, and under slight magnification two concentric layers of different staining intensity. These two layers correspond to the *cortex* and *medulla* of the adrenal body. The following details of histological structure make the diagnosis clear.

A. The Cortical Zone.—This is composed of three layers, recognizable under a low power, which passing from the surface to the center are:

1. *The Zona Glomerulosa.*—This is the most superficial layer, and lies immediately beneath the connective-tissue capsule. It is composed of cellular masses, scarcely acini, composed of cells with dark protoplasm and darker nuclei. This zone, easily enough recognizable in man, forms a dark line at the periphery of the section. Its cells are of an undifferentiated type, that is to say, their protoplasm is homogeneous and scarcely tinted by the eosin.

2. *The Zona Fasciculata,* which forms the greater part of the Fig. 99, B, is formed of parallel columns of cells between which the capillary vessels, easily recognized by the presence of red blood corpuscles, are in intimate contact with the cells. This layer is composed essentially to spongiocytes, or cells in the clear protoplasm of which is an extremely fine meshwork. This appearance is caused by the fact that the cells are filled with fat (neutral fat or lipoid) dissolved out by the usual histological reagents, with the resulting pale and reticulated appearance.

At the bottom of the drawing there are some cells of undifferentiated type with dark granular protoplasm.

3. *The Zona Reticularis.*—Here the spongiocytes completely disappear and the cells have an undifferentiated appearance, and granular protoplasm; they form an extensive network, in the meshes of which are numerous capillaries. Here and there are a few cells containing granular pigment. The zona reticularis is a particularly vascular layer.

The three layers of cells represent different stages in the development of the same cell, whence the variability in the thickness of the layers in different parts of the section, according as the gland is in a state of activity or repose.

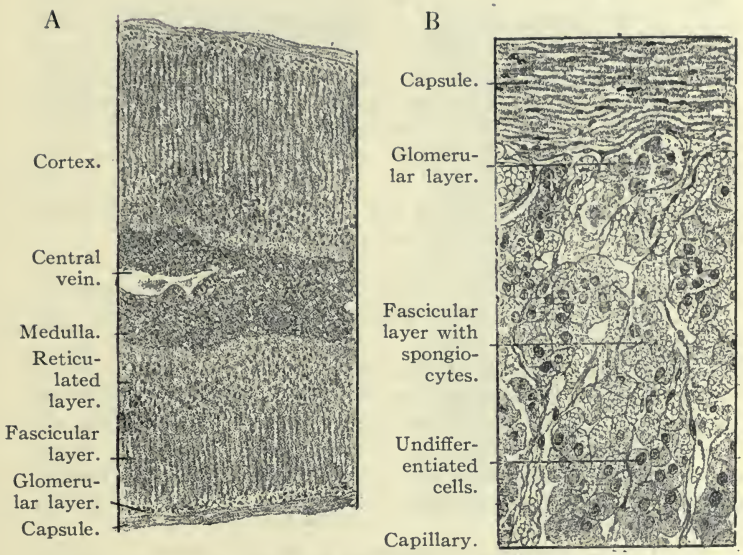


Fig. 99.—Normal adrenal body.

Stained with hematoxylon and eosin.

A.—*Transverse section of the entire adrenal gland magnified* 15 *diameters. The medullary substance occupies the center, the cortical substance being seen above and below.*

B.—*Glomerular and fasciculate layers seen under a magnification of* 200 *diameters. Above is the capsule of the organ; below the drawing continues with Fig.* 100, C.

B. The Medullary Zone.—This, forming the central part of the organ, differs from the preceding in its appearance and by staining a deep blue-violet color in sections stained with hematoxylon and eosin. It consists of an extensive epithelial network in which the elements are separated by capillary blood-vessels. It is broader than the zona reticularis with which it is continuous without distinct separations. The cells have a dark granular protoplasm that takes the hematoxylon strongly: *chromaffine cells*—so-called because they are distinctly browned by salts of chromic acid. The center of the medulla contains numerous vessels, of which the central veins are large and have thick walls.

Lastly it must be pointed out that the medullary substance contains rare and disseminated lymphoid collections.

The stroma of the gland is formed of fine collagenous fibrillæ and of young connective-tissue cells, the former rare except at the periphery of the organ where they are condensed to form its capsule.

Here and there at the periphery of the section, but at points not shown in the drawing, are small cellular masses composed of spongiocytes or undifferentiated cells well isolated from the remainder of the gland by surrounding connective tissue. Such epithelial islands occur in the greater number of adrenal glands, and when the number is not excessive have no pathological signification.

In the periglandular connective tissue it is always possible to find small groups of cells deeply stained with hematoxylon, and of the nervous type. These are ganglionic nerve cells belonging to the sympathetic nervous system.

Résumé.—The histological appearance of the suprarenal gland with its differentiated cell layers and the absence of any ducts is characteristic and easy to differentiate from other blood vascular glands.

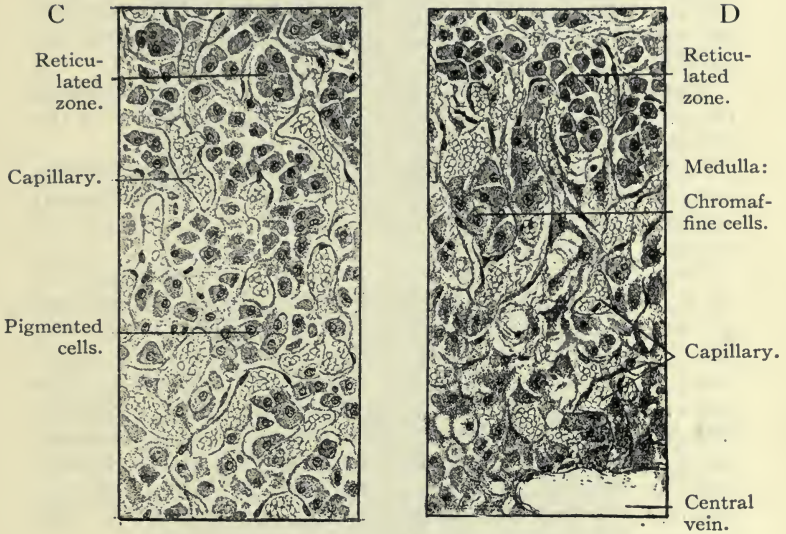


Fig. 100.—Normal adrenal gland.

Stained with hematoxylon and eosin. Magnified 200 diameters.

C.—*The zona reticularis below the zona fasciculata shown in the preceding drawing, with its cells in irregular anastomosing columns. Some of the cells have a finely granular protoplasm, others contain pigmentary granules.*

D.—*The medullary substance. It consists of columns of large cells whose protoplasm contains granules of adrenalin. These granules turn brown upon the application of salts of chromium and are therefore called chromaffine cells.*

HYPERPLASTIC ADRENAL.

Diagnosis of the Organ.—The section passes through all three layers of the adrenal. Above, beneath the connective-tissue capsule, the glomerular layer is scarcely visible; in the center is the zona fasciculata, below this is the zona radicularis, with its undifferentiated cells, and at the bottom is the medullary portion.

Diagnosis of the Lesion.—One is at once struck by the great thickness of the cortex, which is almost entirely formed of the spongiocytes.

Under a higher power lens it is possible to recognize the vacuolar or reticular character of the cells as in the normal adrenal, but the nuclei are larger and sometimes in a state of division.

Toward the right hand in the drawing, the arrangement of the fasciculi has the normal appearance; the cells are arranged in long parallel columns in a radiating manner. To the left, the cellular tubes have lost all regularity of direction, sometimes paralleling the surface of the organ, and tending to arrange themselves in a concentric fashion (*adenomatous hyperplasia*). The zona reticularis, at the right inferior portion of the drawing, is formed of undifferentiated cells in short columns. Finally here and there one sees some pigment cells.

On the exterior of the capsule, at points not shown here, are some large oval masses formed of spongiocytes.

The medulla, which is partly shown in the lower part of the drawing, does not show anything abnormal.

The connective-tissue stroma appears to be a little better developed than normal. One can see very distinctly the thin connective-tissue separations between the columns of cells. So far as the capillaries are concerned, especially in the fasciculus, they are scarcely visible, being compressed between the hypertrophied columns of cells.

Résumé.—The usual histological picture is modified by the great thickness of the cortex, especially in the zona fasciculata in which the spongiocytes are greatly augmented in number and in size. This appearance betrays a condition of hyperplasia and corresponds anatomically with general enlargement of the gland, which instead of weighing 4 to 6 grams may reach 10 grams. From the point of view of physiology it signifies excessive function. It is found in cases of Bright's disease and arteriosclerosis.

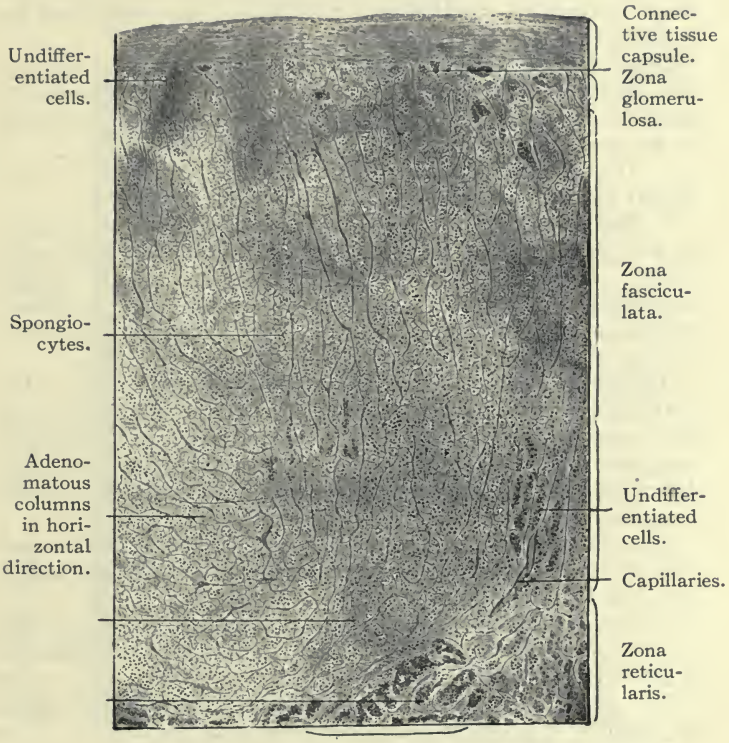


Fig. 101.—Hyperplastic adrenal gland.

Stained with hematoxylon and eosin. Magnified 100 diameters.

The cortical area is greatly thickened, especially in the zona fasciculata, which is almost entirely composed of spongiocytes. Toward the right of the figure the columns of cells are regularly arranged and parallel; toward the left they are confused, and show the beginning of an adenomatous transformation.

HYPOPLASTIC ADRENAL BODY.

Diagnosis of the Organ.—The adrenal body is easily recognized through its division into two layers, the cortex and the medulla, the former with its three portions.

Diagnosis of the Lesion.—One is immediately struck by the diminished thickness of the cortical portion. Comparing this drawing with the preceding, it is found that the thickness of the cortex is diminished by about one-half.

1. The *glomerular layer:* This is scarcely visible, but one should not draw conclusions from this alone.

2. The *fascicular layer:* This shows the cells well arranged in long columns, but they have almost lost their spongiocytic aspect; scarcely a trace of the vacuoles being seen in their protoplasm. The cells are small, retracted and shrunken. In some of them the nuclei show no chromatic structural details and have become pycnotic.

At occasional points, as in the central and upper parts of the drawing, there are oval areas with ill-defined limits, which form pale patches. These have an adenomatous aspect, and are composed of less differentiated cells than those we have been describing, but without vacuolar structure as in the normal spongiocytes.

In addition to the cellular alterations a slight sclerosis dissociates the cell columns; some fine connective-tissue bands isolate the cells from one another.

3. The *reticular layer:* This also contains retracted cells poor in pigment, but whose lesional appearance is less distinct than in the fascicular layer.

In regard to the lesions of the medulla, they are of slight importance.

Résumé.—The histological picture is the reverse of that shown in the last specimen. It is hypoplasia of the adrenal generalized throughout the entire gland, and characterized by the absence of the spongiocytes and the return of the cells to the undifferentiated condition, and by the slight sclerosis that dissociates the cellular elements. This hypoplasia corresponds anatomically to a diminution in the size of the gland, which may not weigh more than 2 or 3 grams, and physiologically to a condition of hypofunctionation.

It is seen in infectious diseases and in the cachexias of cancer and tuberculosis.

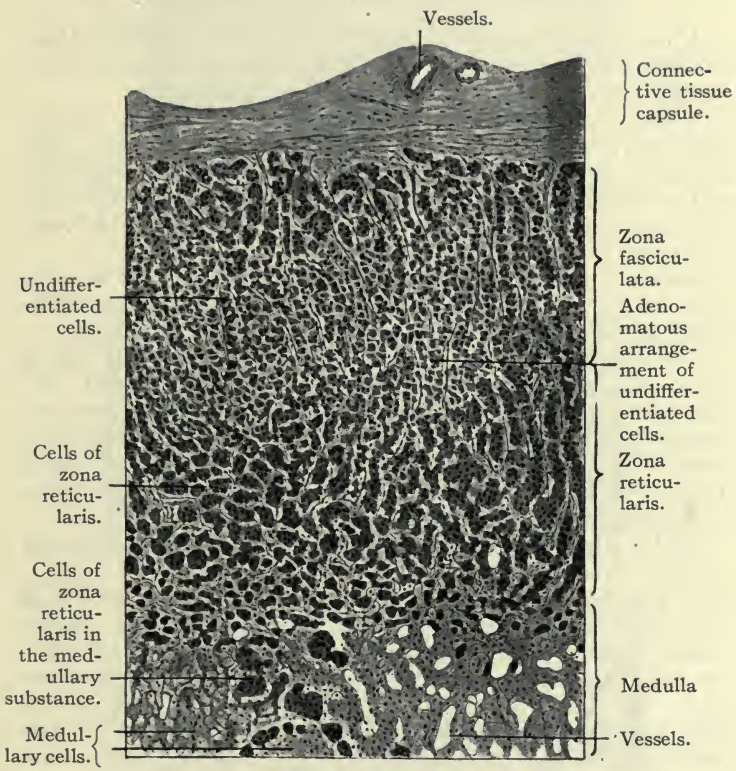


Fig. 102.—Hypoplastic adrenal gland.

Stained with hematoxylon and eosin. Magnified 500 diameters.

The connective-tissue capsule of the gland is thickened, and fine strands descend from it between the cellular elements which they separate (sclerosis). The cells of the zona fasciculata have lost the spongiocytic appearance, and are smaller and darker in appearance: undifferentiated cells.

NORMAL HYPOPHYSIS CEREBRI.

A microscopic section passing through the hypophysis close to the center of the organ, in an antero-posterior direction and having a very peculiar and characteristic appearance.

When examined under a low-power lens (Fig. 103, A), the section divides itself into two distinctly limited portions: one, the larger, is red-violet and rounded, and forms nearly the whole of the section; the other pale rose-red, scarcely colored, ovoid and very small. One of the poles of this latter is partly included in a recess in one edge of the former.

Such a histological appearance is truly unique and at once permits the assumption, even without microscopical examination, that we have to do with a section of the hypophysis.

The hypophysis is then composed of two lobes, the one a great deal larger than the other and stained blue-violet, the *glandular* or *anterior lobe;* the other much smaller, and stained rose-red, the *posterior* or *nervous lobe.* These lobes form in a certain fashion two kinds of glands pressed together, of which the origin and function are different. Between them is a connecting portion, the *intermediate lobe.*

Under a higher power the histological details of the different portions can be studied.

I. **The Glandular Lobe** (Fig. 103, B).—This is formed of a series of cellular elements grouped in different ways. Sometimes the cells form little masses separated from one another by the connective tissue and vessels of the gland; sometimes and more rarely, the arrangement takes the form of acini and recalls more clearly a glandular structure (Fig. 103, C). The columns or masses include two types of glandular cells; some have a clear protoplasm scarcely stained, so that it is only the nucleus that indicates the presence of the cell—*chromophobic cells*—others have protoplasm that stains with avidity and is finely granular—*chromophilic cells.*

Among the latter the greater number stain violet (hematoxylon), and are called basophilic; the others, less numerous, take the eosin and are called eosinophilic. It is probable that these different staining reactions of the granules of the protoplasm express different functional conditions of the cells. It is, however, important to remember that in the normal hypophysis the chromophobic and chromophylic cells occur in about equal numbers and that the basophiles are less numerous than the eosinophiles.

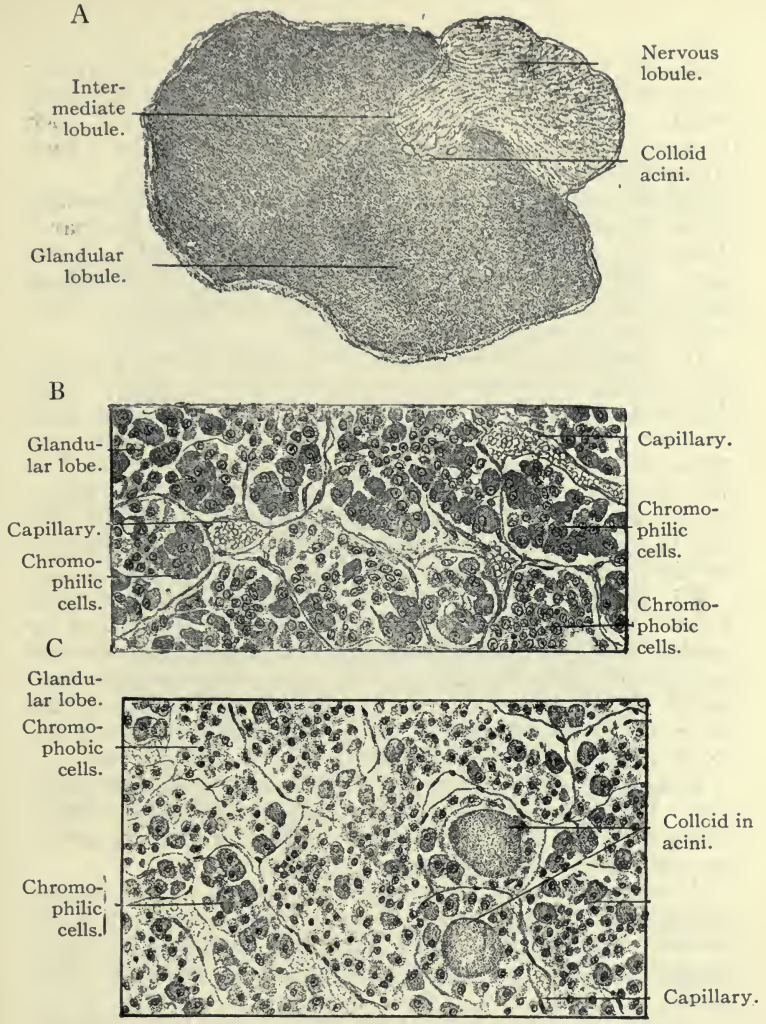


Fig. 103.—Normal hypophysis.

A.—*Vertical section of the entire organ showing its three lobes magnified 5 diameters.*

B.—*Section of the glandular lobe showing the different types of cells, magnified 250 diameters.*

C.—*Another section of the glandular lobe showing two acini filled with colloid.*

In the acinous formations (Fig. 103, C) the cells, chiefly chromophylic, line small cavities in which a colloid substance exactly comparable to that of the thyroid body is found. Such acinous formations are not common, however, in the normal hypophysis.

Between the different cellular components is a fine connective tissue in slender fasciculi, forming the stroma of the gland. Numerous capillary vessels are in intimate contact with the cells. One sees in this the chief characteristic of the glands of internal secretion, which together with the absence of ducts, easily enables the diagnosis to be made.

II. **The Nervous Lobe.**—This presents an individual structure that in no way resembles a parenchymatous gland. It is formed (Fig. 104, D) of fine collagenous fibers and a great number of neuroglia fibrillæ, impossible to differentiate by the ordinary methods of staining, but made very distinct by the special and specific method of Lhermite. In the depths of this fibrillar stroma are numerous nuclei, and finally, here and there some masses of pigmented cells the origin and nature of which are badly known.

III. **The Intermediate Lobe.**—This includes a series of cystic formations of very varied number. They are acini lined by cubical cells filled with a colloid material, sometimes retracted and fissured, sometimes colored rose-red by the eosin, sometimes bluish by the hematoxylon, and whose morphological appearances recall the vesicles of the thyroid body. Between the cysts are cells of the glandular type of the anterior lobe.

Résumé.—The structure of the hypophysis is sufficiently characteristic for its tissue to be easily recognized in a microscopic section. That which is most difficult is to appreciate its normal or abnormal condition.

A large number of chromophile as opposed to the chromophobe cells, frequent acinous formation and a quantity of the colloid substance, added to the increase in the size of the organ, suggest a gland in a state of hypersecretion: *glandular hyperplasia.*

Opposed characters indicate the opposed condition: *glandular hypoplasia.*

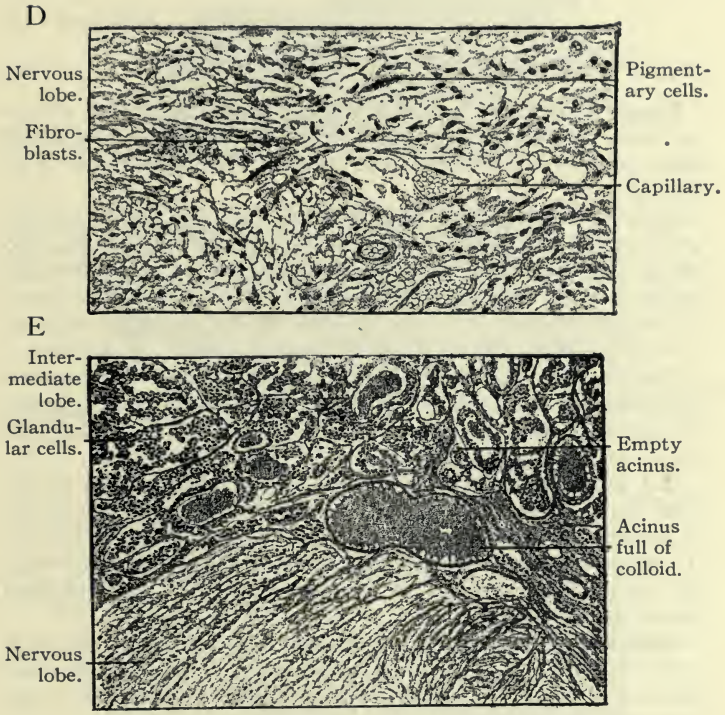


Fig. 104.—Normal hypophysis.

D.—*The nervous lobe, magnified* 200 *diameters, showing its fibers of collagen and neuroglia and nervous cells.*

E.—*The intermediate lobe, magnified* 100 *diameters, with its colloid cysts and glandular cells. Below a fragment of the nervous lobe.*

SCLEROSIS OF THE THYMUS.

Diagnosis of the Organ.—Examination of the section with a low-power lens shows a dense tissue divided into lobules by broad bands of connective tissue that support the bloodvessels (Fig. 105, A).

With a medium power magnification (Fig. 105, B), the lobules are found to resemble the lymphoid organs, the spleen, the tonsils and the lymph nodes, being composed of a reticulum in the meshes of which are an infinite number of lymphocytes. At certain points the reticulum can be seen to be composed of fibrillary prolongations anastomosing among themselves.

The lymphocytes are small cells in which it is often impossible to distinguish more than a nucleus surrounded by a thin coronet of scarcely visible protoplasm. There are, however, occasional mononuclear cells with abundant pale red protoplasm.

But that which enables the organ to be immediately recognized is the presence of numerous small pale masses composed of flattened cells arranged one upon another like the skins of an onion, vaguely recalling the pearly bodies of the squamous-cell carcinoma, known as the *corpuscles of Hassal*, and characteristic of the thymus.

Diagnosis of the Lesion.—The thymus under examination differs from the normal by the presence of *broad* and *dense* connective-tissue trabeculæ that send fine divisions into the interior of the lobes.

Résumé.—It is a chronic inflammation of the thymus or a *chronic sclerotic thymitis*, characterized by:

1. Excess of the connective tissue.
2. Architectural transformation which no longer permits the differentiation of the lymphoid elements into cortical and medullary zones.

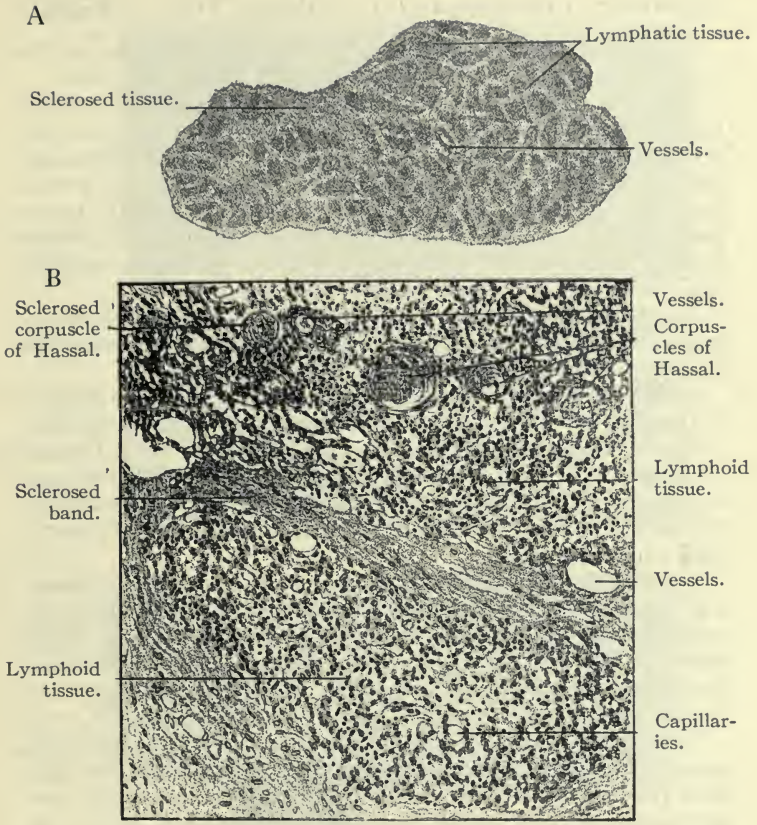


Fig. 105.—Sclerosed thymus gland.

Stained with hematoxylon and eosin.

Portion of a large, firm, sclerosed thymus gland taken at autopsy from an infant.

A.—*Entire section magnified* 5 *diameters.*

B.—*A portion of the same, magnified* 150 *diameters, showing the corpuscles of Hassal and the sclerotic bands.*

NORMAL FIBROBLASTIC CONNECTIVE TISSUE.

In this section we will consider the different stages in the development of normal and pathological connective tissue.

Drawing A represents an embryonal connective tissue, essentially composed of cells, the *fibroblasts*, distinctly visible but not distinctly differentiated. They have abundant protoplasm and pale nuclei relatively rich in chromatin, which at certain points may show a tendency to lobulation which is assumed to be an indication of activity. Between these cells, arranged in parallel fashion, are opaque, undulating, striated bands of variable size, composed of delicate fibrillæ of collagen.

At the left-hand lower corner of the drawing is shown a mononuclear cell, derived either from the blood, or from the fibroblasts through metaplasia.

Such a purely fibroblastic appearance is typical of the embryonal connective tissues, in which there is relatively little collagen.

Similar poverty of collagen fibers is also observed in certain malignant tumors of connective-tissue origin, the *fibrosarcoma* or *spindle-cell sarcomas*. In them, however, are atypical cellular and nuclear formations not found in the normal embryonal connective tissue.

Drawing B shows a more highly developed connective tissue. The fibroblastic cells have become flattened, are without envelopes, and mold themselves to the spaces between the collagen fibers. The nuclei are a great deal darker, the mass of chromatin being condensed. The thickness of the collagen fibers has greatly augmented.

The origin of the collagen fibers is disputed. It is, however, admitted that the fundamental amorphous substance that will later give origin to the collagen is a part of the primitive connective-tissue cell, which, through differentiation may give origin to either collagen or elastic fibers.

In Drawing C the development of the connective tissue has reached an adult stage. The nuclei and bodies of the fibroblastic cells are reduced to a sinuous line of chromatin. The collagen fibers have become much larger and more prominent, and show marked undulation. The fibroblasts seem to have been smothered by the collagen.

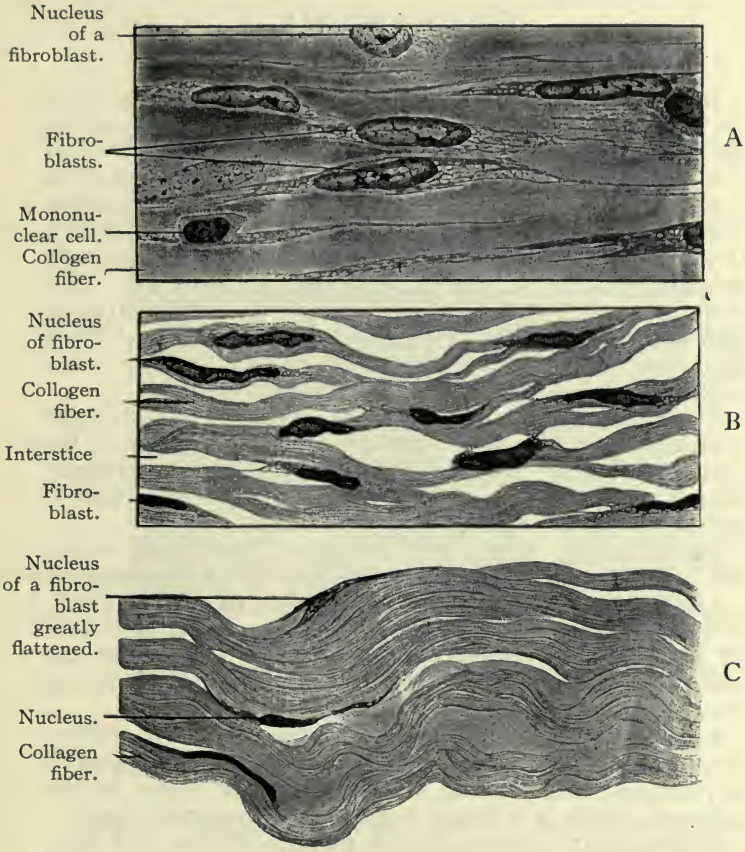


Fig. 106.—Normal fibroblastic tissue.

Stained with hematoxylon and eosin. Magnified 1500 diameters.

A.—*Connective tissue from an embryo, showing numerous cells and few collagen fibers.*

B.—*Embryonal connective tissue in a stage of further development, showing equality in the proportion of cells and fibers.*

C.—*Adult connective tissue. It contains only rare nuclei smothered in the collagenous proliferation.*

FIBROSARCOMA.

Spindle-cell Sarcoma.

Dense tissue, in which the cells are arranged in whorls about the vasculo-connective-tissue axes and occasional red-colored patches betray the presence of small hemorrhages. This is all that can be learned, under a low power, from the topographical study of a histological section taken from a fibrosarcoma. The appearance under a higher power lens is shown in Fig. 107. In the center of the drawing is a section of a capillary whose walls are partly formed of elongated cells with fusiform nuclei. But these cannot be found on the right-hand side of the right-hand limb of the capillary, where the cells of the tumor seem to form the actual wall of the vessel. The capillary contains a few white mononuclear and polymorphonuclear leukocytes.

The greater portion of the section is composed of cells with elongated bodies pointed at the ends—young fibroblasts of the connective tissue—arranged side by side to form parallel fasciculi of cells cut transversely which gives them a rounded appearance with central or peripheral nuclei.

The vegetating nuclei, sometimes constricted at the center, like an hour-glass, and the arrangement of the chromatin in equatorial plates, denote a great reproductive activity.

A tissue presenting a uniform structure of this kind is in all probability a tumor of the connective tissue. But the diagnosis should always be confirmed by information received from the clinic or autopsy.

Résumé.—A tumor of the connective tissue composed of fibroblasts: a *fibrosarcoma* or *spindle-cell sarcoma.* It is regarded as a *sarcoma*, that is to say, a malignant tumor, rather than as a *fibroma*, which is a benign tumor of the connective tissue:

I. Because it is extremely rich in atypical cells with monstrous nuclei and karyokinetic figures which indicate its tendency to malignant development.

II. Because it contains numerous newly formed vessels whose walls appear to be cut into the substance of the tumor.

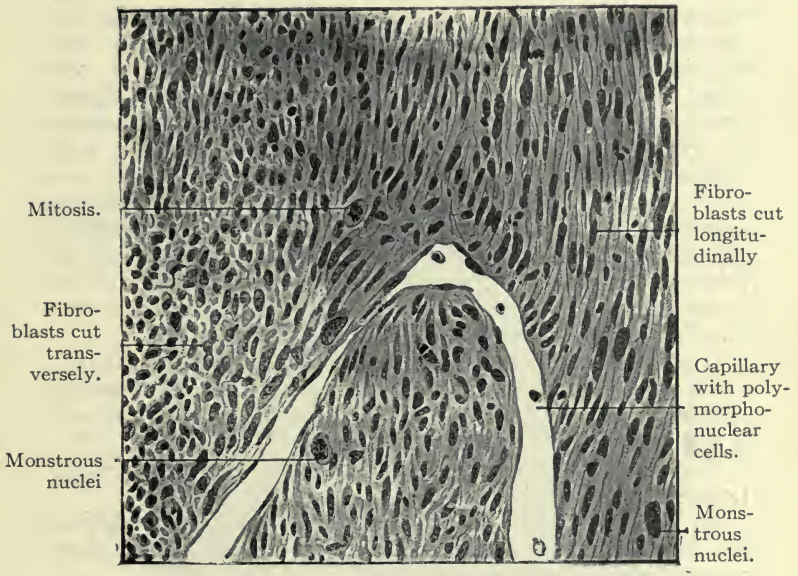


Fig. 107.—Fibrosarcoma.

Stained with hematoxylon and eosin. Magnified 225 diameters.

A fibrosarcoma of the nose, not yet having given rise to metastasis at the time it was removed at operation. Note the imperfect character of the central capillary and the numerous cellular monstrosities. The histological structure of the fibrosarcoma explains its anatomical characteristics; its softness, its vascularity, and its tendency to hemorrhage. Certain inflammatory processes may afford histological pictures very similar to this, but the uniformity of the structure seen here ought to make us incline toward the diagnosis of tumor in the absence of clinical information.

ROUND-CELL SARCOMA.

Sarcoma globo-cellulare.

The tumor is formed almost entirely of cells of variable size and shape, whose general contour is polygonal or circular, whose protoplasm is abundant and without prolongations, whose nuclei are rich in chromatin, and which contain large nucleoli. Sometimes the nuclei are small, sometimes very large, actively multiplying and showing atypical mitotic figures or they may even be multiple—giant cells. The stroma consists of occasional fibrillæ and abundant vessels, with thin walls composed only of endothelium, and often formed by the cells of the neoplasm itself. Such a histological picture does not correspond to that of any known organ and one is brought to the diagnosis of tumor, which it is always well to confirm by information from the clinic or autopsy. It is a tumor of the connective-tissue type in which the occurrence of cell monstrosities betrays the malignant character.

It is then a malignant tumor of the connective tissue, that is, a *sarcoma.* Inasmuch as the cells are round, a *round-cell sarcoma,* or *sarcoma globo-cellulare,* or, if the form of the cells is very variable, a *polymorphous sarcoma.*

Differential Diagnosis.—Round-cell sarcoma must be distinguished from:

(*a*) *Lymphadenoma,* or lymphocytoma, which is recognized by the presence of a fine reticulum in the meshes of which atypical lymphocytes are contained.

(*b*) *Atypical epithelioma,* which can frequently impose itself upon us as a sarcoma. The differential diagnosis is based upon the fact that the connective tissue and the neoplasmic cells are quite independent of one another in the epithelial tumors, and vessels present a normal wall quite independent of the tissue of the tumor.

(*c*) *Inflammatory pseudo-tumors,* "proud flesh," "granulation tissue," which present cells of very polymorphous character, and in which it is usually possible to find the specific lesion—miliary tubercle, syphilitic plasmoma, etc.

Résumé.—It is a malignant tumor, *round* or *polymorphous-cell sarcoma,* developed in the subcutaneous tissue.

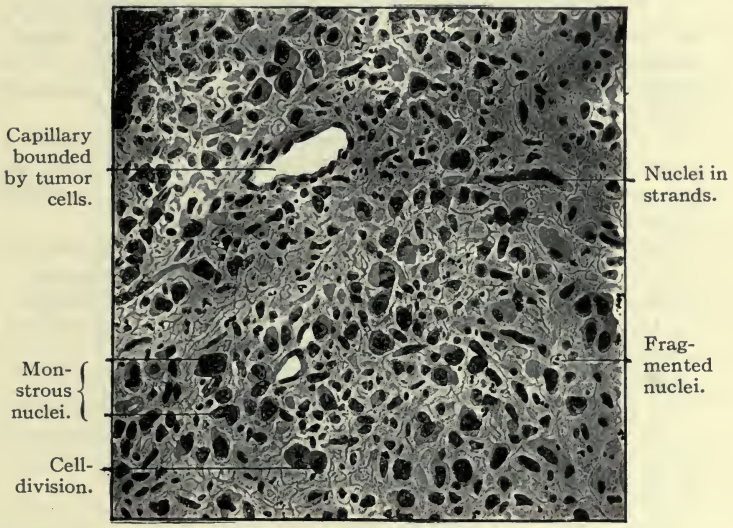


Fig. 108.—Round-cell sarcoma.

Stained with hematoxylon and eosin. Magnified 50 diameters.

A sarcoma with extremely polymorphous cells developed in the cellular tissue of the thigh, and removed by surgical operation. It is a tumor in which the atypical nature of the cells and numerous nuclei showing mitotic change testify to extreme malignancy.

LYMPHADENOMA.

Lymphocytoma.

At the center of the drawing, Fig. 109, there is a triangular section of a capillary vessel. From each of its angles, connective-tissue prolongations extend and circumscribe areas in which are cells and a reticulum.

1. *The cells*, pressed one against the other, are *lymphocytes*, the greater number of which are about the normal size, though some are large, with a greater amount of protoplasm, and nuclei sometimes of monstrous size, bilobed and showing abnormal karyokinetic figures.

2. *The reticulum* is often difficult to see, and is formed of connective-tissue fibrillæ, that stain a rose color and form an immense network that seems to be in contact with the cells either by continuity or contiguity.

Such a histological picture—and, of course, it is understood that the rest of the section has the same general appearance—enables one to recognize the lymphoid tissue, and after eliminating the normal lymphoid organs, to arrive at the diagnosis of a lymphoid tumor.

Differential Diagnosis.—The following are to be excluded:

(*a*) *The Spleen.*—This organ is easily recognized by the presence of the *Malpighian corpuscles*, little collections of lymphoid tissue in the center of which there is usually a vessel, and by its fibromuscular trabeculæ.

(*b*) *The Lymph Node.*—These are composed, especially at the periphery, of a pale tissue (sinus lymphaticus) and a dark central or medullary substance with *lymph follicles having germinative centers*. Lymph nodes subject to chronic inflammation are often difficult to differentiate because of the disturbance of the normal architecture. One then has to look with care for such signs of inflammation as sclerosis, polymorphonuclear leukocytes, or for caseous centers with giant cells.

(*c*) *The Thymus*, which is easily recognized through the presence of the *corpuscles of Hassal*, formations roughly looking like the bulb of an onion.

Résumé.—It is a tumor of a lymphoid structure—*lymphocytoma*, or *lymphadenoma*—a tissue not occurring in the normal organism.

It is further an atypical tumor, in which nuclear monstrosities betray malignant character—*malignant lymphocytoma.*

Fig. 109.—Lymphocytoma.

Stained with hematoxylon and eosin. Magnified 225 diameters.

This tumor was about the size of an egg, and grew in the subcutaneous cellular tissue of the scapular region. It was surgically removed. The reticulum containing lymphocytes in its meshes is to be carefully noted. This network is of extreme importance in the differential diagnosis of the tumor. The presence of cell monstrosities, though not numerous, betrays malignant tendency of the tumor.

OSTEOSARCOMA.

Osteogenetic Sarcoma.

The section, examined under a low-power lens, shows a number of long columns stained a rose-red color with the eosin (osseous trabeculæ), between which are pale blue cartilaginous masses and connective tissue composed of elongated cells.

1. *The Osseous Trabeculæ.*—These are recognized by their undifferentiated and structureless substance (*ossein*), in which the cells or *osteoplasts*, of which no more than the nuclei can be distinguished, lie in spaces.

Most of the trabeculæ are surrounded by a border of large cells—*osteoblasts*. These osseous formations do not have a medullary cavity containing red blood corpuscles and hemopoietic cells, or concentric arrangements forming lamellæ about a Haversian canal like the normal bone. They consist rather of tissue in process of ossification than of fully formed bony tissue.

2. *The Cartilaginous Masses.*—These are composed of homogeneous structureless pale masses of *chondrin*, in which are cartilage cells with pale nuclei, two or three in a space.

3. *The Fibroblastic Tissue.*—This is seen in the left-hand upper part of the drawing and consists of fusiform cells resembling those of the fibrosarcoma. Examination under the higher power will show cellular monstrosities.

Study of the remainder of the section which is found to show the same structure everywhere supplemented by information from the clinic or autopsy brings us to the conclusion that we have to do with a tumor of the connective tissues or *fibrosarcoma.*

But it is a fibrosarcoma of a special structure, inasmuch as it contains bone and cartilage. The young connective tissue has manifested a peculiar property called *metaplasia*, by which, in the embryonal state, it transforms itself into other tissues—bone and cartilage.

Résumé.—It is a fibrosarcoma giving origin to bone and cartilage: ossifying or osteogenetic sarcoma, observed exclusively in connection with bones.

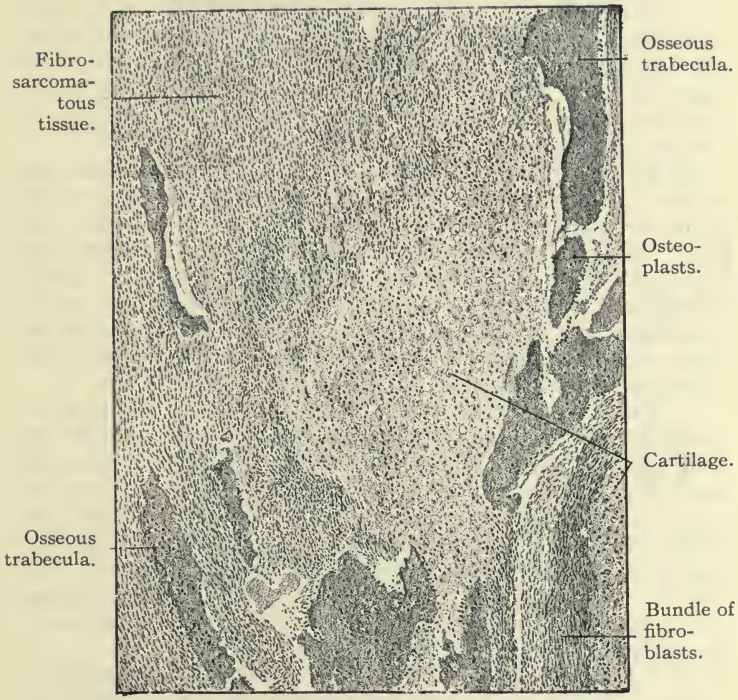


Fig. 110.—Osteosarcoma.

Stained with hematoxylon and eosin. Magnified 50 diameters.

Osteosarcoma of the extremity of the femur of a young girl aged fourteen years. Amputation at the hip-joint; no return. It is an osteogenetic sarcoma showing in the middle of sarcomatous tissue fine osseous trabeculæ and numerous masses of cartilage which indicate the osteogenic property.

EPULIS.

Giant-cell Sarcoma.

Examining under a low-power lens from above downward, one sees the following: A dark line of stratified epithelium which corresponds to the external surface of the structure: a dense mass in which are a large number of large cells, multinucleated cells, the *myeloplaxes* a deep part containing long, rose-red homogeneous osseous trabeculæ.

1. *The Superficial Epithelium.*—This is of the squamous type: a deep basal germinal layer formed of parallel cells, arranged upon a basement membrane, and supporting polyhedral cells with the intercellular filaments of Ranvier, and surface cells filled with granules of eleidin, but nowhere showing a horny formation. This type of epithelium is found in the mouth, esophagus, vulva, glans penis, anus, etc. Beneath the epithelium there is a loose layer of connective tissue, the *corium*, which contains the vessels.

2. *The Dense Tissue Below the Corium.*—This is formed of fusiform cells compactly placed one upon another, fibroblasts, analogous to those of fibrosarcoma, but without monstrosities, and without abnormal mitotic figures. Here and there are *large giant cells*, or *myeloplaxes*—large cells with somewhat basophilic protoplasm, and nuclei in varying numbers, grouped in masses in the center or at the periphery. The myeloplaxes must not be confused with the giant cells of tuberculosis, whose protoplasm is distinctly acidophilic, and whose nuclei form a peripheral coronet like a horseshoe.

3. *The Osseous Trabeculæ.*—These are formed of lamellæ of rose-red structureless material: *ossein* containing *osteoplasts.* Bordering these trabeculæ are the *osteoblasts* which form the bone. The absence of organization in the osseous trabeculæ (concentric arrangement about Haversian canals) suggests that the structure is a neoplasm.

Résumé.—The superficial part of the section is composed of a squamous mucous membrane. The tumor is a fibroblastic tissue like that of fibrosarcoma, but with the addition of the myeloplaxes and the osseous elements. It is *osteosarcoma of the gum*, a tumor described under the name of *epulis.*

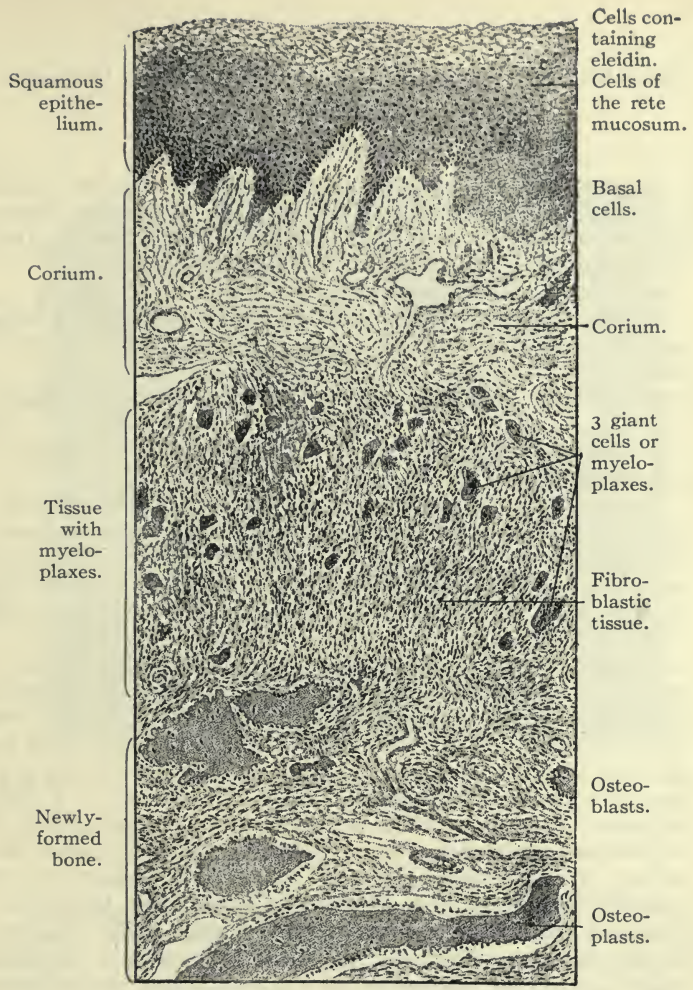


Fig. 111.—Epulis. (Giant-cell tumor of the gum.)

Stained with hematoxylon and eosin. Magnified 80 diameters.

Epithelium and corium covering a fibroblastic tissue with giant cells and containing in the center some osseous lamellæ. It was a tumor arising from the gum of the mandible in a child of eight years that caused the loss of two teeth. It was surgically removed. No return.

SQUAMOUS CELL CARCINOMA WITH EPITHELIAL PEARLS.

Lobulated Squamous Epithelioma.

Diagnosis of the Organ.—Let the section be examined with a low-power lens, beginning at the left. The dark upper border consists of a squamous epithelium with a horny layer in which can be distinguished:

(*a*) *The germinative layer.*

(*b*) *The Malpighian layers* (*rete mucosum*), composed of large cells of polyhedral shape, arranged in several layers upon the basal layer.

(*c*) *The granular layer*, composed of cells filled with granules of eleidin.

(*d*) *The horny layer*, composed of cornified cells—fine desquamating lamellæ of keratin.

Keratinization of the superficial layers of a squamous epithelium can occur in leukoplakia of the buccal or vaginal mucosa; but at one extremity of the section (not shown on the drawing) the connective tissue subjacent to this epithelium is found to contain *fat cells*, which enable the tissue to be recognized as the skin.

Diagnosis of the Lesion.—At the other extremity of the drawing, as the cutaneous epithelium is followed from left to right, there appear in the derm, enormous dark-colored masses that descend deeply and are separated more or less completely by islets and bands of connective tissue. They are not in continuity with the suprajacent epithelium, though of a very analogous structure. They are formed, at the periphery, of cells whose appearance recalls the basal epithelium, and at the center, of polyhedral cells with intercellular spines, of the type of the cells of the Malpighian layer. But that which gives the tissue a pathognomonic appearance is the presence, in the centers of the large cell nests, of enormous spherical masses, frequently malformed, of an ovoid shape, the *epithelial pearls.* They are like onions and are formed of concentric laminæ of cornified epithelium.

Between the epithelial masses is a loose connective tissue which disappears little by little as they grow, until only narrow bands remain. This relation between the stroma and the cells is peculiar to malignant tumors developed from squamous epithelium. The section is one of *squamous epithelioma*, lobulated, and containing epithelial pearls. The epithelium which

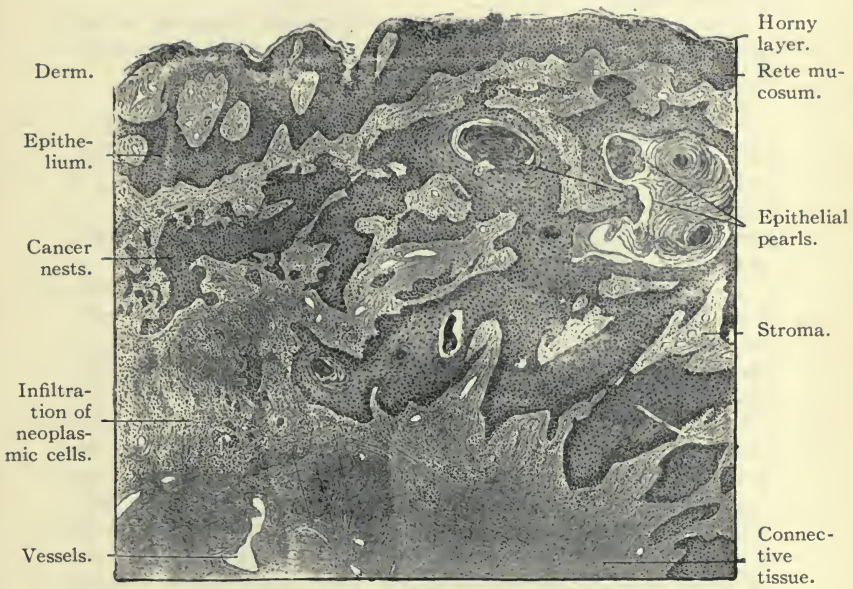


Fig. 112.—Epithelioma spinocellulare. (Squamous-cell carcinoma with epithelial pearls.)

Stained with hematoxylon and eosin. Magnified 40 diameters.

A cutaneous epithelioma of which a fragment was obtained at autopsy. Beneath the cutaneous epithelium with its horny layer there are numerous cancer-cell nests, some of which contain epithelial pearls.

covers the tumor is not ulcerated: it is the infiltrating, not the ulcero-vegetating variety, in which the cancer masses form enormous buds that ulcerate at the surface and bleed upon the slightest touch.

A moderate magnification permits both the diagnosis of the tissue and the lesion to be made: a higher magnification enables the cytological details to be studied.

The epithelial cells contain numerous mitotic figures.

In the neighborhood of the epithelial pearls important transformations of the cells can be seen and serve to explain their formation. The rose-red center of a young pearl (Fig. 113) is composed of polyhedral epithelial cells connected together by protoplasmic filaments, the *intercellular bridges* of *Ranvier*, which give a stippled appearance to the interspaces.

The nuclei stain well and are provided with distinct nucleoli. But in proportion as one passes toward the center of the pearl, the cells become flattened, attenuated and frayed out from one another; their protoplasm becomes paler and here and there small cavities with small masses of chromatin in the center are seen. This appearance is known as *dyskeratosis*, and has often been mistaken for parasitic inclusions in the cells. It is, however, due to nuclear malformation through fragmentation. Occasional cells show small dark blue dots which take the hematoxylon stain intensely; they are granules of eleidin and precede the keratinic transformation of the epithelial cells. The cells flatten more and more, become pale, almost acidophilic, the nucleus disappears, and nothing remains but a mass of hyaline keratinized substance surrounded by flattened cells arranged one upon another like the skins of an onion.

Between the cells and grouped around the epithelial pearls, occasional polymorphonuclear cells, plasma cells and lymphocytes indicate secondary infection, suggesting that there is an ulceration of the tumor at some point not shown in the drawing, or to be found in the section.

Résumé.—A tumor developed from the squamous epithelium and recalling the structure and transformations of the epiderm: *squamous-cell epithelioma* with *epithelial pearls*. A malignant tumor, because of its destructive invasion, the presence of the atypical cells and the frequent occurrence of metastasis to the regional lymph nodes.

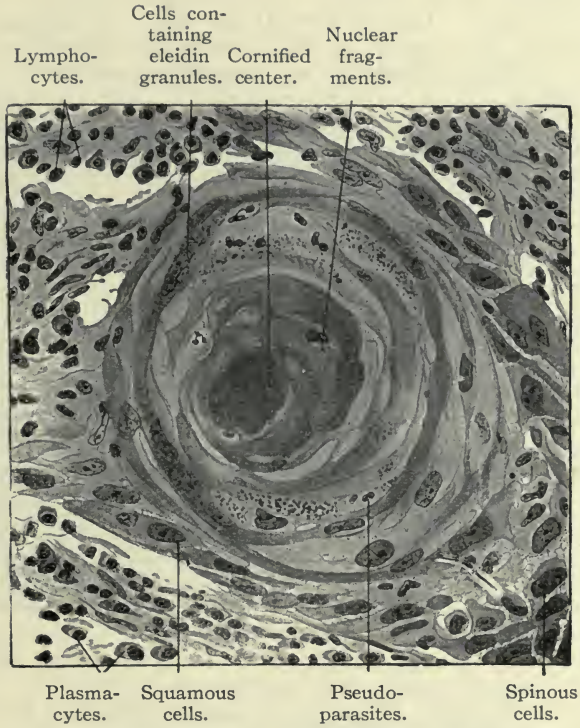


Fig. 113.—Epithelial pearl in an epithelioma of the tongue.

Stained with hematoxylon and eosin. Magnified 425 diameters.

It is one of the epithelial pearls found in the preceding section. In this pearl the keratinic change is only beginning and is far from the large formations that can almost be seen with the naked eye.

CARCINOMA BASOCELLULARE.

Tubular Squamous-cell Carcinoma—Rodent ulcer.

Diagnosis of the Organ.—The preparation can be divided into two parts; that on the left, in which the organ can be recognized, and that on the right, which shows the lesion.

In the left-hand portion are found elements characteristic of the skin: squamous epithelium with a uniform horny layer, supported upon a dense connective tissue in the thickness of which are numerous fat cells; sebaceous glands, with their large pale cells grouped in masses and filled with fine granules of fat; sudoriparous glands with a double row of nuclei in the lining, myoepithelium; hairs cut obliquely and provided with an epithelial sheath.

Diagnosis of the Lesion.—At the right-hand extremity of the drawing, beneath the epithelium, there appear in the connective-tissue stroma below and without the least ulceration, large masses of dark blue which the connective tissue divides into more or less distinct tubular formations. This infiltration of the corium by the epithelium, without distinct limits, indicates a malignant tumor, *epithelioma.*

But the uniformity of the cells which compose its prolongations and the complete absence of epithelial pearls cause this tumor to appear quite different from the epithelioma shown in Fig. 112.

Under a higher power magnification, the tumor is found to be composed chiefly of cells recalling those of the basal layers of the epiderm; cells uniform in their structure and not subject to keratinic change. Everywhere the protoplasm has the same staining quality, and nowhere do granules of eleidin occur in the cells. Occasional monstrous cells may be found.

The absence of all keratinic transformation and the close resemblance of the cells of the neoplasm to those of the basal layer of the epiderm lead one to designate the tumor an *epithelioma basocellulare.* It is sometimes called *tubular epithelioma* because of the tube-like arrangement of its cell processes.

The connective-tissue stroma shows an enormous infiltration of leukocytes in consequence of suprajacent infection.

Résumé.—An epithelial tumor derived from the basal or germinal layers of the epithelium—an *epithelioma basocellulare.*

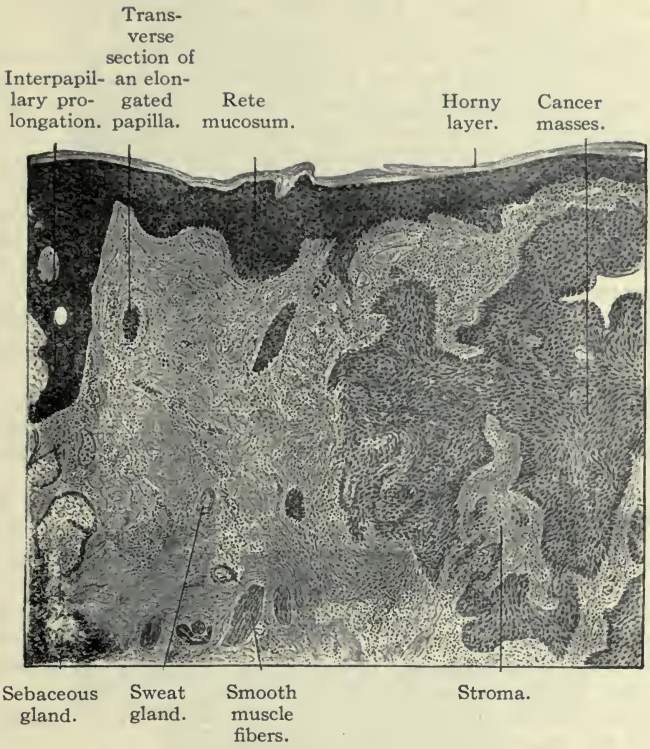


Fig. 114.—Epithelioma basocellulare of the skin.

Stained with hematoxylon and eosin. Magnified 50 diameters.

It is a section of a cancroid or rodent ulcer of the cheek, removed at operation. This form of epithelioma differs from the preceding in the absence of the epithelial pearls and the nature of the cells from which the tumor arises. In the middle and to the left of the drawing there is a little fasciculus of smooth muscle fibers—one of the arractores pilaris connected with the hairs.

NEVUS OF THE SKIN.

Melanotic Tumor. Nevo-carcinoma.

Diagnosis of the Organ.—When the section is examined under a low-power lens, it is found to be composed of two distinct parts; one superficial, consisting of a narrow dark bluish band; the other, deeper and more extended, of an extremely dense tissue. The dark band that borders the upper part of the drawing is a squamous epithelium in which can be found a basal germinative layer, successive strata of polygonal cells, a granular layer and a covering of horny cells. This type of structure together with the presence of fat cells in the subjacent connective tissue characterize the skin.

Diagnosis of the Lesion.—The enormous dark mass that make up the greater part of the section is part of a tumor whose structure is almost unique.

It is composed of elongated cells arranged in whorls and is provided with a large number of newly formed bloodvessels. The appearance recalls that of the fibrosarcoma, and easily leads to an erroneous diagnosis.

These cells are intermediate between the epithelial and the connective tissue types, and are called *nevus cells*, because they are found only in congenital tumors or malformations of the skin—the *nevi*.

But that which gives the section its most unusual appearance is the presence of pigment in granular masses of brown color and irregular form. Nearly all of the cells also contain a large number of minute black granules.

This is a peculiar pigment, *melanin*, which is not derived from the blood pigment (*hematoidin*).

The presence of the elongated cells, young and of an embryonal appearance, and the great abundance of the pigment masses in the neighborhood of the skin, indicate a tumor developed from the nevus and pigment cells, the *chromatophores*, which are also found in the normal skin—the *pigmented nevus*.

Such melanotic tumors can be either benign—*nevus pigmentosus* (birthmarks, beauty spots, etc), or malignant. In the latter case they develop rapidly and cause numerous metastases: *nevo-carcinoma*.

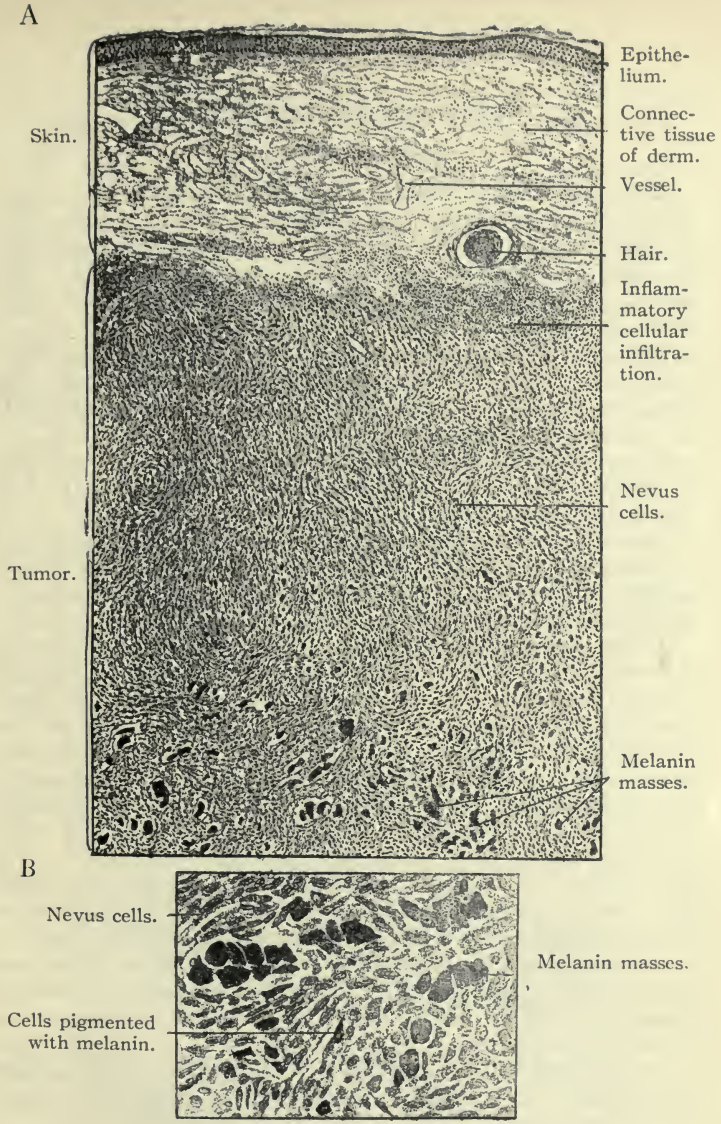


Fig. 115.—Nevus of the skin

A.—*Shows the skin and the suprajacent tumor, magnified* 60 *diameters.*

B.—*Shows the cells and the crowded masses of melanotic pigment, magnified* 200 *diameters.*

CHORION-EPITHELIOMA.

Syncytioma Malignum.

Diagnosis of the Organ.—From the portion of the tumor shown in the drawing it is impossible to discover from what organ the section comes, because, as so commonly happens in practice, the section is of a fragment removed from the uterus with a curette and contains none of the tissue of the organ from which it came.

Diagnosis of the Lesion.—Examination shows that the histological structure of the tissue does not correspond with any organ of the body. Under these circumstances the possibility of tumor should be kept in mind.

If we are informed that the tissue under examination is part of the proceeds of a uterine curettement, the possibility of its being embryonal should be considered.

A medium-power lens shows the section to consist mainly of nondescript cells unlike in size and appearance, and lacking definite arrangement. They are, however, resolvable into two principal varieties:

1. *Pale Cells.*—When these are most distinct they appear of cuboidal shape, the surfaces of contact clearly marked, the nuclei vesicular and palely staining, the cytoplasm pale, sometimes slightly granular or vacuolated. But these cells are not always clearly outlined and separated from one another; instead many of them are indistinctly outlined, and not infrequently great numbers of them are fused together into an indefinite plasmodium which may fade away into necrotic areas in which deformed and gigantic nuclei are common.

2. *Dark Cells.*—These are rarely distinct cells, but rather giant cells and masses of nucleated protoplasm. Their outlines are sometimes distinct, but sometimes fade away into neighboring protoplasmic masses either of the same kind or of the pale kind. The cytoplasm of these cells and masses is distinctly basophilic and the nuclei, which vary in size and shape, are usually deep staining.

In addition to the cells and cell masses described, sections of this tumor usually show extensive necrosis and hemorrhagic infiltration.

The structure shown and described, even in the absence of chorionic villi, which, of course, would be pathognomonic of retained secundines, is sufficient to enable a diagnosis of embryonal tissue to be made.

The pale cells may be decidual, when they descend from the maternal tissue, or chorionic (cells of Langhans), when they are embryonal.

The dark cells are syncytial and embryonal and descend from the trophoblast.

In cases of retained secundines, the cells mentioned not infrequently proliferate, and the syncytium, whose primary function seems to be to erode the decidua and open the uterine blood sinuses to the chorionic villi, may descend deeply into the uterine wall. Such abnormality results in a highly necrotic and hemorrhagic tissue mass classified as a tumor. If it remains local, and eventually disappears by necrosis or fails to reappear after removal by the curette, it is benign chorion-epithelioma or *syncytioma benignum*. If, on the other hand it continues to invade the uterine wall through the erosive action of the growing syncytium, and entering into the bloodvessels becomes disseminated to other organs, a highly destructive and fatal tumor, *malignant chorion-epithelioma* or *syncytioma malignum* results. The microscopic examination of a fragment may not be sufficient to enable the malignant nature of the growth to be determined.

Résumé.—A morbid growth of embryonal tissue derived from the foetal membranes, composed chiefly of chorionic and syncytial cells—*syncytioma malignum.*

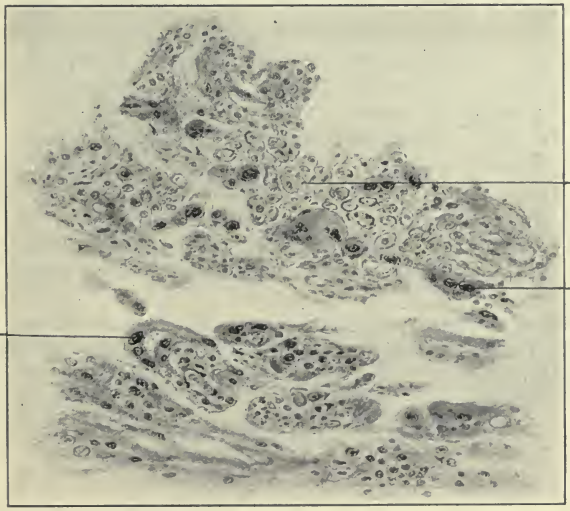


Fig. 116.—Chorionic epithelioma or syncytioma malignum.

SACRO-COCCYGEAL TUMOR.

Mixed Tumor of the Sacro-coccygeal Region.

The section when examined under a low power presents an extraordinary polymorphous appearance whose structure does not suggest any known organ. It is in reality an extremely complex tumor, produced, so to speak, through the juxtaposition of several different elementary tissues. Examined under a medium power, the different tissues of which it is composed can be studied:

(*a*) Dark-colored formations suggesting glandular acini. These are lined with an epithelium, not unlike that of the mammary gland, the thyroid body or the tubules of the kidney.

(*b*) Certain of them are cystically dilated, and all intermediate stages between acini and cysts can be found. The cysts are lined by a more or less flattened epithelium that is rarely stratified, and contain a fluid in which occasional cells with pycnotic nuclei (not shown in the drawing) are suspended.

(*c*) The stroma surrounding these formations is a loose, more or less nucleated connective tissue, some areas in which are infiltrated with fat. As the glandular formations at such points have very indistinct limitations, and the basement membrane is frequently absent, the histological appearance is suggestive of sarcoma so far as the interstitial tissue is concerned, and of carcinoma so far as the glandular elements are concerned. The absence of the basement membrane and the dispersion of the epithelial cells in the cellular connective tissue may suggest the diagnosis of adenosarcoma.

(*d*) In the stroma, and adding to the complexity of the tumor, may be found:

1. Striated muscular fibers cut transversely or longitudinally, and easily recognized by their peripheral nuclei.

2. Cartilaginous masses, forming homogeneous blue-staining areas with numerous retracted cells enclosed in spaces in the chondrous substance (chondrin).

Résumé.—The number and variety of formations and tissues lead to the conclusion that it is a *mixed tumor*—a tumor of multiple tissues of congenital origin—an *embryoma.*

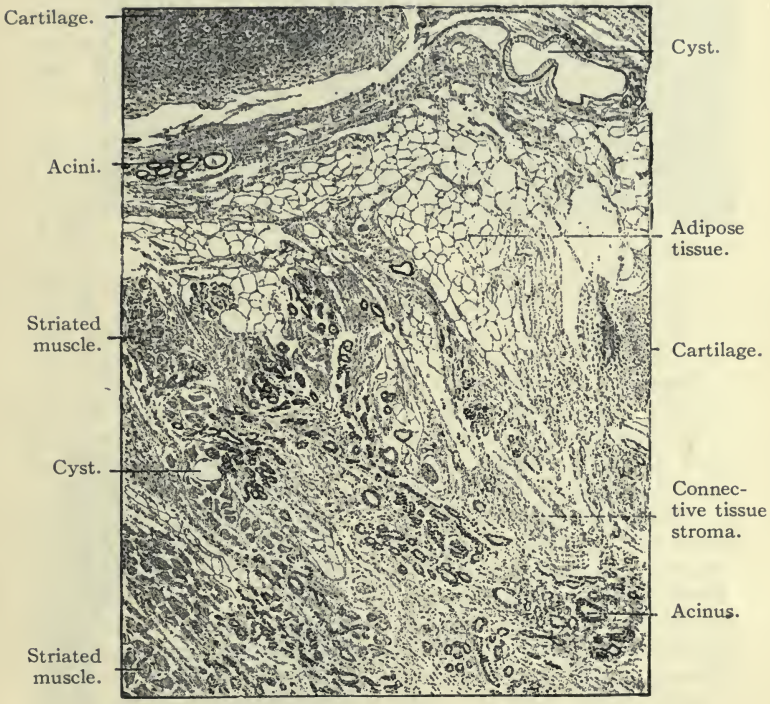


Fig. 117.—Mixed tumor of the sacro-cocygeal region. Embryoma.

Stained with hematoxylon and eosin. Magnified 50 diameters.

A sacro-coccygeal tumor about the size of an orange taken from an infant, aged one year, by resection of a part of the sacrum. Multiple sections made from different parts all showed structure identical with that represented in the drawing.

INTRADERMIC ABSCESS.

Streptococcic Abscess.

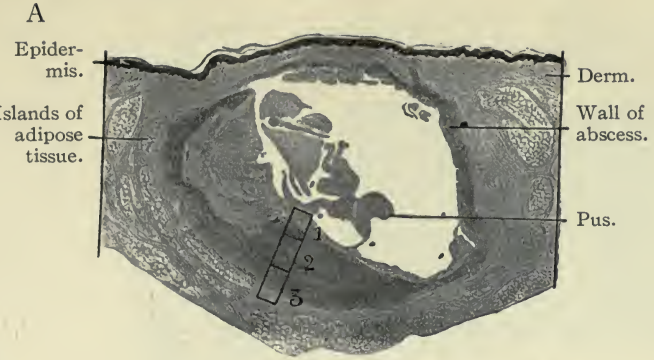
The section passes through an entire small abscess situated beneath the skin. When it is examined under a low power (Fig. 118, A), it is found to be bordered on one side by a narrow blue band (stained with hematoxylon) covering a loose connective tissue. Below this is a large rounded mass, stained red-violet, in the center of which is an excavation.

Diagnosis of the Organ.—Under a medium magnification (Fig. 118, A), the dark blue line can be recognized as a squamous epithelium with a basal germinative layer, a mucous body of Malpighi, elongated cells containing eleidin, and a cornified layer formed of thin desquamating plates.

This epithelium rests upon a dense connective tissue, the derm, in which hairs, sebaceous glands and sweat glands (not shown in the drawing) can be found. The cornified epithelium and the presence of fat cells below, enable the skin to be recognized.

Diagnosis of the Lesion (Fig. 118, A).—The epithelium is normal. The derm alone contains the lesion in the form of a rounded mass. The periphery of this nodule is formed by a thick sheath of inflammatory cells with several patches of red stained substance—small hemorrhages. About the nodule there is a loose connective tissue, rich in fatty vacuoles, with a light infiltration of inflammatory cells, giving the connective-tissue trabeculæ a darkly dotted appearance. The center of the nodule contains an agglomeration of cells to see the structural details of which it is necessary to employ a high power, even an oil-immersion lens. The zones marked by the small rectangles 1, 2 and 3, on the drawing A, should be studied in detail.

Zone 1 (Fig. 118, B).—The débris which lies in the center of the cavity, and the thin layer lining it, are composed of cells with lobulated nuclei, relatively abundant protoplasm brightly stained with eosin, and without easily recognized granules. These are polymorphonuclear leukocytes. Their enormous number is an indication of acute inflammation. The fragmentation of the nuclei, the loss of chromatic details (chromatolysis) and the eosin affinity of the protoplasm show it to be an abscess. In the interior of some of the cells it may be possible to find some of the microörganisms of suppuration (streptococcus, staphylococcus, etc.), hence, the name *phagocytes* and for these cells in particular, *microphages*. Beyond the microphages, in the inferior part of the drawing (B) and frequently mixed with



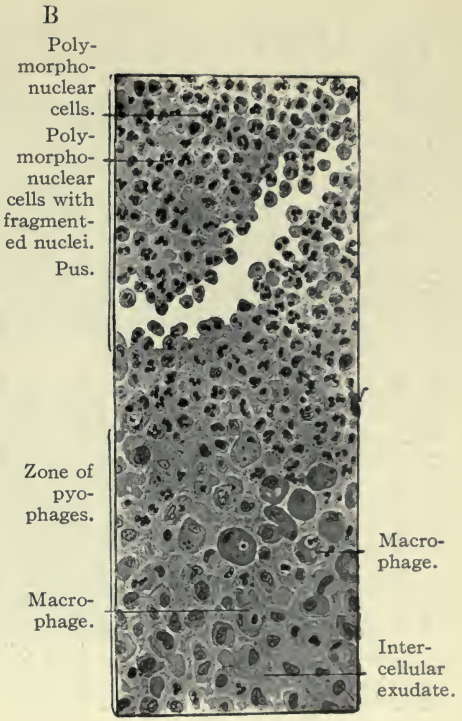


Fig. 118.—Intradermic abscess.

Stained with hematoxylon and eosin.

A.—*The entire section magnified* 3 *diameters and showing the whole abscess. The small rectangles* 1, 2, 3 *show the points from which the other drawings were made.*

B.—*Zone* 1, *magnified* 325 *diameters, oil immersion lens, showing the pus cells in the center of the abscess, and below and outside, the zone of pyophages.*

them, are a number of larger cells with finely granular protoplasm, containing besides the nucleus, chromatin fragments and sometimes even a polymorphonuclear leukocyte. This is another manifestation of phagocytosis—*pyophagocytosis*—these cells being known as *pyophages*. The polynuclears and pyophages may be held by delicate threads of fibrin or simply immersed in a fluid which constitutes the most internal part of the inflammatory nodule, the part completely liquefied, the *pus* of the abscess.

Zone 2 (Fig. 119, C).—Outside of the layer of the pyophages is a zone of organized tissue, rich in newly formed vessels, and in large mononucleated cells of a form intermediate between the polynuclears and the pyophages. These are the *large mononuclear cells*, *macrophages*, some of which, in a state of degeneration, show protoplasm that is homogeneous and acidophilic and have pycnotic nuclei.

Besides the macrophages there are a large number of cells of oval form with polar nuclei, the *plasmacytes*. These can multiply as is shown by the presence of several nuclei in some of them. The much dilated bloodvessels show a thickened endothelium. In a capillary, shown in the central part of the drawing, red blood corpuscles and two polymorphonuclear leukocytes indicate coexistent leukocytosis.

Zone 3 (Fig. 119, D).—The upper part of this zone is a continuation of the preceding. There are three capillaries and numerous mononuclears and plasmacytes. In the lower part the confines of the pyogenic membrane are reached. There are a number of fibroblasts that have formed collagen fibers. In the interstices are some large mononuclears and some plasmacytes.

Résumé.—In this section can be followed in detail all of the stages of an acute inflammation: cellular necrosis, extremely active phagocytosis, and finally the connective-tissue reaction. The abscess is sharply circumscribed by an important connective tissue reaction that tends to limit the extension of the suppuration and make it different from the diffuse phlegmon and the cold abscesses of tuberculosis.

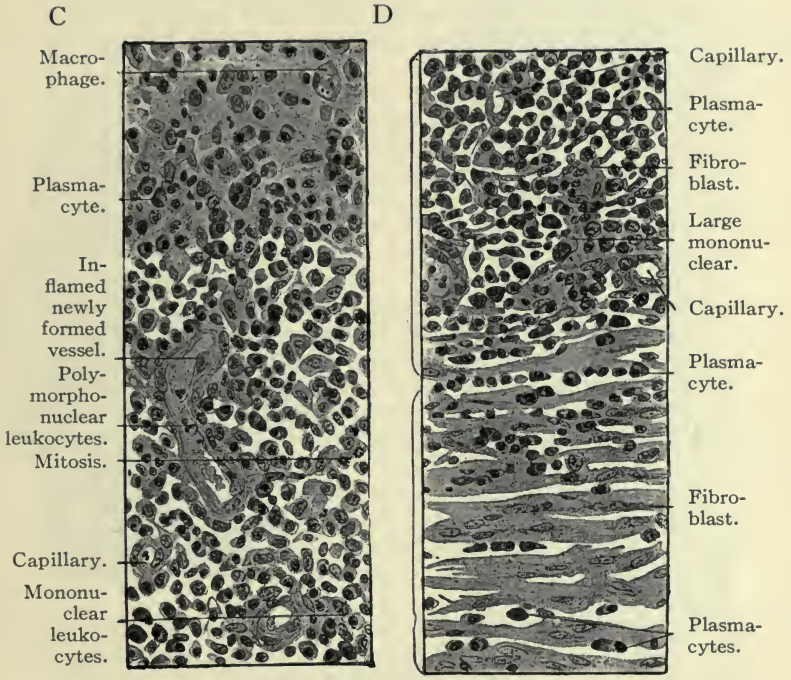


Fig. 119.—Intradermic abscess.

C.—*Zone* 2 (*Fig.* 118) *showing the macrophagic reaction, the plasmacytes and the newly formed capillary vessels with swollen endothelium.*

D.—*Zone* 3 (*Fig.* 118) *showing the fibroblastic reaction forming pyogenic membrane at the outer limits of the abscess.*

SUBCUTANEOUS SPOROTRICHOTIC NODULE.

Diagnosis of the Organ.—An examination of the specimen with the naked eye, and a low-power lens (Fig. 120, A), shows that the section passes through an entire subcutaneous nodule.

The presence of squamous epithelium with its various layers of hair follicles and sebaceous glands are sufficient to make the diagnosis of the skin.

Diagnosis of the Lesion.—In the thickness of the derm and subcutaneous tissue there is a dark blue colored nodule, in the center of which there is an irregular space. It is a circumscribed new formation concerning the exact nature of which it will require a higher magnification to decide.

The Central Zone (Fig. 120, B; No. 1 in Fig. 120. A).—This is a zone of suppuration as is shown by the large number of cells with polylobed nuclei, relatively abundant protoplasm colored distinctly by the eosin, and without appreciable granules. They are polymorphonuclear leukocytes in a more or less marked condition of necrosis, and forming the pus cells or pyocytes. The fragmentation of the nuclei, the chromatolysis, the eosinophilia of the protoplasm are characteristic of pus cells and are the same as in the more common form of suppuration already studied.

At the periphery of this central zone the lower part of Fig. 120, B, pyophages are mixed with the pyocytes. As in the abscess, the pyophages and polymorphonuclears may be held by a fine fibrinous reticulum, or be suspended in the fluid in the cavity.

As the examination proceeds from the center to the periphery the pyophages become more and more rare until they disappear altogether, and a growing connective tissue is reached. It is composed of fibroblasts in process of metaplasia. The collagen fibers are nearly all absorbed, and scarcely anything remains except fine fibrillæ more or less dissociated by edematous fluid. Between fibers and fibroblasts occasional polymorphonuclear cells with pycnotic nuclei may be found.

The Intermediate Zone (Fig. 121, C; No. 2, Fig. 120, A).—This is the zone of epithelioid and giant cells. The drawing shows a number of cells with pale nuclei and scarcely stained protoplasm with peripheral prolongations, and two giant cells; one in the center of the figure, containing two nuclei, the other at the lower part—left-hand part—with a pale center in the early stage of necrosis, and a coronet of nuclei at the periphery.

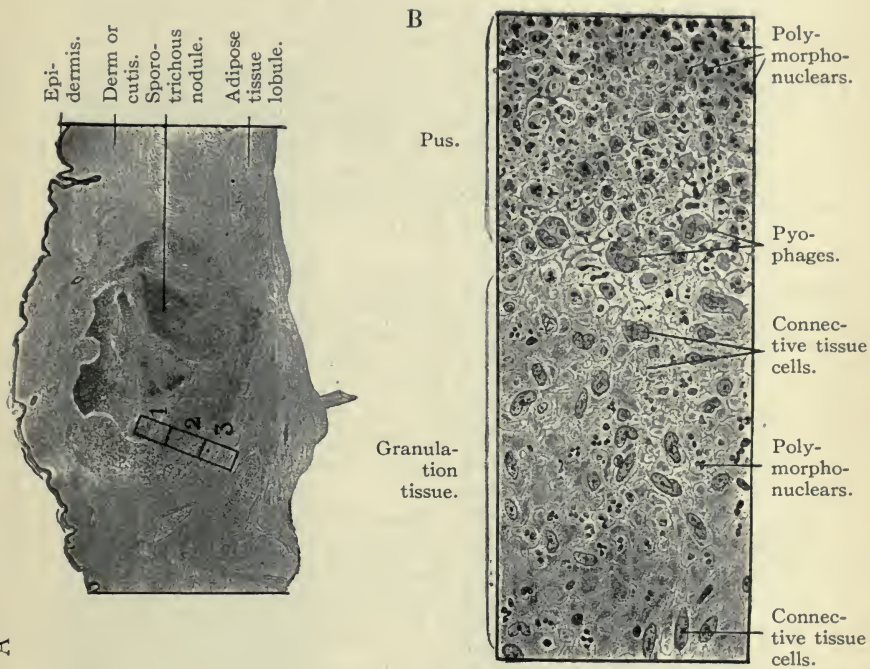


Fig. 120.—Subcutaneous sporotrichotic nodule.

Stained with hematoxylon and eosin.

A.—*View of the entire section, magnified* 3 *diameters, showing in the little rectangles* 1, 2, 3 *the areas from which the following drawings were made under a higher power.*

B.—*Zone* 1, *magnified* 350 *diameters, showing the pus cells in the center of the abscess, and the zone of macrophages outside.*

Scattered among these are also a number of mononuclear and polynuclear cells and occasional fibroblasts.

Peripheral Zone (Fig. 121, D; No. 3, Fig. 120, A).—This corresponds to the external limiting zone of the sporotrichotic nodule. In it appear *plasmacytes* which have an ovoid shape, basophilic cytoplasm, especially dark at the periphery and polar nuclei which are spherical and have a reticulated appearance, and large granules of chromatin pressed against the nuclear membrane or about the nucleolus which is usually quite distinct. The nuclei appear in the center or at the pole of the cells accordingly as they are cut tangentially or perpendicularly.

Sometimes a plasmacyte may have two or three nuclei, indicating cellular division.

There are also sections of capillaries, indicating vascularity. Their walls are formed of several layers of cells, the endothelium being tumified or swollen, unlike the normal condition in which they simply show a single layer of endothelial cells.

In the most external zone (lower part of the Fig. 121, D), the pyogenic membrane is seen to form the external limit of the nodule. It is composed of fibroblasts and collagen fibers more or less dense, in the interspaces of which are a few lymphocytes and polymorphonuclears.

Résumé.—An intradermic inflammatory nodule composed of three zones of inflammatory reaction of different character:

A central zone, composed of pus formed of degenerated polymorphonuclear cells and pyophagous mononuclears of large size.

A median zone with epithelioid and giant cells, recalling the lesions of miliary tuberculosis.

A peripheral zone, intensely vascular, composed of lymphocytes and plasma cells. This histological structure is sufficiently characteristic to permit the diagnosis of *sporotrichosis* to be made. But besides this a bacteriological examination by cultures from the fresh material ought to be made, and should show the specific agent, the *sporotrichium* of Beurmann and Gougerot.

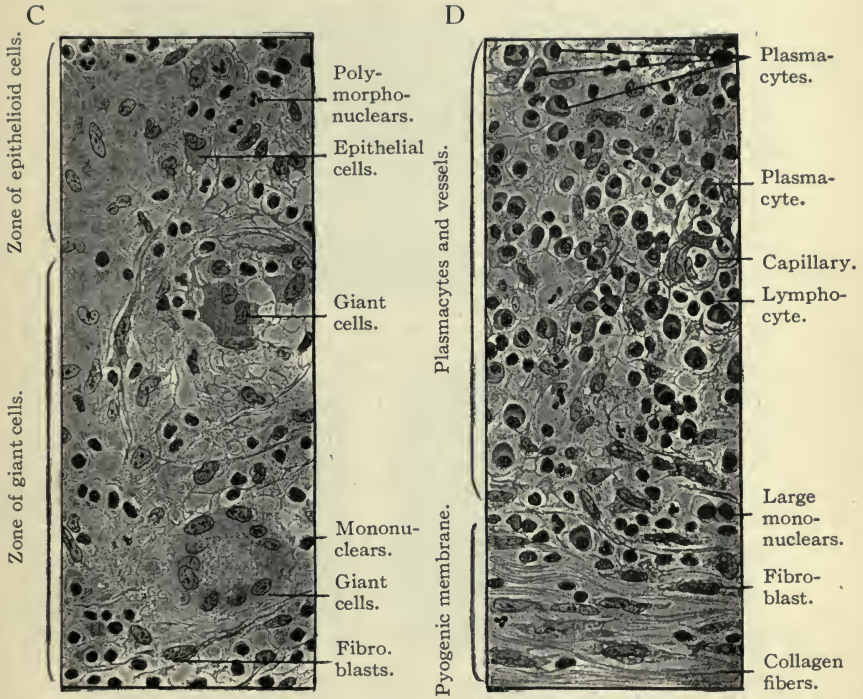


Fig. 121.—Subcutaneous sporotrichotic nodule.

C.—*Zone 2 showing giant cells and epithelioid cells.*
D.—*Zone 3 showing the lymphocytic resection in the connective tissue and the vascularity of the pyogenic membrane.*

BLOOD CAPILLARIES IN INFLAMMATION.

The drawing shows a collection of blood capillaries such as are frequently met with in various normal and pathological conditions.

Fig. 122, A and B, show two different stages in the embryogenesis of blood capillaries.

A is connective tissue taken from an embryo. In the middle of an extremely loose tissue of a myxoid appearance, and composed of undifferentiated connective-tissue cells, there is a section of a long tube, cut longitudinally at the left and transversely at the right. Such cellular tubes, from which the vascular system is developed, are the *islands* or *cords of Wolf* of the embryologists.

In B is shown an embryonal capillary developed from a cord of Wolf, in the center of which is a lumen. Its walls consist of endothelial cells with large nuclei which project into the lumen in which there is a nucleated red blood corpuscle: *normoblast.* The connective tissue about the capillary has acquired a more dense appearance than that shown in Fig. 122, A.

Capillaries with such embryonal appearance are frequently found in the adult in pathological conditions, especially in the course of inflammatory disturbances such as proud flesh.

In Fig. 122, C, is shown a section of adult capillary in a dense connective tissue.

The wall is formed of a single layer of endothelial cells very flattened, in which two fusiform nuclei can be seen. The lumen contains six or seven red blood corpuscles of the adult type.

The connective tissue through which the capillary passes is sclerotic: in it there are very few cells (fibroblasts) and very many collagen fibers.

In Fig. 122, D, is shown a capillary in an inflamed tissue. Diapedesis of leukocytes is distinct. It consists in the passage of the polymorphonuclear and small mononuclear white blood corpuscles through the wall of the capillary vessel. In the drawing is shown the condition known as *margination of leukocytes*, that is to say, their attachment to the inner wall of the vessel, and their passage through it into the neighboring stroma.

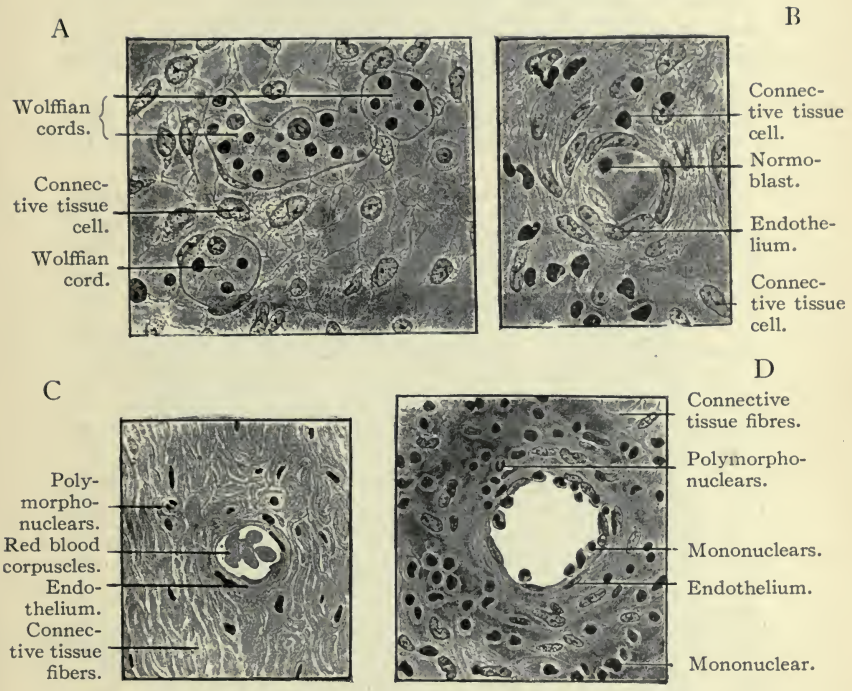


Fig. 122.—Capillary bloodvessels.

Stained with hematoxylon and eosin. Magnified 350 diameters.

A.—*Embryonal capillary showing the cords of Wolf.*
B.—*Embryonal capillary containing a normoblast.*
C.—*Adult capillary in sclerosed tissue.*
D.—*Capillary in inflammed tissue showing the margination of leukocytes and diapedesis of white corpuscles.*

Diagnosis of the Organ.—If in this case it is not possible to determine with what organ one has to do, he can say very definitely that it is a squamous epithelium of which a basal germinative layer, a rete Malpighii and horny scales in process of desquamation can be recognized.

No fat cells are found in the subjacent tissue, nor are there any sebaceous glands, sweat glands or hair follicles. It is the prepuce.

Diagnosis of the Lesion.—Below the epithelial covering, interrupted over a considerable part of its extent, by an ulceration, there is a dark bluish mass which constitutes the principal lesion. It is shown by a blue stippling that indicates numerous cells and a large number of capillary vessels, all lost in a pale rose connective tissue. The stippling and the vessels are distinctly shown in Fig. 123, B. With such a magnification it is difficult to determine further details, except a very definite collection of the cells about the vessels. A much greater magnification, even an oil-immersion lens may be necessary to bring out the nature of the lesion.

Let one of the capillaries with its perivascular infiltration (Fig. 124) be studied.

In the center of the drawing is a capillary with a distinctly thickened wall and swollen endothelium projecting into the lumen, and partly obstructing it. The external wall is also proliferated and is composed of several layers of young connective-tissue cells. An intense vasculitis is expressed by the scantiness of the lumen in comparison with the thickness of the wall.

About the capillary the infiltration consists of large oval cells with excentric nuclei—plasmacytes—which indicate a particular type of inflammatory reaction which is sometimes called "plasmoma perivasculare."

Though very numerous, the plasmacytes do not constitute the only cells in the inflammatory infiltration. There are also a considerable number of lymphocytes, and occasional, but rare, polymorphonuclears, and lastly forms intermediate between the plasmacytes, the lymphocytes and the mononuclears.

The plasmoma characterizes the primary and secondary lesions of syphilis; but it is not specific as it is quite possible to find similar infiltrations of plasmacytes in other types of inflammation, as in sporotrichosis for example.

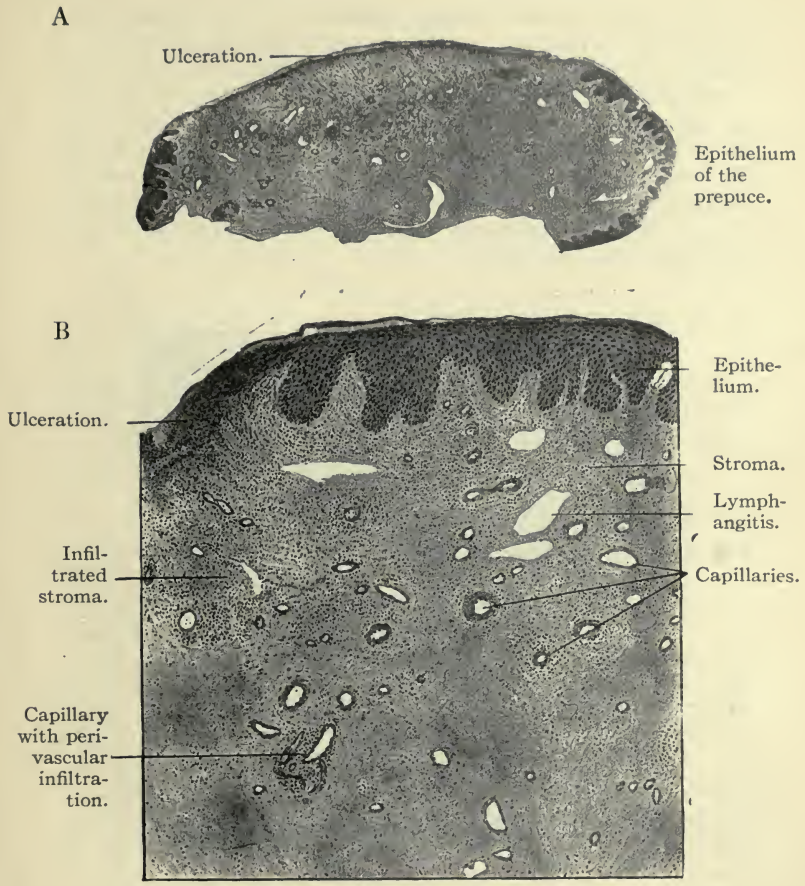


Fig. 123.—Syphilitic chancre of the prepuce.

Stained with hematoxylon and eosin.

Operative removal of the prepuce in the early days of the development of the chancre.

A.—*Showing the entire ulceration, magnified* 20 *diameters.*

B.—*Showing the inflammatory infiltration about the bloodvessels of the stroma, magnified* 40 *diameters.*

The stroma contains large fibroblasts with normal appearing nuclei, and protoplasm which has secreted an abundance of collagen fibrillæ, which give the lesion (*the chancre*) its induration.

Résumé.—Because of the nature of the cells that go to make up the cellular infiltration, and their arrangement about the bloodvessels as well as the importance of the vascular lesions, it is correct to make a diagnosis of *primary* or *secondary syphilis;* a diagnosis to be confirmed later by the discovery of the treponema through the employment of one of the special methods of staining with silver salts.

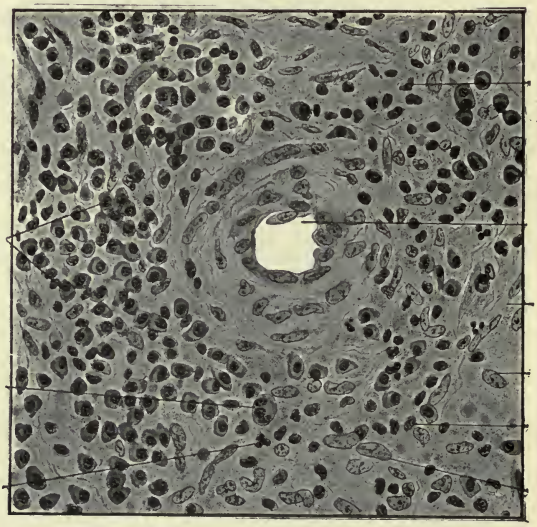


Fig. 124.—Syphilitic chancre of the prepuce.

Stained with hematoxylon and eosin. Magnified 425 diameters.

One of the capillaries shown in the preceding drawing is shown under a higher magnification to show the plasmacytic perivascular infiltration. Note the thickness of the wall of the capillary, in which the endothelial cells are swollen and surrounded by several layers of fibroblasts. About the capillary the tissue is infiltrated with a composition of inflammatory cells particularly rich in plasmacytes.

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