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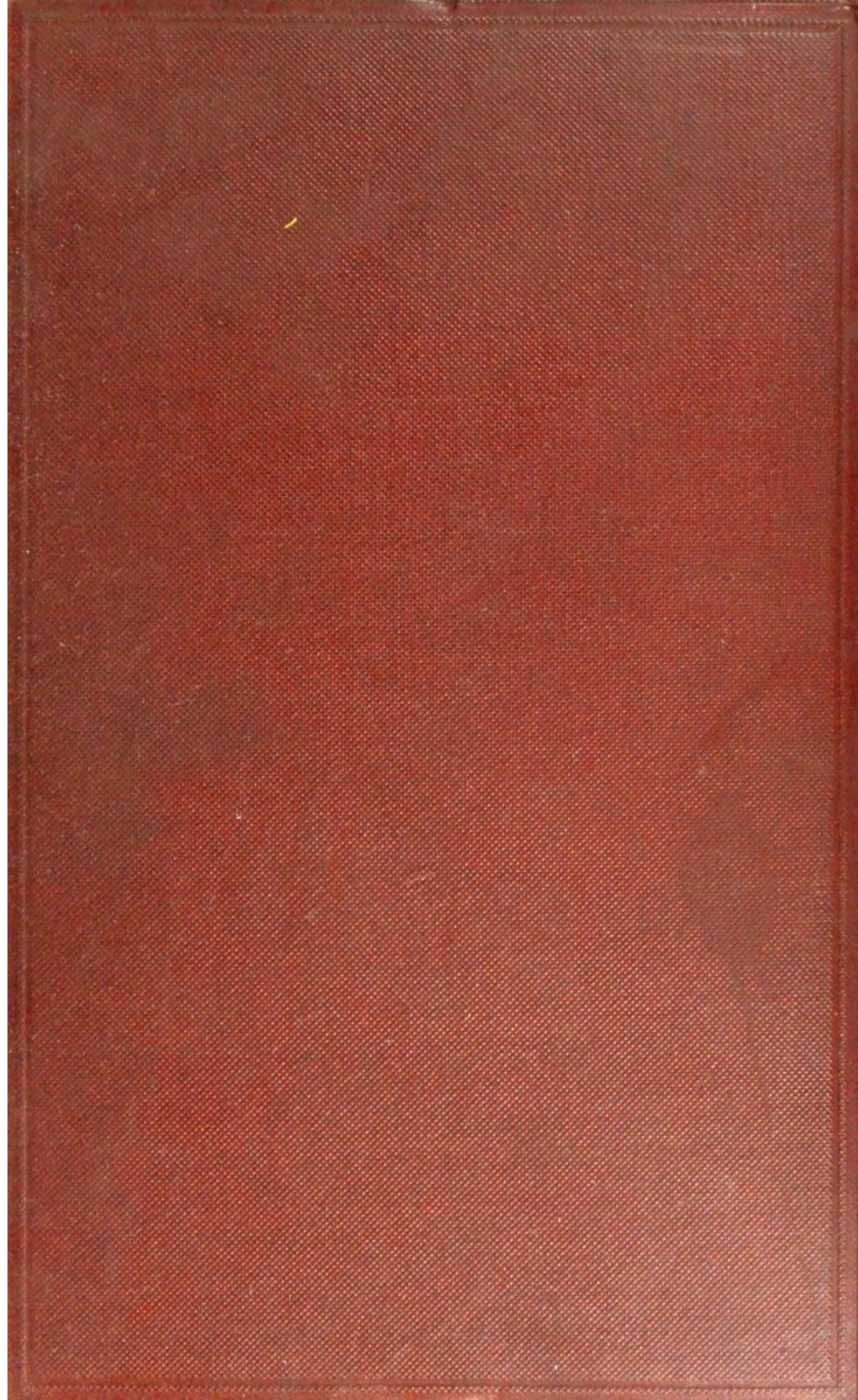
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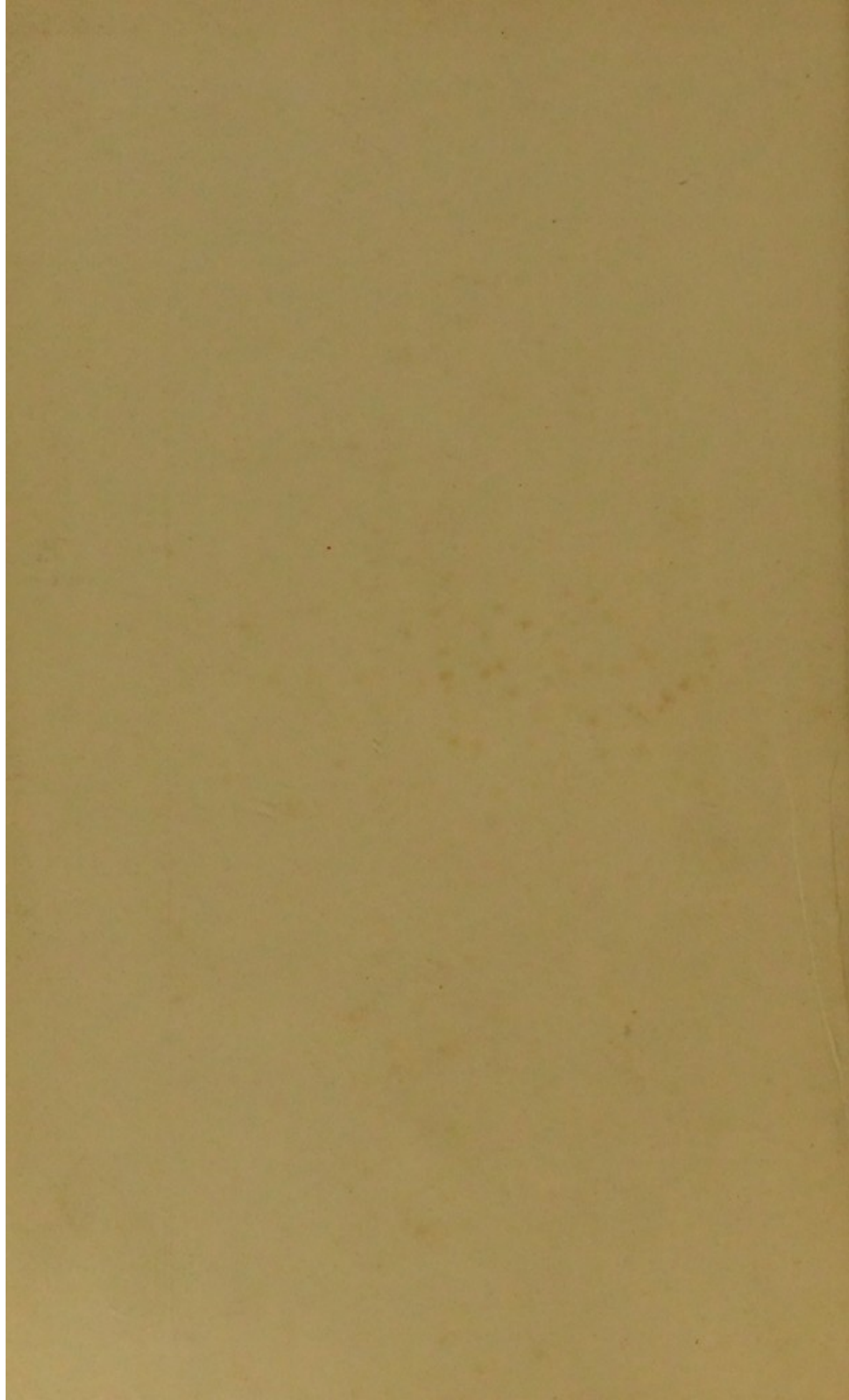


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A TEXT-BOOK
OF
PATHOLOGY
AND
PATHOLOGICAL ANATOMY.

BY
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EXTRAORDINARY PROFESSOR AND FIRST ASSISTANT IN THE PATHOLOGICAL INSTITUTE, MUNICH.

TRANSLATED FROM THE SIXTH GERMAN EDITION

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EDITED WITH ADDITIONS

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35 COLORED INSET PLATES.*

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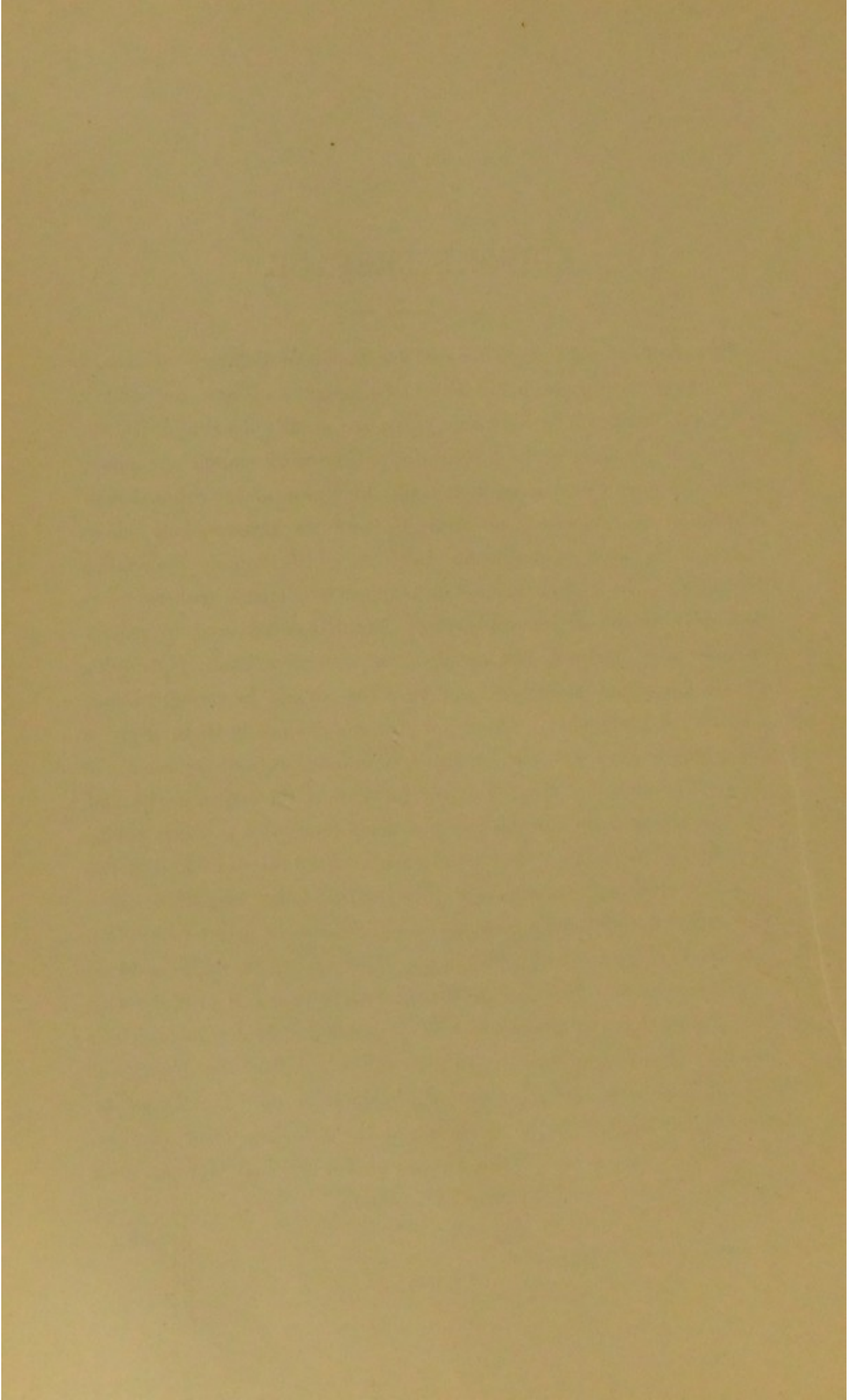
EDITOR'S PREFACE.

THE factors which have secured for Professor Schmaus' *Text-book of Pathology* its great popularity in Germany, and have brought it to a sixth edition in a very few years, are readily discernible in the scheme and manner of its preparation. The work stands out among the well-known Continental text-books by reason of its original close adaptation to the needs of students, and its progressively closer approach to such requirements in each of its rapidly succeeding revisions. The author has not attempted to compete with the more discursive works of his countrymen, but has endeavored to write a shorter, more compact, but equally comprehensive book, embodying all the important principles and facts that should be brought before students of pathology. There is a notable absence in these pages of the argumentative style, the quotation of authorities, and the pursuit of personal opinion that are prominent features in the larger works, and likewise absent is the full discussion of many topics that properly belong to a work of reference. Instead of such material there is found in this volume a condensed statement of present knowledge, amplified with a rich array of aptly chosen instances and references, which the editor believes to be scarcely equalled in any other text-book on the subject.

It has seemed a duty to English-speaking students of medicine that they should have command of a work possessing such great intrinsic merits. The Editor has avoided, as far as possible, any changes in the subject-matter, arrangement or classification, and the Translator has limited himself to the rendering of the text into clear English. To the very rich series of illustrations in the original German some new ones have been added in this translation.

J. E.

NEW YORK, OCTOBER, 1902.



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PATHOLOGY AND MORBID HISTOLOGY.

INTRODUCTION.

By *Disease* we understand a condition of the organism in which the expression of its life varies from the normal type. The science of disease is called *Pathology*. In certain pathological conditions we are unable to demonstrate anatomical changes in the affected region, either in the gross or microscopically, and abnormalities in the blood and lymph and other body fluids are not so distinctive that they entirely explain the symptom complex. Among these purely functional disorders belong many of the diseases of the nervous system, the neuroses, neurasthenia, hysteria, and psychic affections.

In many cases, on the other hand, we find such alteration of the anatomical structure of the organs that it is at once evident that the functions of the part must also have departed from the normal, or there are such variations in the circulation of blood and lymph that secondary lesions in the organs must inevitably follow.

These alterations in the anatomical structure of the organs are the immediate object of pathology, which is concerned, like normal anatomy, with their recognition and description. The history of medicine demonstrates that equally with advance in the perfection of methods of study the territory of the purely functional disorders diminishes, so that for many of these conditions the microscope and its accompanying technique have established an anatomical basis. Thus the domain of pathology is constantly being extended.

Inasmuch as Pathology is the science of disease and might almost bear the name of Pathological Physiology, for symptoms are but the expression of body processes which depart from the normal, so Pathological Anatomy is strictly a part of this science, and, together with Physics and Chemistry, is its immediate foundation, and stands as normal Anatomy to normal Physiology. It is due to practical needs that Pathology is separated from the related sciences, but it must always retain its intimate connections with them. Its main purpose,

to ascertain and establish the actual abnormal conditions, is evidently the only pathway toward adequate interpretation of symptoms, and furnishes the best foundation for diagnosis, therapy, and clinical medicine in general.

Special Pathological Anatomy is occupied with the study of structural changes which the single organs undergo in various diseases. It explains the failure of function, as well as the variations from normal function on the part of the organ. From the facts gathered by such study we can formulate the more abstract general laws which apply to all tissues and organs; such a universal and inclusive view of the subject is called General Pathology, and necessarily trespasses at times upon the domain of pathological physiology, or can hardly be separated from it.

The conditions which render possible this universal view of the organs and the diseases affecting them are to be found in the fact that all portions of the body are constituted of cells or derivatives of cells. Even the fibres of connective tissue, of muscles, and of nerves are the product of cells, while blood and lymph may be regarded as cellular tissues whose intercellular substance is fluid. These cellular elements, the very bricks of the edifice, are the actual carriers of life functions, normal as well as diseased. Hence disease is the expression of the sum of abnormal cell activities. Disturbance of the life of cells occurs in three directions, in their nutrition, their function, and their multiplication, which latter serves for physiological growth as well as for repair.

Since pathological conditions may affect an organ either as an increase or as a decrease of its life process, acting somewhat as normal development or as senile involution, we may distinguish two great groups of pathological disorders. The first are the *regressive*, in which there is diminution of cell activity, and the second are the *progressive*, in which there is an excess. The conditions are not so simple as mere defect or excess, for there is usually a qualitative departure from the normal for the organ and the cells considered, both functionally and anatomically. Regressive conditions may lead to actual death of parts, and a similar death may follow external influences. Such local death is termed necrosis.

The single cellular elements of the body are dependent for their activity upon their nutrition, provided by the supply of blood and by contact with tissue fluids exuded from the blood. Disturbances in the distribution of these fluids are called *disorders of circulation*, and are

marked by abnormal function or loss of function, and in time by anatomical changes in the part. An example is found in the disorders of intellect which arise from simple cerebral anemia, which, if it persists, causes death in certain portions of the brain. Because of its general importance, we shall place the chapter on Disorders of Circulation before the others.

Certain causes of disease may act upon the fetus. There are true fetal diseases resembling those of later life, but since they affect the developing organism they produce marked changes in its form. Especially evident are the results of injury to the developing ovum, either mechanical, or inherited, or spontaneous. The results are malformations and monstrosities, included in the chapter on Teratology.

Imperfect development of a portion of the body, or entire absence of it, may be due to mechanical causes or more obscure conditions. If the organ, as for instance the kidney, remains wholly undeveloped, this is spoken of as *Agenesis*. If its development begins but is arrested, *Aplasia* is the term employed. If the arrest is but partial, *Hypoplasia* expresses the fact, and the organ is found small or distorted. Hypoplasia may not be due to causes operating on the fetus, for in some cases the extra-uterine life has begun. If at a period when an organ should develop further, as the uterus at puberty, it remains in the infantile condition, it is also a case of hypoplasia. Its cause may be fetal in one sense, as when the vascular supply remains inadequate from undeveloped vessels, or it may be acquired at a later time. Like simple arrest, both regressive and progressive lesions may at any time disturb the normal embryonic or the later development.

The essential nature of the anatomical changes and the methods of their production from normal tissues—in other words, the lesions and their pathogenesis—are the questions which immediately concern the pathologist, and which explain, on morphological grounds, both the nature of the disease and its symptom complex.

Every gain in any department of human knowledge opens new and other questions, because each successful investigation forms but a link in the chain of phenomena whose complete comprehension involves a grasp of the foundation of all life; hence after the lesions which explain a disease have been established, the inquiry after their cause follows at once. This branch of the subject is known as *Etiology*. The many external influences which may act upon the organism to its injury lead us to refer disease to an external cause. Long since it was assumed for many diseases that they arise from foreign organisms,

often microscopical, and this assumption has been demonstrated as correct in the last few decades.

Having established an external cause for a disease, our etiological knowledge is advanced, but far from completed, and the essence of the disease is not yet clear. One cannot consider it the simple influence of an alien agent, as for example the activity of a parasite. The agent is not an efficient cause for all consequent results in the body, but rather the disease is an altered condition of the body, depending upon what manner of reaction follows in the organism from the influence of the agent. Hence the action of external agents may vary widely, depending partly upon surrounding conditions, but even more upon the internal disposition of the body. Entirely different causes may in some circumstances produce similar effects, and the identical agent may cause diverse results. Beside the external causes, there exist internal factors also, to which we ascribe many of these variations in causal influences. The group of the inner factors is summed up under the term *Disposition*, and that disease may proceed from these apart from external causes appears in inherited developmental disorders. The external causes are as multiform as the other influences working upon the organism, and cannot be systematically classified either from their nature or their activity. The exception to this rule is formed by the parasites, which will be treated in a separate chapter.

In contrast with the external cause the internal disposition appears less important, for the latter is often a matter of deductive reasoning, and the former is in concrete form; but the essential nature of a disease is found in the abnormal expression of its cellular life, and knowledge of etiology merely informs us what was the stimulus. Hence the importance of investigating the changes in the cells in order to approach the actual comprehension of the disease.

Cellular Pathology is one of the greatest contributions of the last decades, and remains as the groundwork of pathological science despite all momentary contradictions and the etiological progress lately attained.

The Signs of Death. Before attacking the field of pathology proper, it is well to consider the phenomena of death of the whole organism, especially those considered as *signa mortis*.

The cooling of the body—*algor mortis*—depends for its development upon the surrounding medium. The body may reach the temperature of the surrounding medium within twenty-four hours, and before this cooling there may be a slight rise of temperature.

Post-mortem rigidity—*rigor mortis*—is explained as a temporary coagulation of the muscle proteid (myosin), and begins, usually in four to twelve hours after death, in the muscles of the jaw, passing then to the neck, upper extremity, and so downward. It disappears in the same order, in twenty-four to forty-eight hours. Strong muscular action just before death may be followed by rapid rigidity, and the trunk and limbs may then be fixed in the position assumed. In other cases rigor develops more slowly (twelve to twenty-four hours).

The disposition of the blood in the body differs much from that during life. Three factors may be noted:

1. The agonal contraction of the arteries drives the blood out of them and into the capillaries and veins. This spasm is connected with the venosity of the blood, increasing as the cardiac activity ceases, until the vasomotor centre in the medulla is excited and the vessels contract to the minimum calibre. From this spasm of the vessels and the stiffening of the muscles the arteries are usually found empty.

2. The post-mortem sinking of the blood to the most dependent portions of the body causes hypostatic congestion of the organs and lividity of the surface. Thus the lungs and the brain are commonly filled with blood in the lowest parts, and in the alimentary canal there are frequent hypostases which appear in the mucosa as fine branching figures. *Livores*, or spotting of the surface, depend on this sinking of the blood and also on the diffusion of the blood-coloring matter in the tissues. In the former case pressure removes the red color, in the latter it persists. These spots appear on the back or other dependent parts and usually in three to four hours post-mortem.

3. If death occurs with cardiac paralysis the left ventricle is arrested in diastole and is distended with blood. Rigor mortis involves the heart muscle and drives this blood into the aorta and left auricle, the left ventricle remaining empty; this does not occur when a pronounced change has taken place in the heart muscle. The right ventricle is usually found distended, its muscular mass and power being much less than those of the left ventricle.

The blood in the heart and great vessels coagulates after death, at times even in the agony, making clots which are either dark red, as observed in blood drawn during life, or yellow and fat-colored, or fibrinous. The latter decolorized clots are formed during protracted agony, when the heart gradually weakens, the red cells being separated from the other constituents of the blood and the clot forming in slight adhesion to the wall. The blood coagulates less quickly after death

by suffocation, by certain poisons, in septicemia and pyemia, and when it is hydremic.

The cornea becomes cloudy and relaxed a short time after death, and when the lids are not closed it may dry.

When putrefaction begins, with its accompanying odor and greenish or brownish discoloration of the skin, these changes are usually first and most pronounced over the abdomen. Gas collects in the tissues, vesicles appear on the skin, and the blood becomes foamy. The blood pigment becomes dissolved in the serum and is imbibed by the tissues in spots or larger areas. The changes in the intima of the vessels and the endocardium may thus simulate inflammatory congestion. Sulphuretted hydrogen acting on this pigment turns it green or black, as may be noted along the alimentary canal and parts adjacent. Pigment already in the tissues in granules may take the same tinge, and thus resemble the pigment of anthracosis. Under the microscope sulphuric acid produces the well-known changes in color, from black through blue, green, and yellow, as with biliary pigment.

In the stomach and lower end of the esophagus a post-mortem digestion may occur.

PART I.

GENERAL PATHOLOGY.

CHAPTER I.

DISORDERS OF CIRCULATION.

A. HYPEREMIA AND ANEMIA.

THE blood content of a part is regulated by the supply of blood and its venous return. Increased supply depends upon :

1. *Increase in the cardiac activity* (not simply more contractions in a given time), which is followed by rise of pressure in the arteries and more rapid current, unless some obstacle hinders the action of the heart, and its increased action is but the compensatory effort to overcome the mechanical obstruction.

2. *Vascular dilatation or contraction.* The latter is caused by (a) various local stimuli which cause a constriction or a paralysis of the vascular muscle fibres, with consequent variations in the size of the lumen and of the blood stream, (b) or through vasomotor nerves, either vasodilator or vasoconstrictor.

The flow of blood from a part depends on all the influences acting upon the venous circulation ; on the richness of supply, whose physiological increase implies greater flow from the part, with heightened *vis a tergo* ; on the contraction of muscles, relatively low pressure in the thorax, and the determination of blood from the venæ cavæ during inspiration ; and, lastly, on the forces which act against the venous current, as gravity, most evident on peripheral and dependent parts of the body.

Through all these factors the blood circulates under physiological conditions, and each organ is supplied according to its needs. Those functionally active require more blood, and the supply lessens with return to a resting stage. The various influences act in more or less opposition, and thus prevent great variations in any direction. Strong

vasoconstriction is followed by exhaustion of the muscle fibres, and conversely. When this balance is destroyed a part may contain too much blood or too little, the former being called *hyperemia*, and the latter *anemia*.

Hyperemia.

Hyperemia, or congestion, may arise from excess of supply or diminished escape. The former, known as active or arterial hyperemia, acute congestion or fluxion, gives the part a bright-red color from the presence of arterial, oxygenated blood. The second, called *passive or venous congestion*, or hyperemia, or stasis, betrays the presence of venous blood by its dark bluish or cyanotic hue.

Congestive hyperemia occurs wherever there is lessened friction in the arterio-capillary system of the part, as happens with dilatation of these vessels. This increase in lumen may be due to direct action upon the vessel walls or indirect through the nervous system. Paralysis of the vessel wall may follow high temperatures acting locally, mechanical frictions (as of the integument), the application of various chemicals, sometimes with a previous stage of vasocontraction. Thus certain erythemas follow the actions of drugs and the growth of bacteria.

Congestive hyperemia occurs also when there is a sudden relief of the pressure upon a part. Such a secondary fluxion in the pleura or peritoneum sometimes follows removal of large exudates, and may cause marked anemia in distant organs, as in the brain. The probable explanation is that long-continued external pressure has diminished the elasticity of the vessel walls, their contractility is lost, and when the support is removed they give way to the internal pressure. After removal of the Esmarch bandage strong parenchymatous hemorrhage may occur, or marked hyperemia. In general, a violent muscular contraction is apt to end in as complete a relaxation.

Paralysis of the vasoconstrictors or stimulus of vasodilators may cause one variety of congestion. Experimentally this may be demonstrated by section of the pneumogastric, which contains vasoconstrictor fibres; when this nerve is cut in a rabbit, in the neck, there occur on the same side hyperemia and redness of the ear, increased temperature, and contraction of the pupil. Electric stimulation of the upper cervical ganglion is followed by lowered blood supply and temperature.

After section of the splanchnic nerves there is marked hyperemia of the abdominal vessels. In the human subject injury and degeneration

in the sympathetic, compression by tumors, etc., have similar results. The active congestions of Basedow's disease may also belong here. Irritation of the vasodilators with resulting hyperemia is observed in many angioneuroses, where slight and frequent stimuli produce repeated hyperemia of special areas.

Collateral hyperemia is the name applied to congestion which occurs in the neighborhood of anemic parts, as when an artery is closed by ligature or thrombus, and the lateral branches carry more blood. This is rather to be explained as a vasomotor effect than as due to proximal increase in pressure, for this may occur much later, and even when present is distributed over the entire vascular system. Similarly in many cases of collateral hyperemia more blood flows to an organ which has to assume an extra share of work, as to the other kidney when the vessels of one have been ligatured.

Lastly, we observe, often with but slight stimulus, an increase in the blood content of lungs or brain when a hypertrophied heart becomes suddenly more active, as in true plethora—*i. e.*, increase in the total blood with increased arterial pressure. (See Chapter VI., 1.) Severe functional disturbances may be the result.

Within a hyperemic part, as may be directly observed, the blood flows more rapidly, its contact with the tissue is shorter, and hence even the venous channels contain red blood. The strong injection of the vessels makes prominent even the smallest, and the distention of the capillaries gives the part a diffuse redness and increased volume, or turgor, with increased local temperature, most marked on superficial parts.

Further results may be unimportant, for active hyperemia is usually temporary. If protracted, and in certain organs, as the lung and brain, such arterial hyperemia may be dangerous, and diseased vessels may rupture from the pressure. As a rule, active hyperemia does not lead to transudation and edema, though probably slightly more fluid leaves the vessel than normally.

One would expect that dilatation of a vessel would produce a slowing of the stream, but, beside lessened friction, the laws of capillary currents apply, according to which the rate is proportional to the square of the diameter of the stream (Poiseuille).

Passive or venous hyperemia results from diminished outflow from a part. The effect varies with partial or complete obstruction to the stream. In normal circumstances the column of red cells occupies the middle of the lumen of the smaller vessels, forming the axial stream;

nearer the wall flows the plasma, free from red cells, forming the still layer or peripheral zone. In this space the white cells move at a slower rate than the red. It is only in the capillaries, which admit but one cell at a time, that the erythrocytes follow each other in single file.

If now the venous current is suddenly and entirely stopped, as in the frog, by ligature of a femoral vein, the first result must be increase of the blood pressure within the region, for the arterial supply persists, and this pressure rises until it reaches the average arterial. In the vessels of the region there occurs, then, a slowing of the stream, then a pulsating movement, and at last, with each cardiac diastole, a flow in the reverse direction. As the veins fill the plasma space disappears, for the red cells fill the entire lumen and touch the walls. Then these cells become applied to each other and form an apparently homogeneous blood cylinder, with leucocytes scattered here and there. The condition is termed *venous stasis*. (Fig. 2.) With the increase in pressure there occurs an increase in the exit of fluid from the vessels, and after a time single and then numerous red cells are pressed through the wall. This process, termed *diapedesis*, occurs especially between capillary endothelia, where a weaker intercellular substance fills the interstices, which become loosened by the filling and distention of the vessel as the endothelia are dragged apart. Such openings are called *stomata* (*stigmata*). By reason of this diapedesis the exudate becomes hemorrhagic. It occurs only in capillary and small venous channels, not in arterial.

Complete and lasting stasis is equivalent to local asphyxia and death (necrosis) of the part involved, for as no new blood can be supplied no interchange of gases or nourishment of the cells is possible.

In most of the cases observed in practice the stasis is not so complete, only a severe interference with the venous flow existing, with local increase of pressure, dilatation of the vessels, and slight hemorrhagic exudate, but without the worst feature of complete stasis, namely, the necrosis. Then supply and outflow of blood become equalized while the part remains distended with blood and its internal pressure is high.

The causes of venous congestion vary. There may be a mechanical obstacle to the venous flow, or the influences which normally tend to slow it may be increased, or some of the auxiliary influences may be removed. The latter two causes seldom act independently; more commonly they coexist with causes of the first variety.

A mechanical obstacle may cause either local or general stasis. If cardiac weakness prevents entire emptying of the ventricles the aortic system receives less blood and arterial pressure sinks, and on the other hand, blood from the venæ cavæ cannot enter the imperfectly emptied right ventricle during the diastole, and hence there is a regurgitation into the venous system with increase of pressure there. From the decreased arterial and the increased venous pressure there is a marked slowing of the stream and rise of pressure in the capillaries. In similar ways uncompensated valve lesions result in imperfect emptying of the heart, with resulting venous engorgement.

The commonest cause of local stasis is the plugging or compression of a vein with complete closure of its lumen; but because of the rich venous anastomoses about most arteries, a large vein or even several may become impermeable without necessarily producing any stasis in their distribution. Such anastomoses are called *collateral*. Clearly the stasis must be more marked when the collateral circulation is less developed. Hence we observe but slight venous congestion after ligature of a femoral vein, or if it appears it is soon relieved, while closure of a main branch of a portal vein, of the spermatic, or of the great vein of Galen, causes profound venous stasis in the corresponding abdominal organ, testicle, or portion of the brain. With incarcerated hernia the stasis may be complete and lead to necrosis. When at the same time both artery and vein are closed, venous engorgement fails to appear.

A further or greater cause of venous congestion is found in diseases of the respiratory organs. Paroxysms of coughing congest the jugular veins, and when numerous lung capillaries are impermeable, general passive congestion may follow, with imperfect filling of the heart. (See Chapter VI., 1.)

Among the auxiliary influences affecting the venous circulation, whose failure may cause congestion, may be mentioned the *vis a tergo*, derived from arterial pressure, as seen with uncompensated valvular defects, loss of the elasticity and contractility of the venous walls, and insufficiency of the valves in the veins from varicose dilatation. Respiratory disorders also act through interference with the normal inspiratory hiatus. As is well known, contraction of the voluntary muscles, between which the veins lie, aids the venous return.

As an increase of normal conditions which tend to slow the current, may be mentioned gravity, as when with continued upright position there are no movements of the leg muscles, so that gravity gradually

causes varicose dilatation of the veins of the legs. Dilatation of the hemorrhoidal veins causes piles. Such effects are accentuated when cardiac weakness prevents emptying of the venæ cavæ or obstacles occur to the flow in the large veins. Hence varicosities appear frequently in pregnancy, for the gravid uterus compresses the pelvic veins, in the upright position especially. In the internal organs gravity acts with heart weakness to produce *hypostatic* congestion, especially in the lungs, where in dorsal decubitus, with imperfect respiration, the blood collects in the posterior portions of these organs.

Since the blood remains in contact with the cells of an organ for too long a time during venous congestion, it gives up its oxygen completely and takes more carbon dioxide. Hence the blood and parts congested become dark blue, cyanotic, as may be noticed during life on the fingers, toes, and visible mucous membranes. After death the distended vessels appear as distinct branching pictures, more prominent because of the post-mortem hypostasis (p. 21). Pressure in the veins is increased because the arterial pressure is carried over. The temperature of the part is low because of lessened supply of warm blood, and the consistence of the part is increased by transudation or edema. Lack of oxygen gives rise to functional disturbance, as in the brain, where dizziness and depression occur, in the lungs dyspnea, from the kidneys albuminuria, according to the organ involved. In chronic cases sensitive tissue elements may atrophy from increased intracapillary pressure, as in the liver and kidney, and varices may develop in the veins. The wall of the vein and the adjacent fibrous tissue may undergo a fibrous hyperplasia, which with the distended and tortuous capillaries gives the part a decided firmness as well as a bluish color; this is called *cyanotic induration*. As an accompanying condition we may find hemorrhagic infarcts and pigmentation, the latter being the result of diapedesis during the stage of stasis. (See Section B.)

Anemia.

Local anemia, as distinguished from the poverty of blood which is part of a general blood condition, may arise from lessening or stoppage of the arterial supply, the venous flow being free. Diminished cardiac activity, as appears from the former chapter, does not produce anemia of the organs, although supply is lessened, but rather venous engorgement from imperfect venous return. Pronounced local hyperemia receives the special name of *ischemia*.

Local anemia may result from external pressure, but only when this is so severe that both arteries and capillaries are compressed. Slight degrees of pressure affect the thinner walled veins and cause stasis. A good example of pressure anemia is seen with the use of the Esmarch bandage; also in pressure from tumors and large collections of exudate in various body cavities.

Pronounced ischemia occurs with plugging or other impermeable conditions in an artery in regions where supplies cannot be received from other vessels; when, in other words, the closed vessel has no peripheral anastomoses with other arteries, or when these, though present, are insufficient. (See Section E.)

Narrowing of the vessel lumen also lessens the blood supply; this occurs with disease of the vessel wall, and the intima may be thickened to complete closure. *Spastic anemia* is the name given to imperfect blood supply from severe vasoconstriction. This is usually temporary, and follows exhaustion of the muscle fibres from long dilatation, but it may persist and even cause necrotic changes in the tissues. Neurotic influences are engaged in this result as well as local, as can be demonstrated by irritation of the sympathetic, a condition observed in some one-sided migraines with tonic spasm of the vessels. Spastic anemia may be reflex.

The local action of cold, especially associated with rapid evaporation, causes paleness and coolness of the skin.

With congestion of certain parts a compensatory anemia of distant organs must occur; this may be termed *collateral anemia*. Thus rapid evacuation of serous transudates from body cavities may cause disorders of consciousness when accompanied by the secondary fluxion already mentioned (p. 24). Section of the splanchnic nerve has a similar effect in causing marked hyperemia of the abdominal organs (p. 24).

The results of anemia are local paleness, loss of heat and volume, cessation of nutritive and excretory processes, with collection of catabolic products which cannot be removed after the blood current ceases. These symptoms depend upon the degree of anemia, the vascular relations of the part, and the sensitiveness of the organ involved. At first there is an attempt to equalize the circulation, for blood flows in larger amount from the site of the closure or obstacle into the neighboring vessels. This collateral hyperemia comes from the vessels just proximal to the closure, or, in paired vessels, through the unstopped artery. After ligation of one carotid the same amount of blood as

before reaches the brain through the other carotid and the vertebrals, so that the loss through the tied vessel is made good. Ligation of the femoral in the thigh causes widening of the profunda, and the vessels of the leg are supplied through the anastomoses about the knee. Even ligation of the aorta is followed by dilatation of the internal mammaries and epigastrics, so that blood may reach the lower extremities by this road. In such cases, then, there develops a collateral circulation, as also for the veins noted above, which carries blood to the organs in a roundabout way. In many cases this substitute for the normal supply may not be adequate to support the nutrition of the part, which is dependent not only on the number of widened vessels but also on their limit of dilatation and the cardiac force necessary to fill them. The question will be treated again when considering embolic infarction.

If anemia is complete and persistent the tissue must die in *anemic necrosis*. Sensitive organs lose their function at once, as is seen in Stenson's experiment, where ligation of the aorta causes anemia of the lumbar cord and paralysis of the legs. Slight degrees of anemia cause functional disturbances, as loss of consciousness or convulsions when the brain is affected, analgesia of the skin with *cutis anserina* from spasm of the *arrectores pilorum*, and in general anemia local ischemias are common, probably associated with vasomotor influences.

B. HEMORRHAGE.

The word *bleeding* (*hemorrhage*) indicates the exit of blood from the vessels. Gross lesions of the circulatory system, such as incisions, must of course be followed by bleeding, as is also erosion of a vessel by ulcerative processes. The former is called hemorrhage by rhexis, the latter by diabrosis (hemorrhage *per rhexin* and *per diabrosin*).

But without mechanical injury to the vessel wall, as we have seen with stasis, blood may leave the vessel. The red cells do not escape by rupture of the wall, but through places where there is much intercellular substance between endothelia, which loosens and makes stomata as the capillary wall stretches. This kind of exit of blood is called diapedesis, or hemorrhage *per diapedesin*.

Hemorrhages are named according to the organ from which they come or according to their gross appearances. Thus bleeding from the nose is called *epistaxis*; from the stomach with vomiting, *hematemesis*; from the lungs, *hemoptysis*; from the kidney with actual red cells in the urine, *hematuria*, distinguished from *hemoglobinuria*, in

which only dissolved blood pigment is present. Collections of blood in the serous cavities are called *hemopericardium*, *hemothorax*, etc., according to their site. Hemorrhage from the uterus is called *metrorrhagia*; in the brain with sudden loss of function, *apoplexy*. Large amounts of blood in connective tissue, which cause external protuberance, are known as *hematomata*; small flat extravasations in the skin are called *ecchymoses* or *petechiæ*; larger amounts, with alterations in the color, *sugillations* or *bloody suffusions*. The vessel from which the blood is lost gives the terms arterial, venous, and capillary hemorrhage; all three together are called *parenchymatous*, as is seen after artificial anemia by compression, when the bandage is removed and blood pours from the wound surface.

By far the most common cause of loss of blood is a trauma of the vessel wall. Other spontaneous hemorrhages may be explained as due to disproportion between the blood pressure and the vascular support, a disproportion which may come from great increase of pressure or from disease of the vessel walls with lessened stability. Both causes may act together. Increase of pressure occurs with active and passive congestion, and bleeding may follow both. With a tendency toward stasis the bleeding by diapedesis is the more common, giving the accompanying exudate a hemorrhagic character, and, as in strangulated hernia, leading to a complete hemorrhagic infiltration of the part. Here also belong cases where the pressure is too high in a relative sense, as with cupping-glasses, where exhaustion of the air causes a negative external pressure. Ascent above the sea level implies similar relief of atmospheric pressure, and may cause hemorrhages. In both active and passive congestion the tendency toward rupture of the vessel wall increases if it is weakened by disease, as with fatty degeneration (especially of small vessels), varix, and aneurism, so that slightly increased pressure may lead to bleeding. Thus extreme emotion, when the heart is hypertrophied and the vessels weakened, may cause not only small but even fatal losses of blood, and when vessels are young and sensitive, as in granulation tissue, such results are not uncommon.

In parts which have been the seat of ischemia the capillaries tend to give way later, probably because of nutritive disturbances. Thus may be explained some of the hemorrhages which follow plugging of an artery, for after the primary ischemia the capillaries are suddenly over-filled by the collateral circulation. In this way most of the *hemorrhagic infarcts* arise, a name given to uniform infiltration of a part by

red cells. Here we notice only that some infarcts arise from a primary hemorrhage rather than from closure of a vessel.

Many of the small hemorrhages which arise in the course of general diseases may be referred to stoppage of small vessels or alteration of their walls. With this there exists also an alteration in the composition of the blood itself, which favors its passage through the vessel. The group of infectious diseases is marked by such bleedings, especially in the septic and pyemic affections, where plugging of vessels by masses of bacteria or septic emboli occurs, as in cutaneous bleedings with malignant endocarditis; yet this rule does not hold for all such infections.

In acute yellow atrophy of the liver, phosphorus poisoning, severe icterus (cholemia), and other diseases, similar lesions are noted, and many of these may be explained by the fatty degeneration which attacks the capillaries. In the essential diseases of the blood, as pernicious anemia, chlorosis, and leukemia, fatty changes in the vessels have been found, but doubtless the alterations in the blood itself take part in the causation of such hemorrhages. In many of these cases congenital abnormalities of the vessels, as unusual narrowness, may also play a part. A special disposition to hemorrhage leads to multiple spontaneous bleedings or relatively enormous losses after slight injury; this is called the *hemorrhagic diathesis*. In scorbutus there is bleeding from the gums, which are ulcerated and infiltrated with blood, as the result of errors in diet (insufficient supply of vegetables), with bleeding in the joints, skin, and mucous membranes. In the skin such a purpura scorbutica is observed in the form of multiple ecchymoses. *Purpura hemorrhagica*, or *morbis maculosus* of Werlhof, is also accompanied by large bleedings in the skin and organs.

The congenital form of this diathesis is called *hemophilia*, and shows strong heredity (as in "bleeder" families). It is commonest among males, but is inherited through the females, sons of daughters whose fathers were bleeders especially inheriting the tendency. As trifling injuries in such persons lead to great or even fatal hemorrhages, it is assumed that there is a congenital lack of coagulability in the blood as well as a liability of the vessels to tear.

In the aged a *purpura senilis* occurs which may be explained by atheromatous changes in the vessels. Bleeding due to nervous influences is still of uncertain etiology, though it occurs in the lungs when there are severe lesions of the brain, in the skin with marked general neuroses (as in hysteria with stigmata), and, in the case of

vicarious menstruation, from the alimentary or respiratory organs. These are in all probability related to vasomotor influences.

When blood has passed from a vessel into the tissues it undergoes certain regular changes: coagulation, absorption of the fluid portion, loss of color in the red cells and its imbibition by the neighboring structures and solution of the fibrin, leaving a mass of detritus. The blood pigment passes through a series of colors—brownish-yellow, green and blue—and leaves a certain amount of pigment at the site of the bleeding. If the hemorrhage was accompanied by tissue destruction there is a regeneration which ends in cicatricial replacement of the clot. In the brain such foci may organize only at the periphery, while the centre remains fluid, clear, or with detritus and pigment, forming a kind of cyst. Similar changes are noted when blood escapes into a body cavity. The bleeding may be arrested spontaneously by formation of a white thrombus at the opening of the vessel, and this becomes organized and permanent.

The results of hemorrhage may be either general or local (see Chapter VII., A.), and the latter depend both upon the amount of the loss and also upon the constitution of the organ involved; thus in the skin or in connective tissue the results may be unimportant for the general health, but in the lungs or central nervous system loss of function (apoplexy), or even death, may at once follow.

C. EDEMA. DROPSY.

There is a constant interchange between the blood and the tissues about the vessels through the transudation of the fluid plasma into the neighborhood; this, in physiological conditions, makes the *lymph* or *tissue fluid*. The process was formerly regarded as a passive leaking from the capillaries; the accepted view at present refers it to a selective action on the part of the endothelia, a true secretion. The lymph furnishes to the cells of the tissues their nutrition and removes at the same time the products of their catabolism. The spaces through which the fluid passes end in a lymphatic system of vessels, and these pass through lymph nodes to enter at last into the great venous trunks. Lymph may thus be regarded as the tissue fluid which has been altered by reciprocal interchange between it and tissue elements and afterward collected in the lymphatic vessels. Not all of it returns by this system; undoubtedly some is taken up again directly into the blood capillaries. Lymph is distinguished from *plasma* by its lower

percentage of albumin, while its dissolved salts are about the same. It also coagulates less readily because its proteid elements are chiefly serum albumin, serum globulin, and a trace of fibrinogen or fibrin ferment; it contains white blood cells, however. The various parts of the body and the serous fluids which bathe the serous membranes are not uniformly of the same constitution, notably in their albumins.

The special variety of lymph which flows in the lacteals of the alimentary tract bears the name of *chyle*. It is remarkable for its large proportion of fat, which is in microscopical globules and gives it a milky appearance.

When the tissue fluids in a part are collected in abnormal quantity the term *edema* is applied to the condition, and the fluid is called a *transudate*. In general the fluid is of a clear yellow hue, alkaline reaction, and does not coagulate or contains small traces of fibrin. In its chemical composition it corresponds with normal tissue lymph, or blood serum, contains less albumin than does plasma, and has a lower specific gravity. Plasma contains from 8 to 10 per cent. of albumin, edematous fluid but 0.5 to 2 per cent.; but variations in this regard are more marked than in normal lymph. The composition of the blood influences this percentage, for in hydremic conditions there will, of course, be less albumin, and blood plasma may be mixed with the transudate; bile pigment in icterus and urea in uremia are also commonly found in it. Other cell products, as mucin and fat, may also be present.

Edema may be general or local in distribution, and in the latter case its site determines its name. Dropsy, in the strict use of the word, means transudation into the body cavities, and the special names hydrothorax, hydropericardium and ascites indicate that the collection is found in the pleura, pericardium, or peritoneum. In the cerebral ventricles it is termed *hydrocephalus internus*; in the joints, *hydrarthrosis*; and in the scrotum, *hydrocele*. Edematous infiltration involves the tissue spaces of an organ, as the lungs, brain, or muscles, and in the skin, if widespread, is called *anasarca* or *hyposarca*.

The edematous parts are swollen and of soft, doughy consistence, the cells and fibres are swollen, especially in tissues rich in mucin, and the cells may be loosened from their attachments and float free in the fluid. The organs involved are enlarged, and their capsules tense, while the skin also becomes stretched, the elasticity of the part diminished, and pressure as by a finger leaves a marked depression. If an incision is made into it the edematous tissue exudes large amounts of

clear fluid, and gentle squeezing increases this outflow. When large collections compress the vessels the part may also be of a very light color.

The causes of edema are the various pathological conditions which influence the modus of normal lymph production. The exit of fluids from the vessels increases, either because of increased intracapillary pressure and lessened resistance of tissues, heightened permeability and secretive activity of the capillary wall, or from changes in plasma and lymph; or there is an obstacle to the flow of lymph from the part, with rapid accumulation. At times several pathological factors enter into its production, and the collection depends not only on their intensity, but also on predisposition (hereditary dropsy) of the organism and the site of the transudate. This appears from both local and general edemas, for general diseases are not uniform in their production of edema, but affect certain regions by preference. The loose areolar tissue of the eyelids and the external genitals, the dorsum of the foot, the ankles, and legs are among the earliest places to show slight swelling and pitting with general circulatory disorders. The prevailing factor in causation gives the name to the form of dropsy, arterial hyperemia being followed by congestive edema or dropsy, and venous by passive edema.

The *dropsy of stasis* occurs especially with obstacles to the venous current (p. 25), the tissue fluids increasing because of greater pressure in the capillaries and small veins, nutritive changes in their walls, and lower resistance of the tissues. Hence the degree of the edema corresponds with the completeness of the venous hindrances, and may disappear if collateral circulation is at once established. Hence where a collateral route cannot form, as with hepatic cirrhosis and compression of the portal vein, a persistent edema of the peritoneum (*ascites*) usually develops. The communications of the portal with esophageal, renal, spermatic, and parietal veins are insufficient in such cases. In the limbs, closure of even a large vein causes but temporary edema, but pressure of the gravid uterus on the large veins of the pelvis may produce marked infiltration below (p. 27). If the arterial supply is cut off at the same time there is no edema, but if active hyperemia coexists the edema is particularly evident. Hence ligation of the vena cava with section of the sciatic causes severe edema of the legs, because of the arterial hyperemia from paralysis of the vasoconstrictors which is added to the stasis. With uncompensated valve lesions and cardiac weakness of all sorts, general passive edema is almost constant

with the general stasis, but even here there are special regions which are most affected.

A second factor in passive edema is found in hindrance to the lymphatic flow, but this is less important than venous stasis, because with the rich anastomoses between lymph channels a complete stasis of the lymph is almost impossible. Even closure of the thoracic duct may not be accompanied by edema, but with interference with the lymphatics over large sections, as in elephantiasis, lymph stasis may occur and produce edematous infiltration.

As a general rule, acute hyperemia merely tends to increase the amount of fluid transudate; only with added stasis, or inflammatory irritation, or hindered lymph circulation does a pronounced edema follow. Thus the chief element in its production is not so much the hyperemia as the factors which may have been added. This is the case with the collateral edema which develops over a wide extent about foci of inflammation. There is a transition here between the edematous fluid and the inflammatory exudate, the latter containing more albumin, but it may be difficult to define the limits of either with accuracy.

Greater etiological importance may be ascribed to the congestive hyperemia with edema which accompanies certain neuropathic conditions, paralysis, etc. Thus in myelitis, sciatica, tabes, hysteria, Basedow's disease, and others the vasomotor apparatus appears to be involved. Thermic influences (burns with vesicles, edema after freezing), and traumatic and toxic irritation of these nerves and the vessel walls, either direct or reflex, may be followed by edema. If temporary in any one site it may be called *edema fugax*. Probably the affected nerves cause alterations in the blood and lymph, but other elements enter in, such as lessened muscular activity in the paralyzed regions and abnormal secretion and permeability of the endothelia.

All these forms of edema are grouped under the name of *mechanical dropsies*, from the nature of their cause, and these are contrasted with the edemas of dyscrasia.

The latter variety is symptomatic of conditions affecting the blood, as decrease of its albumins (hypoalbuminosis), albuminous losses through the kidneys (albuminuria), relatively increased percentage of water (hydremia), and at times an actual hydremia due to increased retention of water in the body. Such *cachectic* or *dyscrasic edema* is common in chronic kidney disease, amyloid degeneration, scorbutus, malaria, primary and secondary anemias. In the diseases which are marked by decreased renal function it is probable that the body retains

its water, and the fact that edema may not develop even with severe kidney disease so long as another way for excretion of water is provided, by sweating or diarrhea, appears to corroborate this view. Moreover, in such vicarious excretions the presence of urea may be demonstrated and the edema may vary with its proportion.

In hydremia the watery composition of the blood increases the rapidity of filtration and diffusion throughout the body, as may be demonstrated by large transfusions of normal salt solution, increasing thus the lymph and excreted water with edema of certain organs. With persistent edemas the increased permeability of the vessel walls is of even more importance, and with hydremic plethora blood pressure also acts. The tissues suffer in their nutrition because of the abnormal constitution of the blood, and lose their elastic resistance. Certain toxic substances which may enter the blood in many of these diseases act as lymphagogues, and thus, as in scarlet fever, edema may develop either before or with renal complications, from irritation of the secreting capillary endothelia.

The localization of the edema in dyscrasia in special regions appears to be both mechanical and circulatory in origin, and the general edemas of late kidney disease are evidently connected with loss of power in the heart. These are consequently in great part stasis edemas (pp. 27, 35).

Senile and marantic edema belong to this group, depending on imperfect muscular activity of respiratory and circulatory organs, with accompanying cachexia, and also the so-called *hydrops ex vacuo*, which fills out atrophied regions and tissue losses. Thus atrophic dilatation of the ventricles of the brain may be accompanied by *hydrocephalus internus*, and atrophy in the subarachnoidal spaces by *hydrocephalus externus*.

False dropsy is the name given to collections of fluid in preformed mucous cavities, from closure of their ducts and distention, with retained secretions. The fluid may be a thin serous or a thickened mucous collection. The common sites are the gall-bladder, the appendix vermiformis, the uterus, the tubes, and the renal pelvis.

The consequences of edema vary with the location and the organ. Edema of nerves may cause loss of function and even complete degeneration. The cause of the transudation is also of importance. Dropsy of cavities may exert compression on contained viscera, as atelectasis in the lungs, compression of the brain, etc. In the skin, closure of many lymph channels, with inflammation, is observed in elephantiasis.

Lymphorrhagia.

Rupture of lymphatics may set the contained fluid free on the surface of an organ or in a cavity of the body, and if the opening remains unclosed a fistula may constantly discharge lymph. The condition is termed *lymphorrhagia*. The very low pressure under which the lymph flows prevents this result unless large vessels are torn, as when the thoracic duct is compressed or plugged by tubercular or neoplastic material, scars, etc., or opened by trauma. The lymph is held in the pleura, pericardium, or elsewhere, and may be mixed with serum, forming the milky collections called *hydrops chylosus*.

Chyluria occurs when the urine contains fat, albumin, and white cells, giving it a milky look, from the presence of the parasite *distoma hæmatobium* in the lymphatics of the bladder and abdomen.

D. THROMBOSIS.

Coagulation of the blood consists in the change of part of its albumin to insoluble fibrous material, the element in the blood from which it forms being called fibrinogen, and the action being due to the influence of an enzyme, fibrin ferment, or thrombin, which changes it to fibrin. This occurs only in the presence of calcium salts.

The physiology of the process is still under discussion, but it is assumed that fibrin ferment is formed from a prothrombin by means of substances which exist in the red and white cells and the blood plates and are set free by their solution (plasmoschisis). Another condition of coagulation is adhesion of the blood to foreign objects, for in a vessel lined with vaseline or oil it does not occur, nor in a vein between two ligatures unless the wall be injured.

Fibrin separates out as long threads in which the cells are entangled. Thus the clot is formed, the fluid portion remaining is the serum.

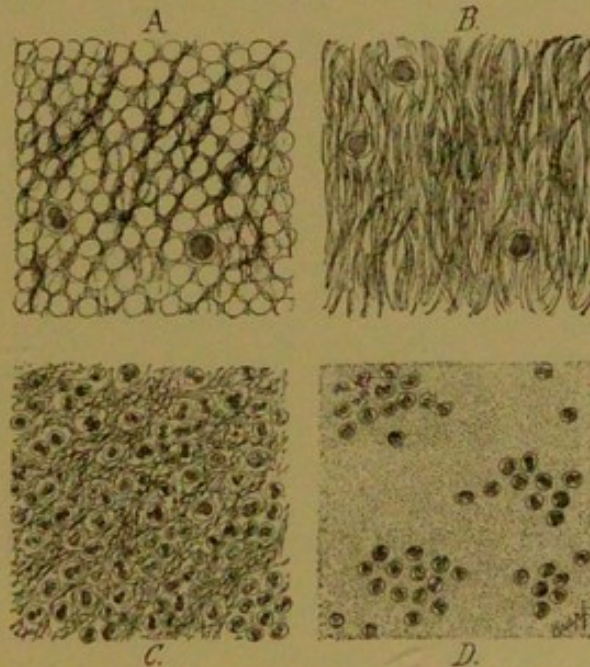
When coagulation occurs slowly the red cells may sink to the bottom of the container, and the fibrin may include so few that the clot is yellow, tough, and elastic, making the so-called fatty clot. (Fig. 1, B.) Such clots are found post-mortem in the heart and great vessels (p. 21).

When there is a coagulation of the blood in the vessels during life the process is called *thrombosis* and the product a *thrombus*, but the process is not identical with clotting outside the body, and has not been wholly explained. It is certain that in thrombi all the elements of the

blood may be separated out, both those normally present and others which enter into the fluid only under special conditions. Among the former are the cells, white and red; among the latter are blood plates and fibrin. It has not yet been determined whether the blood plates are present in circulating blood, or whether they are a precipitate of globulin, or are extruded from the red cells, while white cells are thought to form similar bodies at times. In the recent state the plates are small, colorless, round or oval scales, but very soon they change to finely granular or homogeneous masses. (Fig. 1, *D*.)

Although blood cells, red and white, plates, and fibrin assist in the formation of thrombi, many varieties of the process are known, and the

FIG. 1.



A. Blood clot. *B.* Fibrin coagulum. *C.* White-cell thrombus, with fibrin. *D.* Plate thrombus, with scattered leucocytes.

single elements separate under various conditions. Each of them alone may form a thrombus, but usually all are found. Fibrin especially is an essential part of all large and firm thrombi.

While fibrin ferment may be assumed as present and coagulation is important for some thrombi, others appear to depend upon the tendency of white cells and plates to collect on the wall of the vessel, when it or the blood stream is abnormal, and there fuse to firm masses. Thrombosis hence may occur not by coagulation but by precipitation and agglutination, a viscous metamorphosis of plates and leucocytes, and similar agglutination of red cells has been noticed above under Stasis (p. 26).

The conditions favoring thrombus formation may be divided into three, changes in the blood itself, changes in the blood current, and changes in the vessel walls. In the first of these the essential element is the presence in the blood of substances which provoke coagulation, and it is of great practical importance that the blood of another animal, even though defibrinated, will cause thrombosis when transfused. A second series of foreign materials which have the same effect when found in the blood includes ferments, decaying substances, albumin, etc. Of more importance is the fact that after extensive traumatism of tissues a substance like fibrin ferment, derived from the destroyed cells, may be absorbed and cause fever (aseptic wound fever), and, in large amount, thrombosis.

FIG. 2.



Plate thrombus. *f* Fibrin. *p* Blood plates massed as fine granules. *z* Leucocytes. $\times 49$.

The chief alterations in the blood stream are its slowing and the formation of eddies at special intravascular sites. The most important of this variety are the *stagnation thrombi* which occur with slow or stagnant blood currents, but simple cessation of the flow is not enough in itself to cause it. Careful ligation of a vessel (without a branch between the ligatures) may not be followed by coagulation even during weeks, so that it is evident that trauma or nutritive changes in the vessel are required in addition to stasis.

A slow change which disposes to thrombosis occurs, in the case of simple ligation, in that part of the tied vessel lying between the ligature and the nearest branch, proximal in arteries and distal in veins.

After application of the ligature most of the blood must be diverted into the branch mentioned, but that contained between must slowly coagulate. In passive congestions thrombi are very apt to form in the peripheral veins.

Compression of the veins acts like stasis and produces *compression thrombosis*.

In many regions of the blood channels there are normally very wide sections, as above the venous valves and in the cardiac chambers, while varices and aneurisms cause pathological dilatation. In such places vortices form from the sudden widening, and, with these, lessened energy of flow, disease of the walls, and blood changes, combine to form clots called *dilatation thrombi*. *Marantic thrombi* form in consequence of cardiac weakness, together with ferment action and toxic influences, especially in the auricles, their appendices, the apices of the ventricles, and the valve cavities of veins.

Changes in the vascular endothelium acquire great importance in thrombosis if we consider that normally these cells prevent coagulation. Roughened places give the blood cells and plates an opportunity to adhere and agglutinate; hence any influences which attack the endothelia lead to thrombosis, whether mechanical or chemical, inflammatory or atheromatous, varices or aneurisms, but especially atheromatous ulcers and calcareous deposits. In the aorta, even with marked roughening from atheroma and great cardiac weakness, it is unusual to find thrombi, while in the smaller vessels slight lesions cause them to form. A similar result follows the entrance of foreign bodies into the vessels and wounds of their walls or of the intima alone.

Thrombi gradually formed by the precipitation of material on the wall or in the valve pockets may be called *parietal* or *valvular*. When these increase to occlusion of the vessel they are called *obstructing* or *obliterating thrombi*; when the increase follows along the course of the vessel it is said to be *propagated thrombus* as contrasted with *autochthonous*, formed *in situ*.

Within the heart the thrombus may become loose and rounded by constant attrition during systole, forming a *ball* or *spherical thrombus*.

The best practical division of thrombi is into red, gray or white, and mixed. The structure of the thrombus depends upon the conditions in which it forms, whether the blood was in rapid movement or stagnant. When the blood is included between two ligatures the clot resembles a post-mortem coagulum in all respects, and includes red

and white cells in about the normal proportion, far more of the red than the white. Between the cells are threads of fibrin (Fig. 1, A), and thus occurs the *red thrombus intra vitam*. After one to two days the thrombus becomes paler, drier, brittle, and more firmly attached to the wall, while the post-mortem clot becomes looser.

In capillary stasis, from any cause, the red cells may fuse to homogeneous cylinders from loss of water and compression by the advancing arterial wave. Such results follow loss of the *vis a tergo* in cardiac weakness, changes in the vessels, vasomotor disturbances, and

FIG. 3.



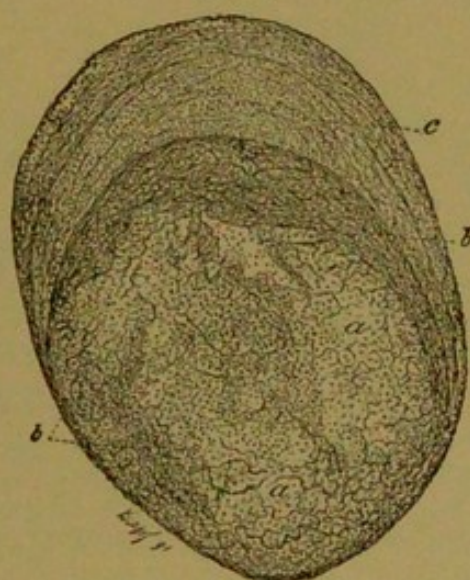
Capillary stasis from a beginning gastric ulcer. *a*. Vessel containing red cells, still preserved. *b*. Stasis. *c*. Stasis with a few blood cells. *d*. Submucosa. *e*. Superficial layers of mucosa; in deeper portions the tissue is partially necrosed, showing no nuclei. $\times 110$.

other slighter influences, and with these may be combined external pressure (decubitus), and trifling injuries (senile gangrene). High temperature, extreme cold, corrosive chemicals, and bacterial products, produce similar results, and in these cases there is probably a chemical change in the agglutinated red cells and partial coagulation of their proteids. For a time the adherent cells may separate and resume their flow if the causes are removed, but in higher grades they are beyond recovery.

Stasis over a large extent of tissue causes in the supplying arteries an increase of pressure, in the corresponding veins a decrease. The former may lead to solution of the stasis, the latter is accompanied with the signs of stasis, transudation, and diapedesis. Complete lasting stasis results in necrosis of the part. In the vessels leading away the stream is so slowed that the white cells collect along the walls and display the parietal disposition of the leucocytes.

Thrombi formed in flowing blood begin by deposit of plates and white cells on the wall, while the red cells pass on, and the amount of fibrin present is relatively large, making a true coagulation. Hence *white* or *gray thrombi* are formed, containing fibrin, leucocytes, and

FIG. 4.



White thrombus formed by leucocytes. *a, c.* Layers rich in cells. *b.* Fibrinous layers. $\times 40$.

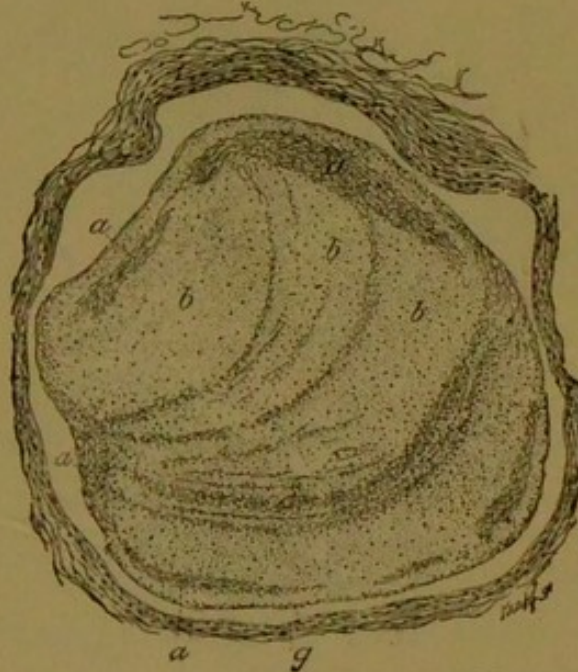
blood plates. The latter commonly lie in heaps, the plates soon losing their usual form and fusing to a homogeneous or granular mass. (Fig. 2.) Pure blood-plate thrombi and pure white-cell thrombi may occur, the latter especially in leukemia. (See Chapter VII., A.) Pure fibrin thrombi are also probable, but commonly we find the coagulum made up of several elements. The plates are to be recognized only in the fresh state, for finely granular precipitates may be formed out of fibrin and leucocytes as well. At times the fibrin threads appear to be arranged in radiate lines about white cells as centres.

The nearer the stream approaches stagnation the larger is the proportion of the red cells mixed with the thrombus, for they have time to

settle and adhere to the wall during its formation. Since in the flowing blood the admixture of the cells is not constant, and thrombi do not form suddenly, we find in parts of the clot more red cells and in other parts more white, so that there is a clear striation or stratification of the thrombus (Fig. 5), and to this the name *mixed thrombus* is given.

Red thrombi, then, more closely resemble blood clots, the white resemble fibrinous coagula. The former, beside the characteristics noted above, differ from a clot in the larger proportion of the included white cells, but if formed in stagnant blood they may contain no more. The mixed thrombus is notable for its colors, layers, and structure.

FIG. 5.



Stratified thrombus, chiefly red. *a.* Layers with fibrin and leucocytes. *b.* Red cells.
g. Vessel wall. $\times 40$.

The white variety might be confounded with fibrin coagula, but differs in being firmer, brittle, dull gray, dry, and more firmly adherent to the vessel. The fatty clot contains little beside fibrin, while the microscope shows in the white thrombus more cells and blood plates, in alternating layers. (Fig. 2.)

Thrombi often present softened portions, especially the plate thrombi, and the entire mass or only its axial portion may be puriform. When the plates and fibrin become dense and transparent the thrombus is called hyaline. When once formed it is common to have secondary clots collect about a thrombus, and after a time new connective tissue grows into it from the vessel wall, with new vessels, and it is said to

become organized. (See Chapter III., C.) Softening is common when thrombi lie in foci of inflammation. (See Chapter III., B., 5.)

Embolism and Metastasis.

Pieces may break from a soft and recent thrombus, or from a softened one, and be carried on with the blood stream until a passage is reached which is too narrow. Here the fragment, called an *embolus*, lodges, and the process is *embolism*. In the superficial veins mechanical influences may break off such particles.

In an artery an embolus is frequently caught at a point of bifurcation where the lumen suddenly narrows, and long emboli may reach into two branches, riding upon the fork. If the vessel is entirely closed by the embolus, or by secondary coagulation about it, the results

FIG. 6.

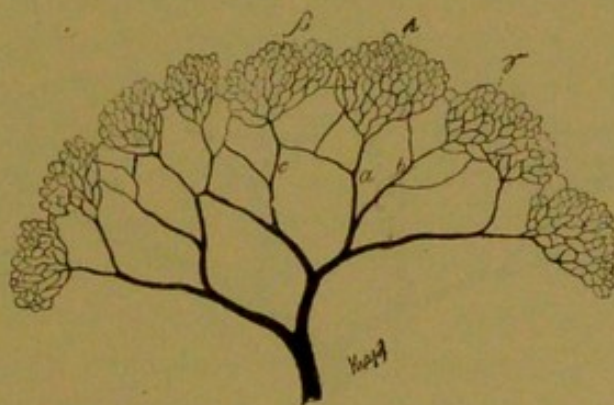


Diagram of branches with free anastomoses. Both the vessels, *a*, *b*, *c*, and their capillaries communicate with each other freely.

are arterial anemia in the distribution of the vessel and collateral hyperemia of adjacent arteries. If anastomoses are abundant between the branches and capillaries of the plugged artery, blood makes its way into the anemic region, with immediate hyperemia and an equalization later.

In other cases the closure of the artery leads to lasting disorders of circulation in the part, with nutritive lesions. There are hindrances to the blood flowing in from the neighborhood, not all of which are of the same kind nor wholly understood. Thus if the part is already in a condition of venous engorgement and high pressure, the pressure is increased by the collateral hyperemia and the capillaries are dilated to their maximum (p. 26). In other cases capillary stasis and thrombosis prevent the entrance of new blood, probably because of changes in the endothelia from the anemia. Lastly, the venous

stream may return in the reverse direction, into the capillaries, and thus oppose the collateral supply.

All these factors which influence the entrance of new blood are especially operative where the vascular supply of a part is naturally poor, where the arterial anastomoses are few and small, because the hindrances to collateral hyperemia are not easily overcome. (Fig. 7.) At times the distention and stasis in the capillaries lead to diapedesis in such measure that the previously anemic part becomes infiltrated with red cells and takes on a dark-red color. Thus occurs the apparent paradox of severe bleeding from closure of an artery. This condition is named *hemorrhagic embolic infarction*. The tissue in which it occurs suffers nutritive changes, becomes necrotic and dies, so that no nuclei may be found in it (p. 54).

FIG. 7.

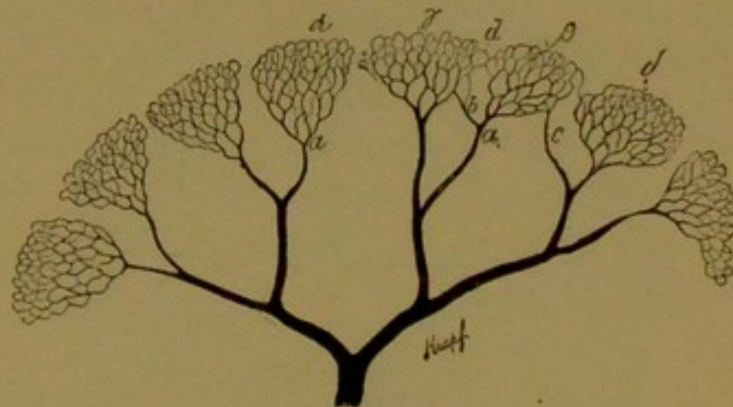


Diagram of "end arteries," with few anastomoses. On the left, true end arteries, *a, a*. On the right, few anastomoses of vessels and capillaries.

In a second variety of embolism the injection of the part by red cells is absent, either because the capillaries have no communications with their neighbors, or because the anastomoses are impermeable from disease, or because cardiac weakness fails to fill them. Then the collateral hyperemia penetrates for only a short distance along the edge of the anemic area, forming a red or even hemorrhagic margin. The infarct itself remains wholly anemic (see Ischemia), and its nutrition ceases, its death is inevitable, and the name infarct, originally meaning hemorrhagic infiltration, is coupled with the adjective *anemic* to distinguish this variety, the *embolic anemic* or *white infarct*.

Beside their origin from closure of an artery, the two varieties are alike in occupying peripheral parts of organs, because the vessels branch more frequently in this direction. Their form is usually conical, with the apex inward and the base on the surface of the organ.

Their extent varies, but seldom is smaller than a pea, for closure of the smallest vessels is usually compensated by collateral supply. The anemic infarct is light yellow, dense, and looks as if the dead tissue were coagulated. Microscopically there is loss of nuclei in the part even in twelve to twenty-four hours.

The central nervous system is peculiar in its behavior after embolism. Infarcts seldom develop, but the anemic area forms a focus of softening, the dead tissue undergoing liquefaction. In its genesis such a softening corresponds with infarction.

The end arteries mentioned above are found most frequently in the brain, heart, liver, spleen, and kidney. In the lung and alimentary tract the arteries may not be strictly end arteries, but their anastomoses may not be adequate in case of plugging, and hence they are called functional end arteries.

Organs with two or more large arteries, with frequent anastomoses between them, seldom are the seat of infarcts.

Corresponding with the anatomical distribution of the arteries, certain forms of infarct are common in special organs, hemorrhagic infarcts being regularly found in some, and anemic in others. The less completely the collateral hyperemia can develop in any case the more likely is the infarct to be anemic, while with more blood from the neighborhood the exit of cells is the more probable, and with immediate and complete restoration of the circulation both infarction and tissue necrosis are prevented.

In the brain the foci of softening are usually anemic. In the kidney, infarcts are most often anemic, unless occurring where an artery passes from the capsule into the renal tissue. Anemic infarcts of the retina are the usual form. In the spleen both varieties are found. In the stomach and intestine hemorrhagic infarcts are easily formed because of the free anastomoses, but they form only when main arteries are occluded. In the lungs in most cases infarction does not occur, because of anastomoses between the pulmonary, pleural, and bronchial vessels; but where the vessels are altered by chronic stasis, so that the blood cannot flow away, infarction may follow. Hepatic infarcts are comparatively rare. (See Chapter X., D.)

Thrombosis and other causes of arterial occlusion can also end in infarction.

The further changes in the infarct are absorption of the necrotic tissue, replacement by new fibrous tissue, with shrinking of the focus and depression of the surface. The new granulation tissue forms an

embolic cicatrix, which is dense, fibrous, and grayish, and still retains the wedge form. In other cases a cyst develops. (See Chapter III., A, 3.) With incomplete temporary occlusion the more resistant interstitial elements of the part may remain uninjured and take part in the replacement fibrosis. In glandular organs the edge of the focus may show gland proliferation. In hemorrhagic areas the hemoglobin undergoes a change to brown pigment, which for a long time may mark the site of the infarct.

With embolism is closely connected the process which is termed *metastasis*, a word of wider signification than embolism, including the transport not only of particles of thrombi but also of all pathological products within the organism, from the primary to a secondary location. The vascular and lymphatic channels may be the path travelled (as well as the tissue spaces).

Corpuscular elements which enter the blood current are carried by it until they reach a part of the vessel which is too narrow, which may be a capillary. Such *capillary emboli*, unless from an infected source, may have no bad effects; if extensive, however, both circulation and function of organs may suffer severely. It is evident that the occlusion of many small or capillary vessels in a part must have the same effect as plugging the main artery by thrombosis or embolism, namely, anemic or hemorrhagic infarction and necrosis. Very small bodies, as single cells and bacteria, may pass the lumen of capillaries or be arrested by their walls, especially in organs like the spleen where the blood flows slowly. But even in organs with end arteries infarction may not result.

The path which the foreign particle travels depends upon the direction of the flow; from the peripheral veins the embolus passes to the right heart and a branch of the pulmonary artery. If the foramen ovale is open or the embolus is small enough to pass the rather wide pulmonary capillaries it may reach the left auricle and ventricle and so the systemic circulation, to be laid away at last in some inner organ or peripheral part. The same is true of particles from the lung or the left side of the heart.

The portal branches form a separate circulation in the liver and are the points of deposit for all emboli coming from the territory of origin of the portal branches.

The lymph takes up material coming from outside the body, as well as that formed within it, and carries it by way of the tissue spaces and lymph vessels to the nearest lymph node, where it may accumulate.

The node then acts as a filter, but its efferent vessels may carry the foreign matter further and empty it into the great veins. In this process the cells of the lymph are active, taking up the granules, carrying them elsewhere and setting them free by their own destruction (*phagocytosis*).

As a rule, the metastasis follows the direction of the lymph flow, but in some pathological conditions there is a reversal of the current, when there is an obstacle to it, which causes a flow in the opposite direction. Thus with carcinoma of the liver or stomach metastasis may occur in the retroperitoneal nodes. With mammary carcinoma it may invade the skin, and these cases cannot be explained otherwise than as due to retrograde flow of the lymph. Thus, also, the regional metastases about malignant tumors develop. In the inferior vena cava a retrograde metastasis into the hepatic vein may take place. It has been assumed that a reflux of the blood might be caused in these veins by alterations in the pressure, the usually negative pressure becoming positive, especially with lesions of the tricuspid and enforced expiration, as in coughing. According to Ribbert, there occurs in general venous engorgement at every cardiac systole a slight reflux wave in the veins, which, by its repeated impulses, may carry a small object along the vein wall gradually toward the periphery, even into a small branch of the vein.

Beside particles of thrombi, all kinds of small objects formed in the body or derived from outside may be carried as emboli, but especially bits of tissue torn off, as from a necrosed valve, products of softening, globules of fat, and living cells.

Fat embolism occurs with lacerations of the subcutaneous fatty tissue or with fractures involving the marrow, if the fat gains entrance to the vessels. Even severe contusions of bones may have the same result. The fat carried through the veins is brought to the right side of the heart and deposited in the capillaries of the lungs. Extensive fatty embolism with large quantities of fat may cause paralysis of respiration and sudden death.

Malignant tumors may break into the blood or lymph vessels, and loosened portions are carried as emboli, like unorganized or necrotic material; but the consequences are worse, for the emboli are living cells, and wherever they lodge produce tumors similar to the primary growth, and thus *metastatic tumors* arise. (See Chapter III., E.)

Air embolism implies the entrance of atmospheric air into the veins, as may happen with wounds of these vessels, pressure in them, at

least sometimes, being negative. The air sucked in reaches the right ventricle and is beaten with the blood to a froth, so that when the heart is opened under water, its vessels first being tied, bubbles are seen to emerge. The difficulty of driving the air out of the right ventricle exhausts it at once or later, and death may follow from weakness of the heart. There may be no air in the heart after death, and the post-mortem appearances are those of asphyxia, the blood being fluid and dark, the veins distended, especially in the abdominal organs, with edema of the lungs and ecchymoses in many organs. The entire removal of the air from the heart depends upon its amount and upon the condition of the heart, small amounts being usually absorbed without injury.

Divers and laborers in caissons under increased air pressure are liable to the formation of air bubbles in the blood, and the condition sooner or later may have a fatal result. The entire circulatory system as well as the heart may be overwhelmed by the air bubbles, and death follows from accumulation in the right ventricle and lungs.

Injuries of the uterus, especially during childbirth, may be followed by inspiration of air into the venous sinuses, and sudden death.

In considering such cases it must be remembered that frothy blood in the right ventricle and air in the blood do not always depend upon air embolism or gas formation in the blood. In the course of the autopsy air may enter the opened veins in the neck, reach the brain, and appear as large bubbles in the vessels of the pia, easily moved along by pressure. Frothy blood is also connected with putrefaction, due to the presence of certain bacteria, which even during the last hours of life may produce gas in the blood of various organs (liver). (See Chapter V.)

Both inorganic and autochthonous *pigment* is frequently the object of metastatic processes through blood and lymph vessels, and phagocytes often carry it from part to part.

Of the organized foreign matters which may be carried by tissue fluids, *parasites* may be mentioned, both animal and vegetable, at times transported from the point of entry, at times from the site of development, secondarily and in complicated ways. Thus cases are known where an echinococcus cyst of the liver has perforated a hepatic vein, entered the right heart, passed through an open foramen ovale and reached the greater circulation. By metastasis certain vegetable parasites may be carried throughout the body and cause multiple abscesses. (See Pyemia, Chapter V.)

CHAPTER II.

REGRESSIVE PROCESSES.

A. NECROSIS.

THE terms *necrosis* and *mortification* apply to the local death of tissue within the living organism. If the part dies slowly, with some of the characteristics of the terminal life processes, it is spoken of as *necrobiosis*.

The causes of such tissue death are multiple.

All circulatory disorders which reduce the blood supply of a part below a certain minimum, and which cannot be compensated for within a certain period, must end in the death of the tissue affected. This is called *indirect* or *circulatory necrosis*. The circulatory disturbance may be due to many causes, as has been mentioned above (p. 45), where the conditions were reviewed which result in local ischemia, with persistence of the same and anemic infarct, or hemorrhage and red infarct. Ligation of arteries and other occlusions act exactly as do emboli and thrombi of the same vessels.

All tissues are not equally liable to injury from temporary ischemia. Thus the epithelia of the kidney die within two hours after the renal artery is tied, while the stroma of the organ remains normal if the ligature is removed after a longer time. Nerve fibres and neuroglia die after a short time in anemic necrosis. Venous engorgement and stasis, and extensive capillary stasis, may lead to a hemorrhagic necrosis in the site of passive hyperemia. Mechanical, thermic, and chemical influences may produce similar effects upon both vessel walls and contents.

In other cases the circulatory disturbance follows abnormal action of the vasomotor nerves. Constriction of an artery by stimulation of its muscle fibres may cause a spastic anemia which in time leads to necrosis, and the symmetrical gangrene observed in anemic, nervous individuals, and the necroses with ergot poisoning, are to be thus explained. A disproportion between vasomotor action and the blood pressure, decrease of the latter and increase of the former, may occur in the course of marantic and nervous diseases, with disorders of the general circulation and localized gangrene. Probably in such cases

there are obstacles to the lymph circulation also, for lowered arterial pressure tends to delay the latter.

Connected with pathological innervation of the vessels are the neurotic necroses observed with certain diseases of the nervous system, in lepra, herpes zoster, and after section of the trigeminus. Possibly certain nerve fibres are specially concerned with nutrition, as appears from certain forms of atrophy which follow removal of nervous control. (See Chapter II., C.)

With great certainty we can name chemical, thermic, and mechanical agencies as immediate causes of direct necrosis. Severe pressure upon a portion of the body, contusion and tearing, are often followed by the death of large areas, and strong jarring of the body may be followed by necrosis of many ganglion cells and nerve fibres. In very sensitive organs the trauma resulting from copious bleeding is enough to lacerate the tissue and cause necrosis, as seen in the extensive destruction of the brain after apoplexies.

Among chemicals, concentrated mineral acids determine the coagulation of the tissues at the point of application, and thus produce the so-called corrosive eschars; as is observed when they have been swallowed, lips, buccal mucous membrane, and stomach being thus coagulated and dead in places. By imbibition of altered blood pigment the parts may take on a brown or black color. Caustic alkalis produce a swelling and partial solution of the upper layers of parts attacked. In many cases of poisoning the absorption of toxic substances causes necrosis in distant organs, as in the excreting intestine and kidneys (mercury and chromic acid).

Thermic action, burns and freezing, may directly produce cell necrosis. (See Chapter VI., 2.)

For necrosis with inflammation, see Chapter III.

The various forms in which necrosis appears differ much among themselves according to the constitution of the area attacked, the cause of the lesion and the external influences to which the necrosed part is exposed. The simplest case is where necrosis occurs in a region of tissue by the sudden stoppage of the circulation or by mechanical agency, and the part is then protected from all external influences. This happens in thrombotic and embolic infarcts, especially in the anemic kind, where the collateral diapedesis is absent. The dead tissue is not left to itself, but is exposed to the influence of surrounding tissues and hence does not behave like a portion of the body removed and dead or a portion of a dead body.

Microscopically an important change may be detected after twelve to twenty-four hours which distinctly indicates the death of the tissue. This is the complete disappearance of the nuclei of the cells, which cannot be restored or found by use of acetic acid or staining methods.

This disappearance of the nuclei begins as a karyolysis, the chromatin losing its affinity for staining fluids. (See Chapter III., Introduction.) Then the chromatin, often after peculiar rearrangement of its particles, breaks into non-staining fragments (*karyorrhexis*). The dying nuclei

FIG. 8.



Recent anemic infarct of the kidney. *a*. Nuclei lost in most epithelia. *b*. Karyorrhexis. *c*. Condensation (pycnosis) of desquamated epithelia and their nuclei. *d*. Leucocytes in capillaries between tubules. $\times 350$.

may become smaller and more dense (*pycnosis*), with more intense staining reaction, and dissolution may then follow. The achromatic portion of the nucleus and the cell protoplasm become altered so that they cannot be distinguished from each other, but form a finely or coarsely granular mass, with vacuoles, in which no trace of a nucleus can be found. Other changes may be so slight that the tissue can be recognized as glandular or vascular, or the entire region may become converted into a mass of homogeneous or granular, structureless material.

The loss of chromatin may depend upon the lymph streaming into the part from the neighborhood, dissolving out the chromatin. When such lymphatic flow through the part is absent the nuclei may remain for a longer time unchanged.

In the gross the necrotic tissues differ according to their structure. Dense tissues, like elastic tissue, cartilage, and bone, show no visible changes for a time after they die. Where anatomical changes occur

FIG. 9.



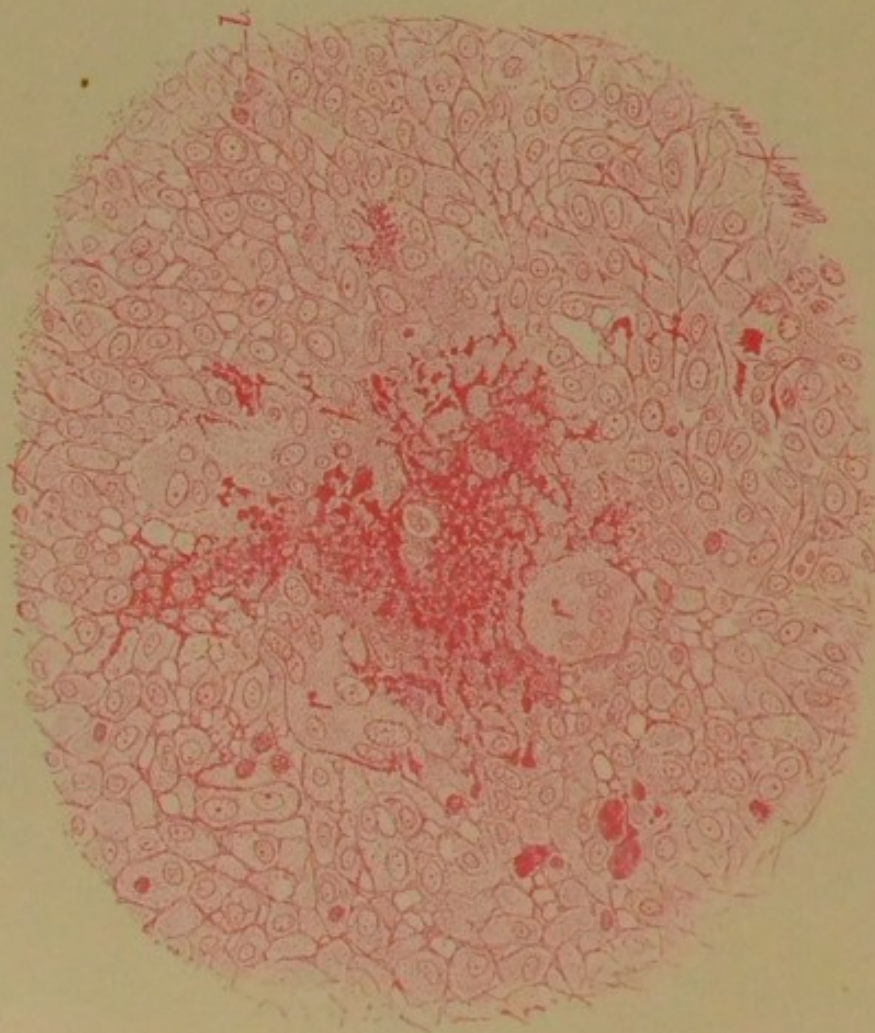
Necrosis of bone. On the right (a) sequestrum formation; on the left (b) osteophyte formation with osteomyelitis.

the distinction is clearer, as in bone, where the dead portion is hard to recognize in itself, but the adjacent healthy bone is not the seat of periosteal thickening and formation of osteophytes as is commonly observed about the dead portion. The absence of circulating blood and the alterations in the contained blood also characterize a necrotic part.



PLATE I.

FIG. 10.



Young Tubercle of the Liver, with Beginning Formation of Fibrin-caseation.

r. Giant cells. *l.* Lymphoid cells; the remaining cells are epithelioid, and between them is a fine network of fibrin.

FIG. 13.



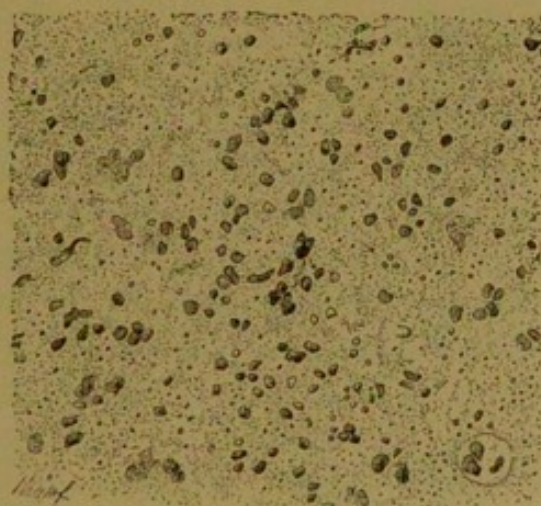
Section of a Recent Anemic Focus of Softening in the Brain; Marchi Method.

The fat is colored black by the osmic acid, the remaining elements are yellow. *a.* Swollen axis cylinder. *b, c, d.* Myelin. *e.* Fatty granular bodies. *c.* Tissue in granular degeneration, with scattered yellow hyalin particles.

Softer tissues present more marked and early growth alterations, usually being denser and drier than normally. An excellent example of this is the anemic infarct. In consistency it resembles coagulated albumin, its color is often light yellow, its volume is slightly increased, and it swells up over the cut section. Similar changes may be noted in the hemorrhagic infarcts, but the dense infiltration with blood makes them appear deep red.

The peculiar firmness of the necrotic part is referred by Weigert to a coagulation of the cell protoplasm, rather than to a pouring out of fibrin between the cells from the lymph flowing through the region. Hence he terms the condition a *coagulation necrosis*. Afterward from loss of water the part becomes inspissated, dry, and shrunken. Finally, when gradual softening and absorption of the dead cells are complete, a fibrous scar remains. (See p. 48, and Chapter III., A.)

FIG. 11.



Section from a caseous tubercle of the lung. Advanced stage with granular and flaky destruction; one cell with three nuclei preserved, the others in fragments and detritus. $\times 250$.

A process which is very similar to the necrosis described is that known as *caseation*, from the firm, yellowish, and opaque look of the part, suggesting the appearance of cheese. An area recently become caseous is slightly enlarged, dry, and apparently coagulated.

In this form of necrosis the separation of a coagulating substance from the blood appears to be of more importance than in the former variety, for in very fresh cases we find through the part a finely fibrous or hyaline material, lying between the cells, which gives the staining reaction of fibrin only in part, and may be termed hyaline or fibrinoid. (Fig. 10.) Somewhat later we find a flaky or granular, dense mass

which consists in part of the fibrin and in part of the altered tissue elements more or less fragmented and coagulated. Scattered through the tissue there may be fragments of chromatin, many of which are derived from leucocytes that have wandered in and been destroyed. The further change is continuous division of the elements present into finer particles, so that under the microscope it appears as detritus of minute granules. Addition of acetic acid gradually clears up the picture and thus proves that the opacity was essentially the result of albuminous coagulation. At the same time fine globules of fat appear, but fatty degeneration does not actually belong to the caseous process, and must be regarded as an accident.

Caseation does not occur in physiological conditions, but only in tumors, gummata, tubercles, and exudates. It does not destroy a region rapidly, as does anemic necrosis after occlusion of a vessel, but

FIG. 12.



Teased preparation from a focus of cerebral softening. *a, a*. Partly naked axis-cylinder with swollen medulla. *b, b1, b2*. Partly naked swollen axis-cylinders. *b2*. The same with granular opacity. *c, c1*. Myelin. *d*. Ganglion cell with fat drops degenerating. *e, e1, e2, e3*. Wandering cells. *f, f1*. Fatty granular cells. *g*. White cell containing four red cells. *h*. The same with myelin globules. $\times 250$.

slowly and as a progressive degeneration, and hence may be considered a necrobiosis.

The caseous tissue may become wholly or partly absorbed, or it may soften or become calcified. With softening, by taking up water anew, the caseous material may become puriform and contain many leucocytes. (See caseous inflammation.) In other cases the focus remains dry, shrinks as its water is lost, and by infiltration with lime salts becomes of mortar-like or stony hardness.

The opposite process to the necrosis mentioned is *liquefaction necrosis* (*colliquatio*), a softening of the dead tissue by the entrance of water. Anemic necrosis in the brain thus rarely appears as an infarct, though formed as are other infarcts, but as a focus of swelling with liquefaction of the tissues, determined probably by the peculiar constitution of nervous tissues. Maceration of the dead fetus in the uterus is a

similar case; at first the epidermis is softened and lost, and then the deeper portions.

The following forms of necrosis are peculiarly the result of external influences:

Superficial parts dry after their death by evaporation of their water, and become stiff and hard, a condition called *mummification*. This occurs in some cases of senile gangrene with the changes of old age in the vessels and decreased vigor in the cardiac muscle, or with plugging of an artery, or from vasomotor disturbances, or, lastly, following mechanical injuries. This form is common in the feet and toes. A physiological case of such dry necrosis is observed in the stump of the umbilical cord.

Another variety of tissue death resembles *colliquatio* in the liquefaction of the parts affected, but differs from it in the development of a disagreeable odor from the formation of gases, together with peculiar changes in color, and of poisonous properties in the products of decay. This form arises only when there are putrefactive organisms present which enter the dead region from the air, or through the blood from other sites of gangrene. Imbibition of altered blood pigment gives the part a dirty green or even black color. In the decayed portions, especially in their fluids, there are leucin and tyrosin, crystals of triple phosphates, fat crystals, and amorphous and crystalline blood pigment. The cell nuclei perish early. The gas accumulates in the soft tissues, and hence the condition is called *emphysematous gangrene*. Certain tissues resist the process for a long time, as bone, cartilage, tendon, and connective tissue, shreds of which sometimes hang free in the fluidified portion. (See Bacteria, Chapter V., A.) All combinations of necrosis and putrefaction are grouped under the term *gangrene*.

Adjacent to the decayed parts there is often a marked reaction which limits the process and prepares for the separation of the dead from the living tissues. Such a demarcation in bone aids in the formation of sequestra which often lie loosely in a bony framework. (Fig. 9.) In some cases the separated portions undergo absorption, in others there is a growth of young connective tissue through the part. (Chapter III., A.)

After superficial portions have died and separated, a defect remains in whose base the necrotic process may persist, and thus a variety of *ulcer* forms, but the strict meaning of the word ulcer is a loss of substance from the gradual death of minute portions by molecular necrosis, as distinguished from death of a relatively large mass. Hence the

name bony ulcer is given to those cases where the death of the bone proceeds as molecular caries rather than as a destruction of a large area at once, for which the name necrosis is preferred.

The following ulcerative processes may be mentioned in some detail here :

Round ulcer of the stomach, *ulcus rotundum*, forms a cone-shaped loss of substance reaching into the wall of the organ and corresponding to the distribution of a branch of the artery. The explanation is probably that some local disorder of circulation causes a necrotic area which is then digested by the gastric juice. (See Chapter X., B.)

Perforating ulcer of the foot (*mal perforant du pied*) is also due to a local obstacle to the circulation, probably of vasomotor origin, with also an element of trophoneurosis. Attending some mechanical injury a callous spot appears, and afterward a rapidly extending ulcer which bores deep into the foot.

Bed-sores, or ulcers of decubitus, are the most important of these processes. They follow long-continued pressure on exposed parts of the body, as over the spinous processes of the vertebræ, the occiput, sacrum, and heel, or over the trochanter, anterior superior iliac spine, elbow, and external malleolus, when the subject lies upon the side. Local disturbances of circulation act in producing necrosis, together with the pressure, with weakened heart action and vasomotor influences. At first the spot turns livid red from imbibition of the blood pigment, and afterward it becomes black and eschar-like, or soft when the gangrene involves wider areas and penetrates deeper, even laying bare the bones and involving them.

B. DEGENERATION.

Distinguished from necrosis, or local death of the tissue, pathological disorders of the life of cells may be called degeneration, in all of whose forms there is a regressive change with diminution of assimilating powers and other functions. In one series of these changes the effect is an accumulation within the cell of the products of its imperfect catabolism, instead of the completion of the physiological process to the usual end-products. This condition is called *infiltration*, and resembles the accumulation of incompletely elaborated material in certain cells during the process of digestion. A certain storing of reserve material is physiological for some cells, and we shall consider in the infiltrations how far we may assume that such conditions are patho-

logical. In other cases a foreign substance which does not belong to the normal cell products may gather in or between the cells, as in hyaline and amyloid degeneration.

Here belongs a third group, also characterized by gradual degeneration of the cell elements and the formation of products of decay out of their own substance. This is the condition indicated by *degeneration* in the strict use of the word as opposed to necrosis, and a good instance of it is seen in fatty degeneration.

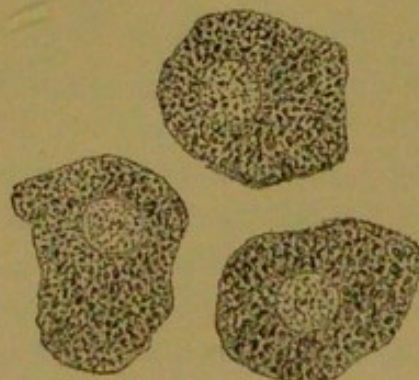
Lastly we reckon *pigmentation* of the tissues among the degenerations, inasmuch as the pigment itself may be a product of such lesions or its deposition may cause manifold disturbances in the organ, as in blood and lymph organs. We include also impregnation of a part with organic or inorganic matters, as precipitates, for it may be followed by regressive disorders.

A clear division between these various processes is not always possible, for they merge into each other and there is no absolute limit between infiltration and degeneration. In accord with the usual custom, the various processes will be described in connection with the main product of the abnormal metabolism and the kind of impregnation observed.

1. Cloudy Swelling.

In this condition the cell protoplasm presents a more markedly granular structure than normally, and when examined fresh is opaque, as if covered with dust. The granular look and opacity depend upon the deposit of countless fine particles, and as the volume of the cells is increased the name cloudy swelling has been given to the condition. The albuminous nature of the granules is evident from their clearing on the addition of acetic acid, so that the nucleus, if present, becomes visible. Potassium hydrate solution also clears the cell but destroys the nucleus. This reaction distinguishes albuminous granulation from fatty degeneration. Other names for the condition are parenchymatous or albuminous degeneration. If pronounced, the change can be recognized in the gross, for the fresh cut surface of the organ has an appearance as if boiled.

FIG. 14.



Liver cells in cloudy swelling. $\times 350$.

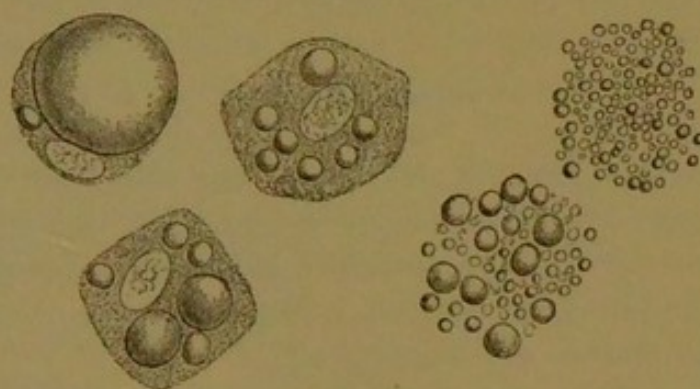
It has not been determined whether this process is an excessive absorption of nutritive material, that is, an active cell condition, or whether it is a metamorphosis of the protoplasm by the precipitation of some of its proteids and changes in its finer structure. It tends, however, to further regressive lesions, as shown by frequent transition to fatty degeneration.

Cloudy swelling, as will be explained under Inflammation, affects both the epithelia of the large organs (liver, kidney) and also the muscle fibres, whose striation becomes indistinct or even lost. The parenchymatous organs are especially liable to the change in general infections and intoxications with various poisons. If the lesion is moderate it may disappear with the cessation of the main disease, but in many cases it is followed by fatty degeneration.

2. Fatty Changes in Cells.

Deposit of fat in an organ has a vastly different significance according as it represents a simple increase of reserve store in an organ which

FIG. 15.



Fatty cells from the liver. To the left three cells with drops of fat-infiltration. To the right destruction of the cells and remaining detritus—degeneration. $\times 350$.

normally contains fat, or results from pathological infiltration of a part normally free from fat. There may be no marked impairment of the life of the cells, or there may be complete destruction of them. The former condition is termed a *fatty infiltration*, and is often a physiological process. Thus the liver cells in normal conditions contain a certain amount of fat, and a slight increase of this cannot in itself be considered pathological. As long as the fat is proportional to the general fatty condition of the whole body and causes no disorder in function, it lies within the boundaries of physiological variation, increasing during digestion and lessening after the completion of the

same. In the kidney, also, and in the muscle fibres, small collections of fat drops may at times be observed which neither interfere with function nor threaten the life of the cell.

At times, however, fatty infiltration may reach a degree which is pathological. This is surely the case when it is in marked excess, as in the liver of the Strasburg goose and in the same organ in alcoholic patients, or when an abnormal storage is observed, for example, in the liver of a tuberculous patient who is otherwise emaciated.

Fatty degeneration is distinguished from fatty infiltration by the destruction of the cells and the deposit, usually, of fine globules of fat. This is a regressive change which is normal in the formation of milk and sebum and in uterine involution, but in pathological cases it may involve almost any tissue of the body. The fibres of muscle, especially of the heart, the epithelia of glandular organs, the media and intima of vessels, the endocardium and nerve fibres may be affected, and fatty degeneration in the renal epithelium is the essential element in parenchymatous nephritis. A similar change is observed in the absorption of all parts which have been affected by circulatory or inflammatory processes beyond their powers of resistance. Pathological products of all varieties may undergo this form of degeneration, as necrotic exudates and thrombi, and in senile involution it appears in many organs, as in the arcus senilis in the cornea, in the epithelia of the testicle, and elsewhere.

Fatty degeneration begins in cells or fibres with the deposit of minute granules which by their strong refraction, insolubility in acids and alkalies, solubility in ether and alcohol, are demonstrably of fat. They may hide the finer structure of both cells and fibres.

A satisfactory distinction between fatty degeneration and fatty infiltration is difficult to formulate. In the liver the infiltration often precedes the degeneration, and in muscle fibres fat drops are always smaller than in the kidney. Consequently we must consider whether the outcome of the process is the destruction of the cells, leaving mere collections of fat drops or diffusely distributed fat, together with other elements of tissue death.

The products of the cell destruction are in part taken up by wandering leucocytes, which at times contain so much fat that they appear to

FIG. 16.



Fatty degeneration of heart muscle.

consist wholly of it and at last may break up into fat particles. Where fat collects in large amount, as in foci of necrosis, or in body cavities, there is a precipitation in the cadaver of the insoluble fat and margarin crystals, which lie in single or grouped needles, as they sometimes occur also in fat tissue. In similar conditions cholesterin crystals form as thin rhombic plates, often arranged in layers, and if numerous, visible in the gross as pearly flakes in the tissue.

FIG. 17.

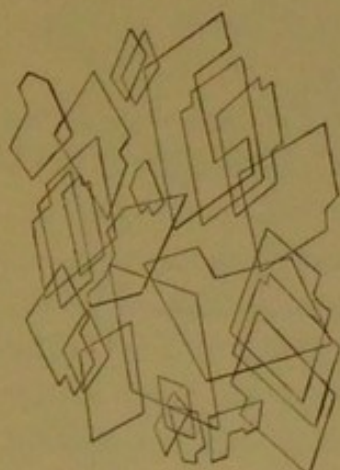


(After SEIFERT-MÜLLER. Diagnosis, tenth edition.)

A mixture of five parts sulphuric acid with one part water turns these plates carmine red and then violet, beginning at the edge. After-treatment with iodine colors them gradually violet, blue-green, and blue. Probably cholesterin is a product of the splitting up of albumin, and hence occurs with cell destruction.

Extensive fatty degeneration of many organs is observed after cloudy swelling in many infections and certain poisonings (as phosphorus and arsenic), and also with acute yellow atrophy of the liver.

FIG. 18.



Cholesterin plates.

Another example of widespread fatty degeneration is found in many anemias, especially with the pernicious form, and after severe hemorrhages when parenchymatous organs and the walls of vessels and even the endocardium are affected. It is not always possible to connect the lesion directly with lack of blood, for in many anemic and cachectic conditions of marked degree it is absent.

From the forms mentioned, of fatty infiltration and degeneration, we distinguish other cases in which there is an increase of the fat which normally occurs between organs and in their interstices. This is called *lipomatosis*, and will be treated in the section on Hypertrophy.

3. Mucous Degeneration.

The term *mucin* includes a number of bodies which are viscous and ropy, which swell but do not dissolve in water, and which precipitate with acetic acid in threads and flocculi, but do not dissolve with an excess of acid. Alcohol precipitates them, also, but the addition of water dissolves them again. The true mucins belong to the glycoproteids and break down into albumin and a carbohydrate. They dissolve readily in alkaline fluids. On boiling with dilute acid, mucin is converted into a substance which reduces copper oxide. Many other bodies are grouped under the name mucin, which are only mucoid and are more or less completely separable from mucin. Of these *pseudomucin* is found in cystic tumors of the ovary, chondromucin in cartilage, and para-albumin is probably a mixture of mucin and albumin. True mucin occurs in the umbilical cord, the mucous membranes, the large mucous glands, and in connective tissue.

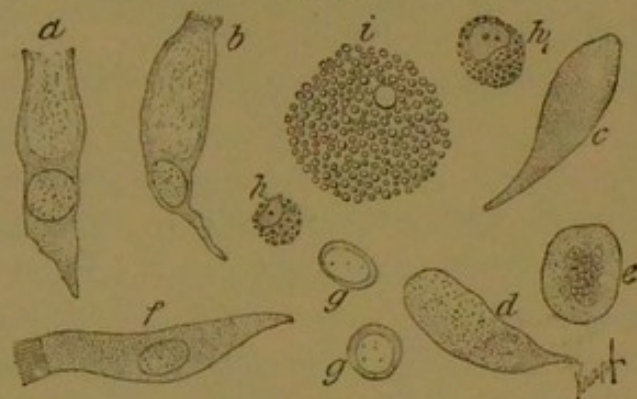
Physiological production of mucin occurs on the surface of mucous membranes and in the muciparous glands, by a metamorphosis of the cell protoplasm into mucin, the latter collecting in transparent glassy drops and making its way out of the cells. Cylindrical cells thus become converted into beaker cells (Fig. 19), the drops of mucin collecting in the upper portion of the cells and passing out, leaving a hollow space like the cavity of a beaker, while below it are the nucleus and the unchanged portion of the protoplasm. With increased formation of mucin these beaker cells become more numerous, and their protoplasm may be entirely consumed. In the epithelia of the muciparous glands the entire cell may be occupied by a transparent globule of mucin, while on the wall of the alveolus there are crescentic masses of protoplasm with nuclei. These become granular and then change into mucin, and the entire cell may become thus transformed. In the produced mucus the so-called mucin bodies are found, which are large round cells, much swollen and transparent.

Pathological production of mucin is an abnormal excess of the physiological process, as may be observed on inflamed mucous membranes (see Chapter III., B.), and may be induced artificially in the submaxillary gland by stimulation of the chorda tympani and sympathetic. In the secretion large numbers of mucin bodies appear, with degenerating epithelia swollen with mucin and free mucin. Other sites of pathological mucin formation are epithelia of many cystic tumors, epithelial tumors of mucous membranes and various glands.

There may be enormous increase in the number of beaker cells or this may be slight, and the process may lead to the mucous degeneration of all the cells, so that in the interior of a carcinoma there may be cavities entirely filled with the mucin. When the ducts of large mucous glands are closed, continued excretion may lead to the formation of large retention cysts, and the pressure may flatten out the epithelial investment of the part. The fluid itself may become thin and watery. Such mucous cysts occur about the buccal cavity and in the gall-bladder, and may lead to hydrops of the part.

Mucin formation in bone, cartilage, and connective tissue is a different process. Here there is a metaplasia of the basement substance of the part, which swells to a structureless homogeneous mass while the cells are not occupied in producing mucin. Through such

FIG. 19.



Cells from the secretion of catarrhal bronchitis. *a*. Beaker cells. *b*. Cylindrical cells with partial mucous change in the protoplasm. *c*, *d*. Epithelia in mucous degeneration. *f*. Normal ciliated cells. *e*, *g*. Mucin bodies. *h*, *h*, *l*, *i*. Cells in fatty degeneration.

a process in the subcutaneous tissue arises the condition known as myxedema. Similar changes in joint cartilages, usually preceded by fibrous changes in the stroma, occur in various articular lesions. In the aged the process attacks the fatty marrow in long bones, and such a degeneration is common to many of the connective-tissue tumors.

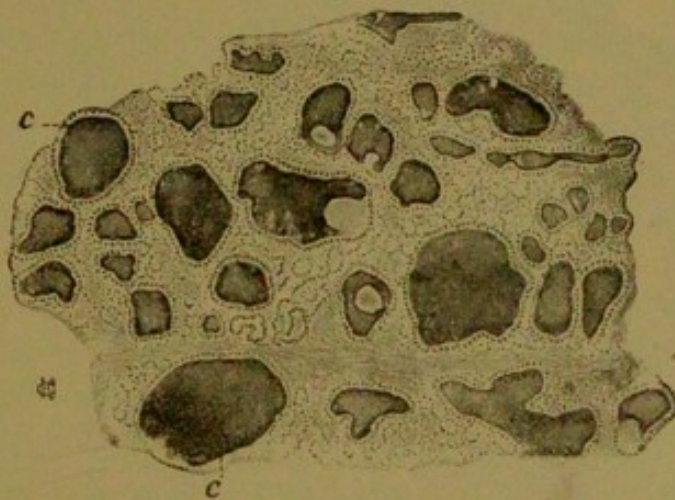
The Charcot crystals found in the sputum of bronchial asthma and in leukemic blood chemically resemble mucin. (See Chapter IX., B.)

4. Colloid Degeneration.

Colloid somewhat resembles mucin, but is of greater density, like glue, and has a yellow or even a brown color, and does not precipitate with acetic acid; but colloid is not always a uniform product. Pseudo-mucin is closely related to it.

The chief site of colloid formation is the thyroid gland, in whose follicles, especially in the aged, the material may accumulate and cause atrophy of the epithelia by pressure. The colloid substance appears first, with the aid of the local cells, as small sago-like bodies which fuse and form larger masses; these may cause atrophy of the septa of the gland and convert it into a multilocular cyst. The follicles often contain firm lamellated bodies, called colloid bodies, which sometimes include cells. With hyperplasia of the gland the production of the colloid material may reach enormous proportions.

FIG. 20.

Colloid goitre. *c*. Colloid masses in dilated gland spaces. $\times 40$.

Colloid is formed in retention cysts of the cervical mucous membranes and urinary tubules, in the adrenals, and in many ovarian tumors and other neoplasms.

5. Amyloid Degeneration.

The deposit of amyloid material in an organ is called *amyloid degeneration*, and the new element is characterized by its firmness, elasticity, transparency, and refraction. Chemically it consists of chondroitin-sulphate and an albumin, and it is very resistant to both acids and alkalies. With several substances it displays characteristic color reactions. Thus iodine solution stains it mahogany brown and the remaining tissue light yellow. Iodine followed by slow addition of sulphuric acid stains it dark red, then violet, and lastly blue, and it is from this that the amyloid takes its name, since starch (*amylum*) gives the same blue reaction with iodine and sulphuric acid. Methyl violet stains amyloid parts ruby red and others bluish-violet; iodine green stains it ruby red and other elements bluish-green. By means

of these color tests amyloid may be distinguished from other substances, such as hyalin, which resemble it.

The form in which the amyloid is deposited varies from flakes to small lumps lying outside the cells in the basement substance. It shows a preference for certain tissues and organs; but amyloid degeneration may be one of the most extensive in the whole body. The commonest site for amyloid is the walls of vessels, especially of the small arteries and capillaries. (Fig. 21.) In the former it appears first in the media, whose muscle fibres are thus destroyed; in the capillaries it occurs as a homogeneous mass which gradually occlude the lumen. This degeneration attacks the connective tissue also, as in the spleen and lymph nodes, whose reticulum is converted into thick, irregular trabeculæ, and whose parenchyma atrophies. (See Part II., Spleen.) In glandular organs, beside the vascular site, the basement membrane under the epithelia, as the membrana propria of the urinary tubes, may be attacked. If epithelia themselves are ever involved it is only very seldom. Lastly, amyloid may occur in the matrix of cartilage.

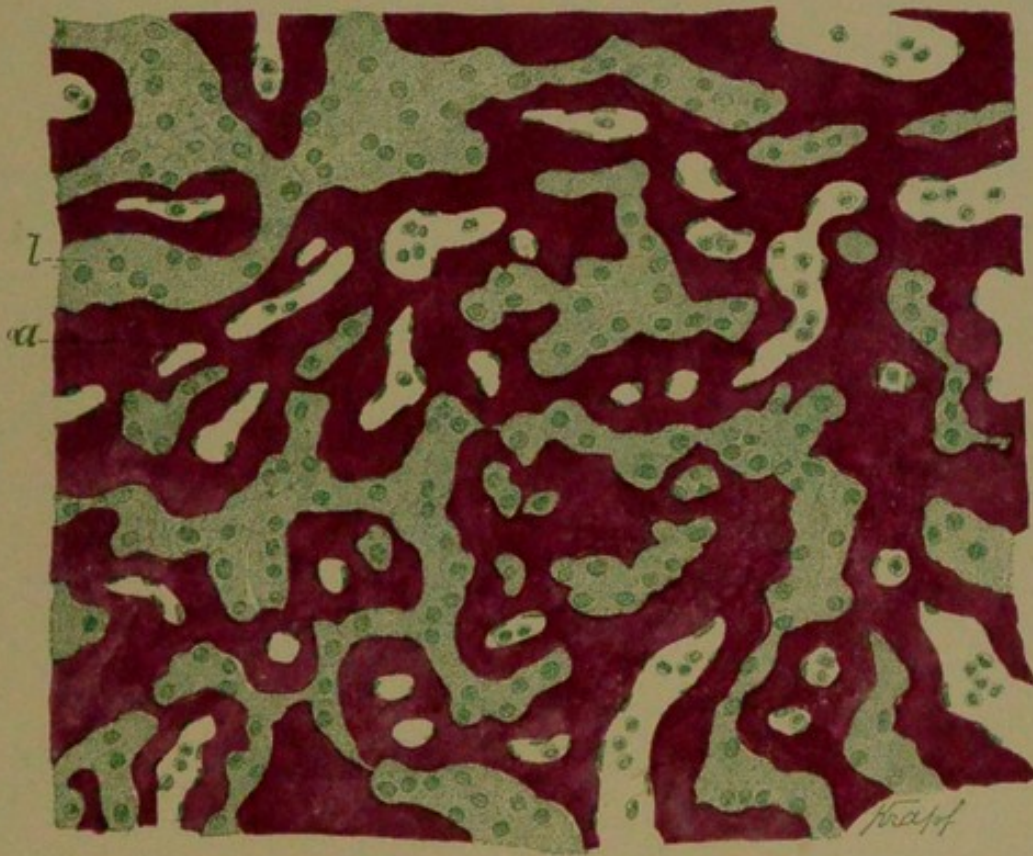
With pronounced amyloid degeneration the gross appearance of the organ changes; it is large, dense, semitransparent, and resembles fresh bacon, or, if the deposit is not diffuse, there appear to be grains like sago scattered through it. The latter appearance is well marked at times in the spleen, in which the follicles are very large and give the organ the name of "sago" spleen.

With amyloid degeneration the other elements suffer atrophy or fatty degeneration, the vessels lose the muscle fibres of the media, the renal glomeruli become homogeneous, non-nucleated spheres, and the renal epithelium is fatty. In the spleen the pulp atrophies. This disappearance of parenchyma is partly explained by the occlusion of bloodvessels (as in the glomeruli of the kidney), partly by the mechanical pressure of the dense amyloid upon the less resistant parenchyma.

Among the organs those most often attacked are the kidney, spleen, and liver, then the adrenal and intestine, less often the intima of great vessels, heart muscle, skin, ovary, uterus, etc. The lesion appears in one or many places, and as a widespread lesion it may occur with cachexias, of which chronic tuberculosis, especially with suppurating lesions of bones and joints, syphilis, malaria, and malignant tumors, are most often accompanied by this degeneration. The origin of the material is not fully determined; possibly it is deposited in the organs

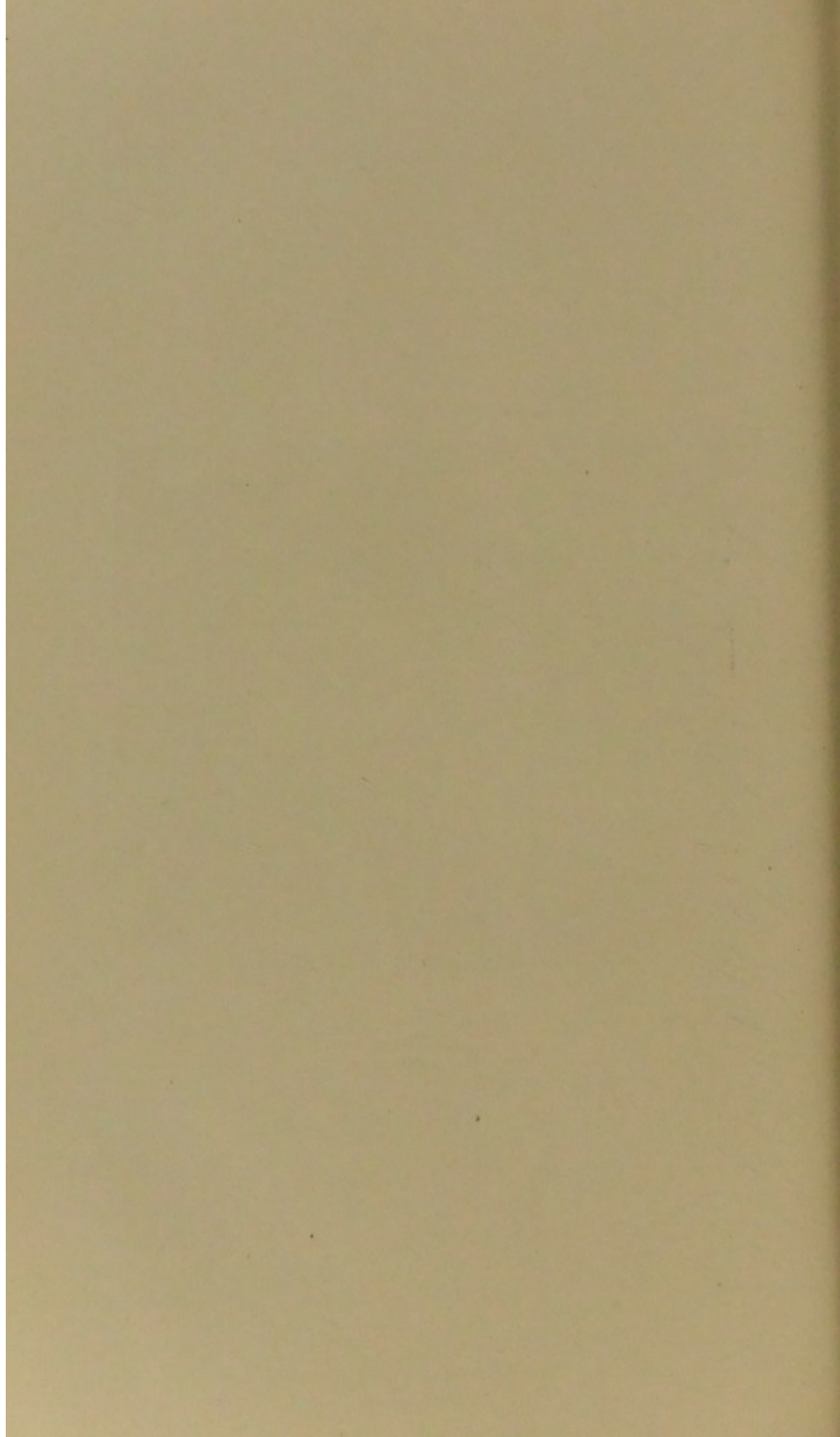
PLATE II.

FIG. 21.



Amyloid Degeneration of the Liver. $\times 300$.

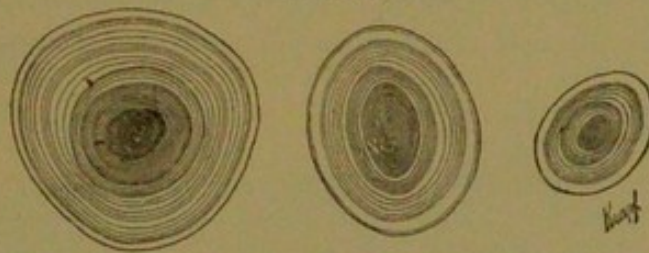
a. Amyloid material. l. Liver cells. Stain—iodin-green.



from the blood, possibly material is extruded from the cells which aids in its formation.

Corpora Amylacea. In various tissues small microscopical bodies are found of concentric lamellation or more homogeneous, usually round, which turn blue with iodine at times without the addition of sulphuric acid. They are common in the central nervous system under the ependyma and in the olfactory tract, especially in the aged; also in cicatrices and old infarcts. In the prostate they reach a large size

FIG. 22.



Corpora amylacea.

and may be deep brown in color. They are closely related to amyloid, and probably result either from material extruded from cells, or, in the nervous system, from degenerated nerve fibres.

6. Hyaline Degeneration.

Mucin, colloid, and amyloid form more or less homogeneous deposits in the tissues, but differ among themselves and from other homogeneous substances by their physical and chemical characters. Beside these there are pathological products of various origin and constitution which are grouped as hyalin and whose formation is termed *hyaline degeneration*. These occur either as scales, fibres, or longer masses which often enclose vacuoles, and are characterized by their homogeneous, glistening appearance, their refraction, and their resistance to acids and alkalies. Their staining reaction is less constant, but many of these substances have a marked tendency to stain with acid dyes (as eosin). They differ from amyloid by the absence of the peculiar reaction (p. 65).

Hyalin is formed in the following cases :

1. **Hyalin Fibrin.** By coagulation of exuded plasma a hyaline substance may form which resembles fibrin. It is not disposed in delicate threads, but as larger homogeneous masses, or as a reticulum of coarse septa with irregular contours. (Fig. 23.) Transitions to normal fibrin are common, but the hyalin does not give the fibrin staining

reaction (Weigert's). A fibrin which has been in delicate threads may take on the homogeneous character by fusion of its filaments to thicker masses, and this altered fibrin is found with fibrinous inflammations of serous surfaces and mucous membranes (see Chapter III., B. 2 and 4), and in the lung it is encountered with both pneumonia and tuberculosis. The so-called hyaline casts probably come from coagulated albumins excreted by the glomeruli. Similar material is found in thrombi, either homogeneous or fibrous.

2. **Hyalin from Cells.** According to von Recklinghausen, under certain conditions, small masses of hyalin may be extruded from cells, especially wandering cells, and these join to form homogeneous masses,

FIG. 23.



Hyaline fibrin from a croupous membrane of the pharynx. In the spaces between the hyaline trabeculae are a few leucocytes. $\times 250$.

or the entire cell becomes hyalin and fuses with others. In thrombi both leucocytes and groups of blood plates may undergo this change. This would be an example of hyalin formed by agglutination rather than by coagulation.

3. **Hyalin from Necrosed Tissue.** Very frequently necrotic cells and tissue elements give rise to hyalin, as epithelia and muscle fibres, losing their normal granulation or striation and taking on a scaly appearance, after the loss of nuclei and finer structure, and later tending to show lines of cleavage. If such masses lie adjacent to each other they may form a homogeneous collection, perhaps with lines of fission, and permeated by a fluid which coagulates in fine or coarse threads. In the renal tubules dead and desquamated epithelia may

form such masses as casts. Extensive necrosis and hyaline degeneration occurs in the regions affected by hemorrhagic infarction, and here the connective tissue suffers the lesion. Hyaline degeneration of the mucosa occurs with severe diphtheria (*q. v.*), and with various inflammatory tissue lesions, as in endocarditis.

4. Hyalin of Connective Tissue and Vessels. (*a*) The fibrillæ of fibrous connective tissue lie in a loose arrangement, or gathered in bundles, which are disposed in a network or run parallel with each other, as in tendons. In many places, as in the cutis, the fibres lie so closely together that they do not appear as fibrillæ but as large homo-

FIG. 24.



FIG. 25.



FIG. 24.—Necrosis of muscle with hyaline and fatty degeneration. To the left is the fibre still striated, but split lengthwise; in the middle there is a transverse rupture. $\times 350$.

FIG. 25.—Hyaline degeneration of the intima of the aorta in atheroma. $\times 350$.

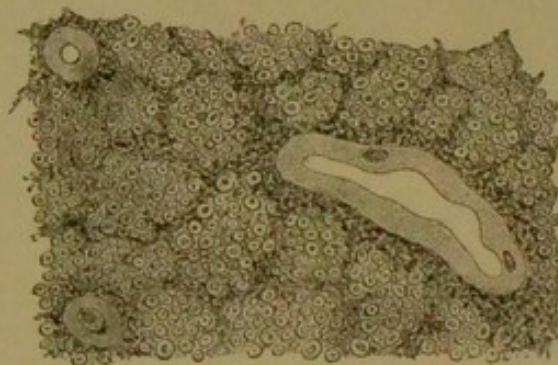
geneous fibres. Hyaline change in such tissue, also called sclerosis, is accompanied by a loss of fibrillary structure and the appearance of thick and homogeneous masses which lie close together and leave but very narrow spaces between, in which nuclei may be found with but little protoplasm. The sclerosis may be only a more intimate arrangement of fibrous bundles and fibrillæ, but in many cases there is evidently a homogeneous addition between them. This lesion is found in the stroma of many organs affected by chronic inflammations of the interstitial type, about tubercles, in many tumors (as fibromata), and in the intima of vessels with obliterating endarteritis or atheroma.

(See Chapter VII., C.) This form of hyalin stains a deep red with picrofuchsin (Van Gieson's).

(b) In reticular tissue there is a network of stellate cells with delicate processes, and in the spaces there are lymphocytes; this tissue occurs in the lymph nodes and has been called adenoid tissue. In tuberculosis hyaline lesions of this reticulum change it to thicker and homogeneous septa with narrower meshes, the contained cells in great part destroyed, and the staining reaction as already given. The picture resembles that of amyloid change, but the characteristic staining test fails. The interspaces may be completely obliterated by the swelling reticulum, so that large areas appear homogeneous.

A similar thickening is observed in certain connective-tissue membranes, as the capsule of Bowman, even after they have already become hyalin; this occurs in chronic interstitial inflammations.

FIG. 27.



Hyaline degeneration of small vessels in the cord. $\times 350$.

Another variety of hyalin is found in the walls of capillaries and very small vessels, and the result strongly resembles amyloid changes in the same parts. The wall is thick and homogeneous, the lumen is narrow or lost, and the nuclei at first lie prominently on the inner side, as if the hyaline change began on the outer, and then they are lost.

Hyalin in its various forms is common in certain tumors, as fibroma, myoma, and psammoma; and in cylindroma the peculiarity of the tumor is such a change in its vessels and septa.

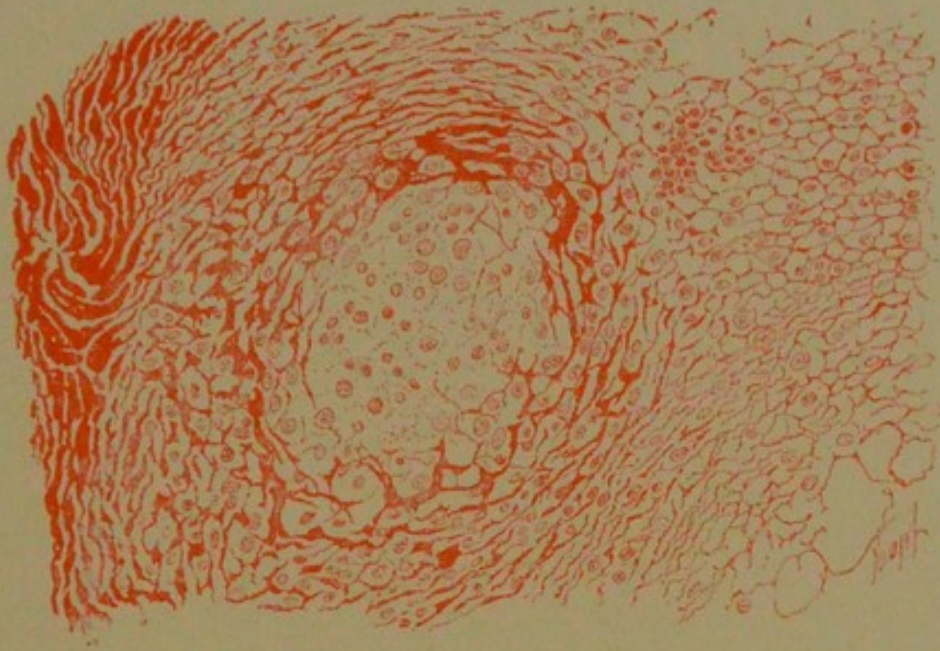
The great variety in the kinds of hyalin partly explains the fact that this lesion often precedes amyloid degeneration. Nearly all hyalin shows a tendency to become calcified after a time.

7. Glycogenic Degeneration.

Glycogen is chemically related to dextrin and occurs normally in several of the tissues, especially in the liver and muscles, while the

PLATE III.

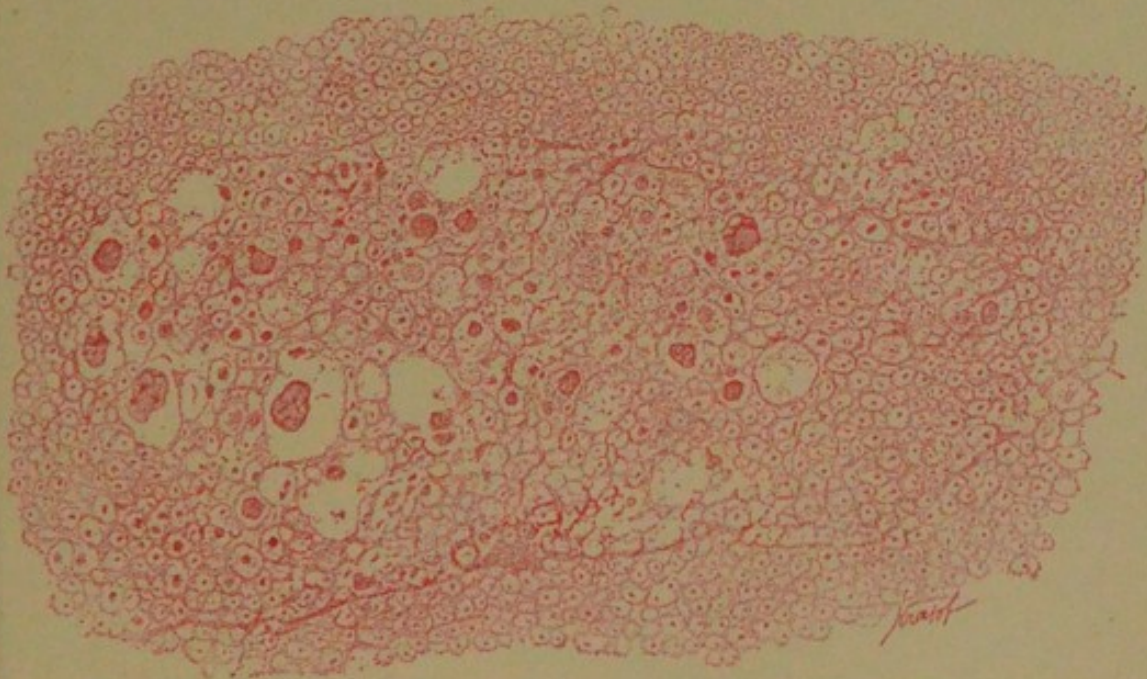
FIG. 26.



Hyaline Degeneration in the Reticular and Fibrous Connective Tissue of a Lymph Node about a Tubercle. $\times 350$.

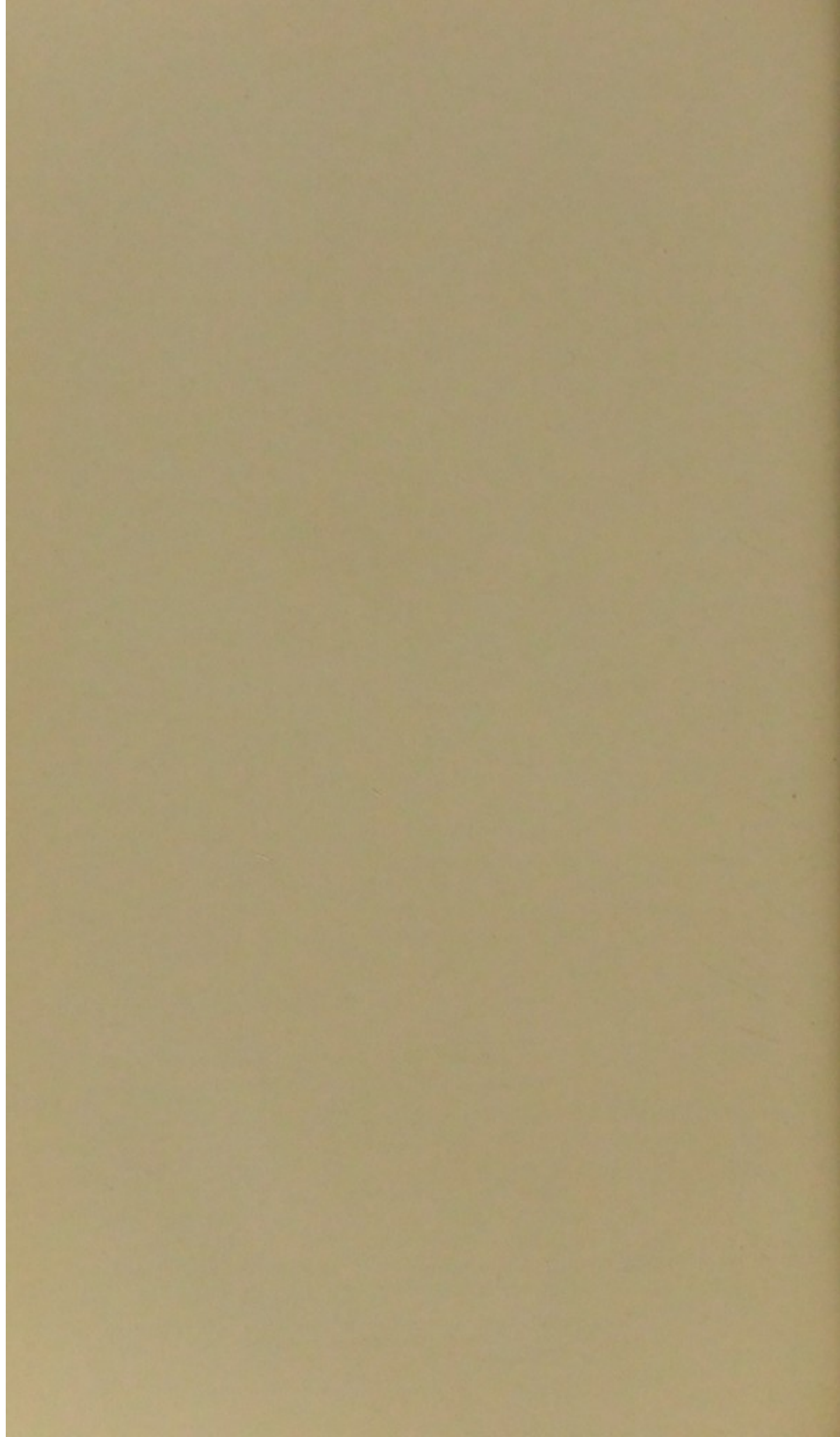
At the left, thickened fibrous and reticular tissue, on the right normal reticulum. The tubercle appears as a lighter area.

FIG. 28.



Focus of Hydropic Degeneration in the White Substance of the Cord; in Chronic Nephritis. $\times 50$.

The meshes of the glia are widened and contain swollen, irregular bodies derived from nerve fibres. The nerve tissue in the neighborhood is normal.



embryonic tissues are richly supplied with it. In pathological conditions glycogen appears as homogeneous material which either uniformly infiltrates the cells or is found as drops and globules within them. With iodine it turns dark brown and it is soluble in water.

The most important occurrence pathologically is in the hepatic and renal epithelia during *diabetes mellitus*. In the kidney the cells of Henle's loops are especially involved. It is found in many tumors, as carcinoma of the testis, rhabdomyoma, chondroma, and hypernephroma. Possibly the local excess of glycogen may be explained as increased cell catabolism.

8. Hydropic Degeneration.

When cells take up an abnormal amount of fluid and become swollen, lighter colored, and vacuolated, the process is called *hydropic degeneration*, and may end in their destruction. In pronounced edema of the central nervous system the axis-cylinders regularly present this change, and in passive or inflammatory edema, epithelia, connective-tissue cells, and glia cells are similarly affected.

9. Petrification.

Deposit of mineral salts in the tissues, usually as a metastasis, receives the name of petrification. The commonest material of this kind is calcium salts, which as a physiological process are deposited in cartilage and developing bone, and these two sites present two different kinds of calcification which may be repeated in pathological conditions. One of these, the deposit in bone, is uniform and homogeneous; the other, observed in cartilage in the calcifying zone, is a deposit of granules which under the microscope appear as discrete particles.

The transition to pathological calcification is given by the impregnation of cartilages and vessel walls in old age. As a general rule calcification affects dying or dead tissue. Among the examples are necrotic epithelia (Fig. 28) and ganglia, fibrous capsules, hyaline and colloid masses, cardiac valves, and atheromatous bloodvessels, old exudates, especially when caseous, and neoplasms which start in bone and cartilage. In extra-uterine pregnancy the dead fetus may be calcified in its external layers and thus form a lithopedion.

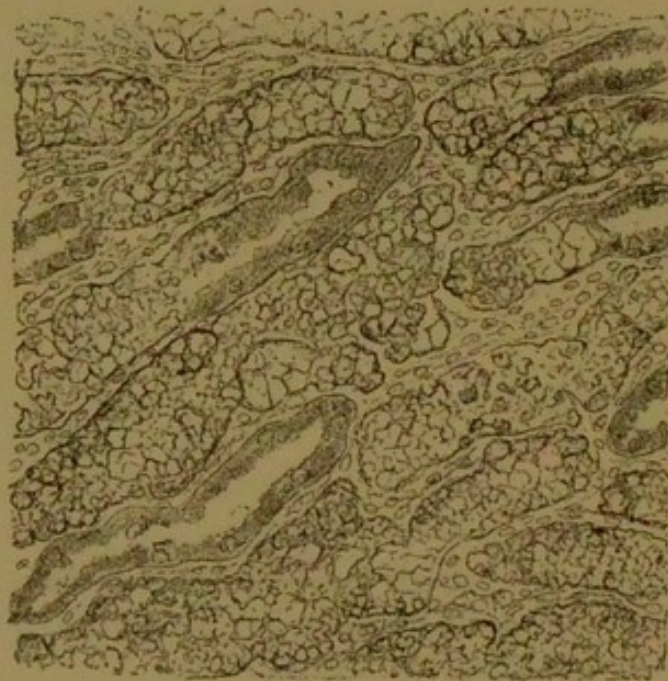
The salts are carbonate and phosphate of lime and magnesia, and are usually extracellular. With hydrochloric acid they dissolve and the carbonates give off bubbles of CO_2 ; with sulphuric acid, crystalline needles of gypsum may be seen to form (calcium sulphate).

When dissolved lime salts flow freely in the blood, as from tumors that destroy bone, granules of lime salts gather in the urinary tubes and form a kind of infarction, or the lime may be found in the epithelial cells; both forms occur frequently in mercurial poisoning.

Smaller or larger concretions of lime occur in other tissues, as in lymph nodes in chronic inflammation, old exudates, fibrous membranes, while in psammomata they form the well-known "sand grains" which characterize these tumors. (See Chapter III., E.)

Other material than lime may form metastatic deposits, as uric acid and its salts in the uric acid diathesis. Here cartilages of joints, the

FIG. 29.



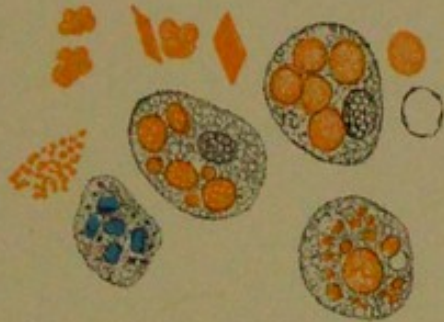
Calcareous infiltration of renal epithella. From the edge of an old infarct; a few tubules still to be recognized. $\times 250$.

fibrous structures about them, the vessel walls, the endocardium, and the cartilage of the ear are common places for deposit in amorphous or crystalline form. Thus also the tophi of gout are formed.

Concretions. When physiological secretions and excretions precipitate their contained salts, either by increased density or by decreased solubility, concretions may form, often in concentric layers about a nucleus. Thus in the urine copious sediments of urates occur, and in the gall-bladder biliary calculi. In jaundice bile pigment may be deposited in the renal tubules. The concretion causes or receives new deposits, which may differ in nature, and hence the calculus is formed of various layers. The commonest seats of such formations are the

PLATE IV.

FIG. 30.

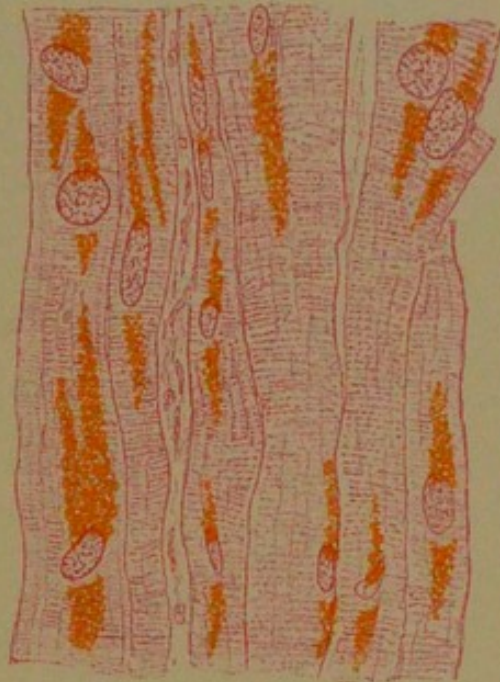


Red Cells and Pigment, Free
and Inclosed in Cells.

× 300.

Above to the left, amorphous and crystalline hematoidin; to the right, cell holding red corpuscles and an empty red cell; in the middle a wandering cell with dark, shrivelled red cells; below to the left a cell with hemosiderin with blue reaction; to the right a wandering cell with a granular hematoidin. (After Dörck, Virchow's Arch., Band 130.)

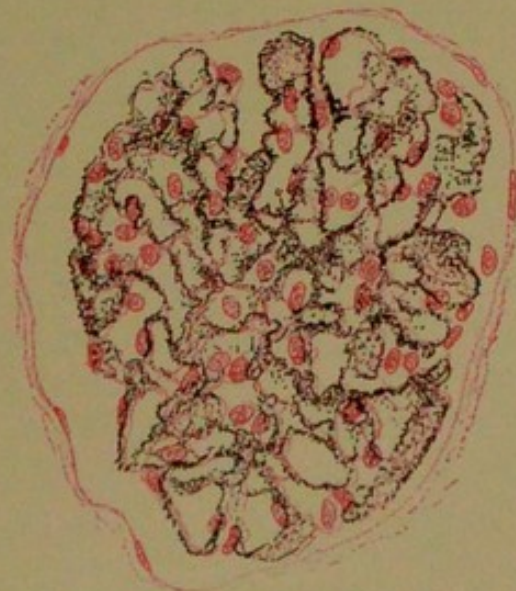
FIG. 32.



Brown or Pigment Atrophy
of Cardiac Muscle.

× 250.

FIG. 33.



Silver Infiltration of a Glomerulus in Argyria of the
Kidney. × 350.

A fine precipitate of black silver in the walls of the capillaries.

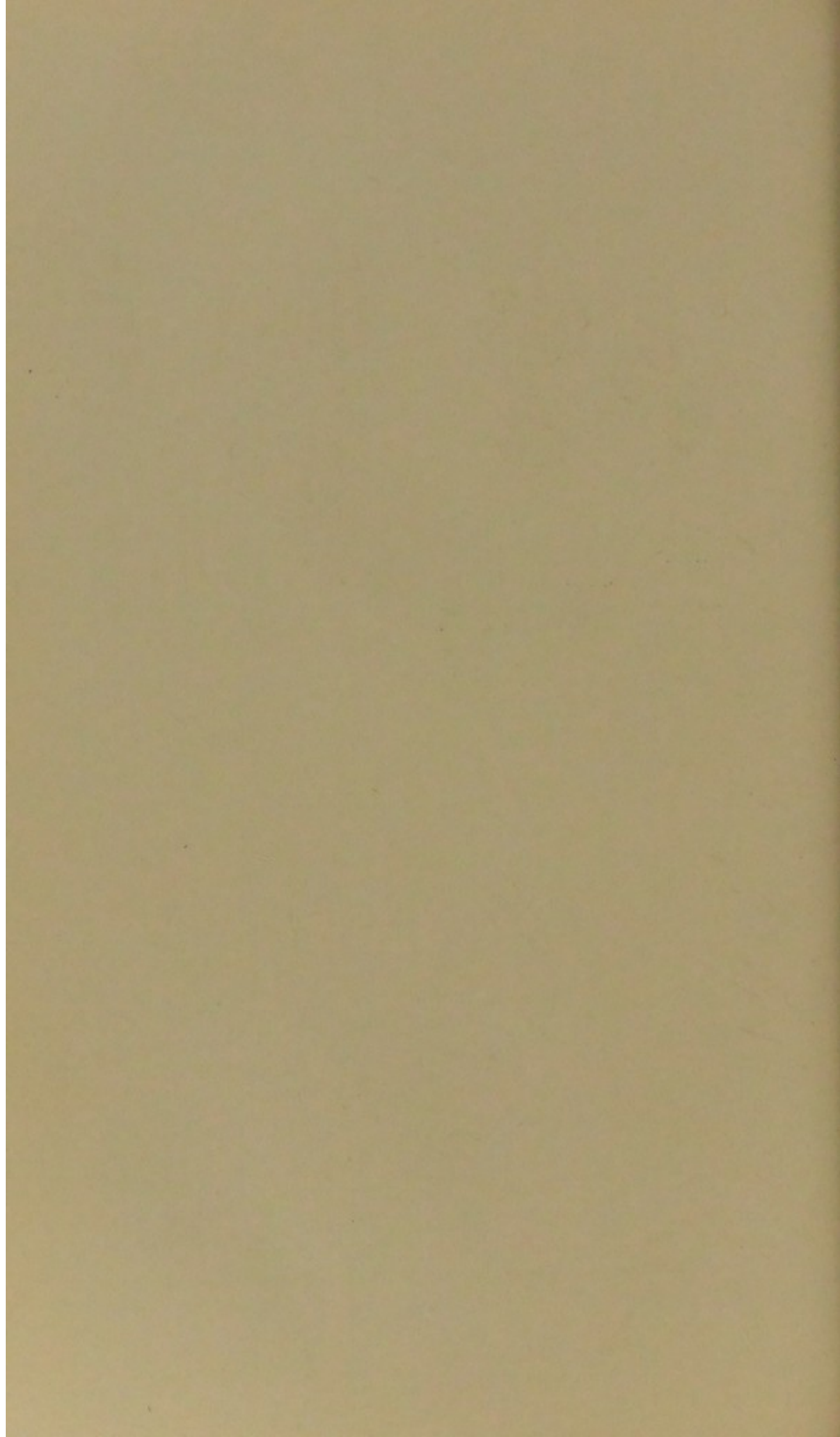
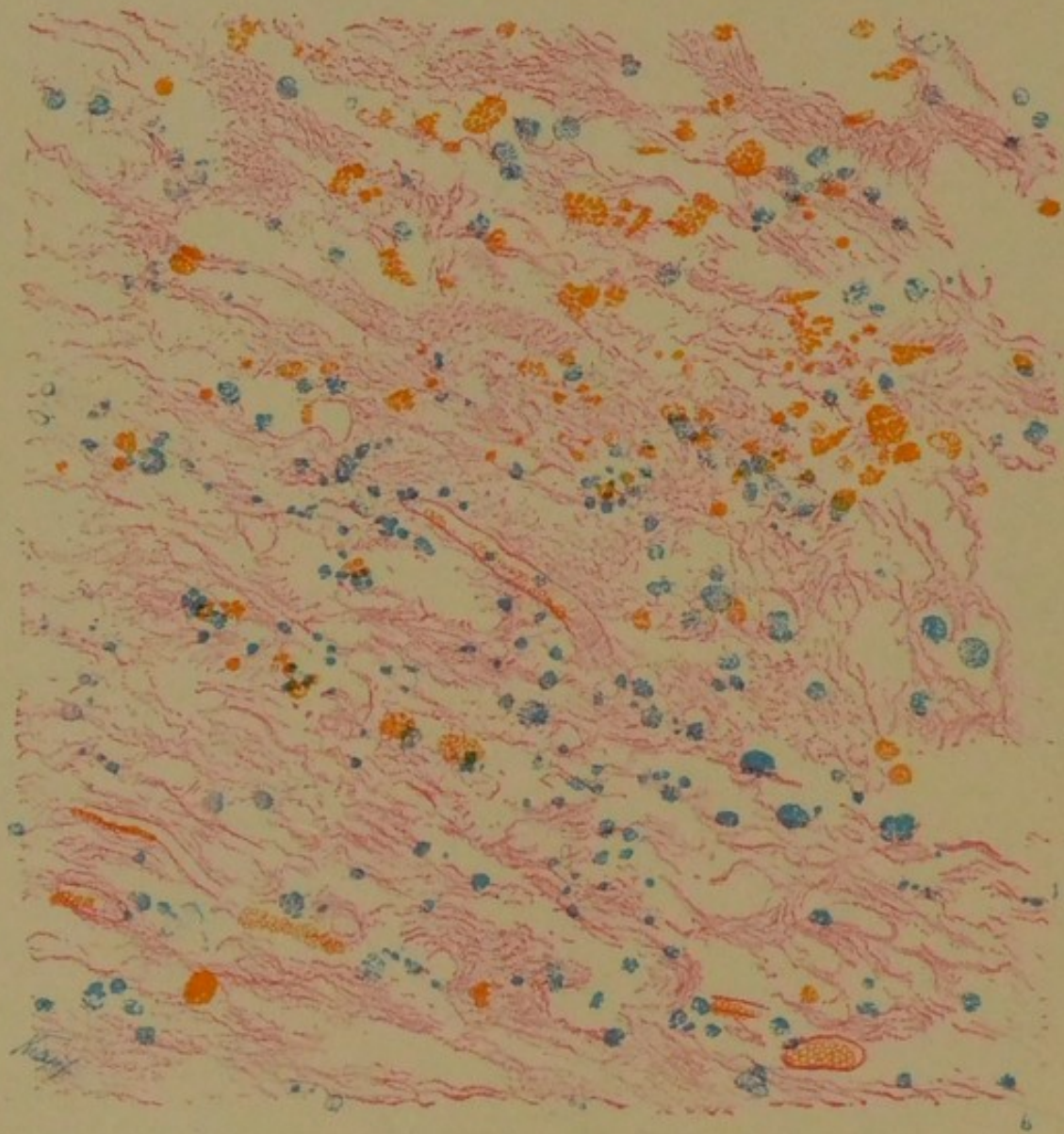




PLATE V.

FIG. 31.



Apoplectic Scar Several Months after Cerebral Hemorrhage.

× 250.

Treated with potassium cyanide and hydrochloric acid and stained with picro-fuchsin.
Hemosiderin blue, red cells and hematoidin yellow, tissue red.

biliary passages and bladder, and the urinary channels, less often they form in the pancreas and salivary glands.

Concretions which lodge in the renal tubes make urate or lime or pigment infarctions, the material lying in the capsule of Bowman, in the convoluted tubes, and especially in the straight collecting tubes of the pyramids, where the converging lines of different color are easily seen in the gross. Uric acid in the newborn, lime, hemoglobin, and bilirubin, are the commonest of the substances found. (See Chapter VI., and Part II.)

10. Pigmentation.

At many different sites in the normal body there are cells which contain more or less granular or diffuse pigment whose color varies between black, yellowish-brown, and a light brown. A dark pigment called *melanin* occurs normally in the rete Malpighii of the skin, in the choroid, sclerotic, and retina, and a yellowish-brown *hemofuscin* is found in muscles and many glands. The coloring matter of fat is called *lipochrome*. Pigmented ganglion cells are common in which the accumulation of pigment may be referred to the function of the cells, which elaborate it from the blood. Its exact nature is not known, but probably some of it is the altered blood pigment.

An excess of normal pigment occurs in physiological conditions, as in pregnancy, the term *chloasma uterinum* designating such excess in the areolæ about the nipple and along the linea alba.

The chief sources of pathological pigmentation are three—increase of the physiological pigment and manufacture from either blood-coloring matter or bile pigment. The presence of iron in such pigment is important in deciding its origin, for it then probably comes from the blood. The test is the Berlin blue reaction, with hydrochloric acid and ferrocyanide of potassium, by which the iron becomes blue. (Figs. 30 and 31.) But iron may be found by chemical tests in pigment which does not give this color test, and blood may at times furnish an iron-free pigment.

Hematogenous pigmentation follows the transformation of extravasated blood, for wherever a hemorrhage occurs the red cells, unless absorbed, undergo alterations which lead to the formation of various pigments. The cells are exposed to the lymph which bathes the part, and this extracts the hemoglobin and diffuses it in adjacent tissues, the red cells appearing empty within a few days after the extravasation, while the stroma of the red cells persists as a shadowy vesicle

for a short time and then disappears. The imbibition of the dissolved hemoglobin gives the region a reddish or yellowish tone, and the pigment suffers a chemical transformation, for it soon gives the blue reaction mentioned, which the living red cells do not give. It is assumed that the iron in the latter, if present at all, is in firmer chemical combination.

The altered hemoglobin which gives the blue reaction is called *hemosiderin*, and it permeates not only the site of the extravasation but also the wandering cells which soon enter it. (See Chapter III., A. 3.) Then after a time there is a precipitate in the part of amorphous or crystalline granules of pigment which have lost their iron. A *hematoidin* free from iron is thus formed from the iron-containing hemosiderin. It may remain for a long time as yellow or brown pigment, and if present in quantity may give the tissue a more or less reddish-brown tint.

Another portion of the red cells is taken up by the ameboid cells which enter the region even during the first few days. These are partly leucocytes, partly derivatives of the fixed cells. Having been englobed by these ameboid cells the red corpuscles undergo regressive changes; they shrink and become darker, break up into various sized fragments of yellow or brown pigment, which are at first hemosiderin and later hematoidin. By the destruction of the containing cells the pigment granules become free and form at times crystalline needles and tables. Such pigmentation from blood occurs in marked degree in organs which are the seat of stasis, either local or general in origin.

A form of pigment infarction occurs in the kidney when hemoglobin is deposited, in hemoglobinuria, as amorphous, brownish masses within the lumen of the urinary tubes; this is called a hemoglobin infarct. A hematoidin infarct may be similarly formed after renal hemorrhages.

Hemochromatosis is the name given to general and widespread deposit of pigment in the organs, as is observed during certain blood diseases, as malaria and pernicious anemia, and after destruction of red cells by poisons, as chlorate of potassium. Since the pigment usually contains iron the name *hemosiderosis* might also be used. The pigment in these cases is usually yellow, and is found in the liver, spleen, lymph nodes, and bone marrow, at times in the cells, at times in the connective tissue of the organ. The deposit may be so copious that on gross inspection the organ is spotted with brown or yellowish areas.

Hemofuscin is a yellow pigment, free from iron, which occurs in smooth muscle fibres of the stomach and other organs in various

cachectic conditions, as with malignant tumors, old age, tuberculosis, and in many hemorrhagic diseases, whenever, in short, we may assume great disintegration of the red cells. The pigment is assumed to have some relation to the blood-coloring matter, but its origin is connected with a specific activity of the cells containing it.

As a pigmentation of pathological origin hemofuscin is deposited in many atrophic and regressive conditions, especially in old age. This "pigment atrophy" is especially common in the cardiac muscle and in the liver, and is known as *brown atrophy*. In both situations it is in the form of small yellow or brownish granules and differs from hemosiderin in its resistance to acids and alkalies, and from fat by its darker color, its insolubility in ether and alcohol, and its lesser refraction.

During the formation of bile pigment in the liver there is a destruction of red cells and a transformation of their pigment to biliary pigment, of which bilirubin is the most important representative and whose chemical composition is identical with that of hematin. When the bile enters the blood (cholemia) it produces a discoloration of the body fluids, and hence a general yellow, yellow-green, or even olive-green color in the organs, as may be observed during life in the skin, conjunctiva, and mucous membranes. This discoloration is called *icterus*. Resorption of bile occurs in the liver either through the lymphatics or the smallest bile and blood capillaries, and commonly after closure of large bile channels. This may follow swelling of the mucosa, as in gastroduodenitis, pressure from tumors and scars, or occlusion by gallstones and closure of bile channels in the liver. The latter condition is explained by the fact that bile is excreted under very low pressure, and hence may be easily retained in the ducts. Beside the bile pigment the biliary acids also enter the blood and are excreted with the former by the kidney. The most pronounced icterus occurs in the liver, where biliary stasis precedes the general jaundice.

While such cases of retention jaundice are easily explained, it is more difficult to understand other cases in which icterus develops without discoverable hindrance to the flow of bile into the intestine, and the feces, usually acholic with retention jaundice, are of the dark color which comes from sufficient admixture of bile, while the liver itself may not show a very marked discoloration.

Pronounced icterus may thus occur in diseases associated with extensive destruction of red cells. The same condition may be induced experimentally by injecting agents which destroy red cells, such as

blood which has been frozen and then thawed, arseniuretted hydrogen, and toluylenediamine. In the same conditions hemoglobinemia and hemoglobinuria are observed. A similar icterus develops in many septic diseases, after transfusion of blood, in the course of infectious diseases, in slight degree with hepatic cirrhosis, in certain heart lesions, and almost physiologically in *icterus neonatorum*. The observation that agents destructive to red cells would cause icterus, and the similarity in chemical composition of hematoidin and bilirubin have led to the assumption, now largely abandoned, that hematogenous icterus arose from formation of bile pigment within the circulating blood.

It is certain that hematoidin may be formed from blood outside of the liver, but never in such volume that it would color the tissues of the entire body. It is more natural to refer the production of the pigment to the liver, in which we know that it is the product of a physiological process. The demonstration of the importance of the liver in the causation of jaundice is given by removing the organ from birds, which do not die immediately after the operation. With geese thus treated injections of toluylenediamine and arseniuretted hydrogen no longer produce icterus.

If we conclude that every icterus takes its origin in the liver, is *hepatogenous*, it remains difficult to explain those cases of jaundice in which there is no retention of bile. Various suggestions have been made, as of a relatively enormous supply of bile, particularly rich in pigment, which cannot be entirely excreted; or that an inspissated, mucous condition prevents its flow from the liver, due to an assumed catarrh of the bile passages; or that there is a swelling of the hepatic cells, as in passive stasis with heart diseases, so that dilated blood capillaries press upon the biliary capillaries and hinder the flow of bile, and thus lead to its resorption.

Contrasted with these explanations, none of which is wholly satisfactory, a recent suggestion seems more plausible, although it still rests upon hypothetical grounds. This hypothesis ascribes a second function to the liver, beside that of producing bile, comparable to the internal secretion of certain glands, because of which its cells constantly furnish to the blood, urea, sugar, and other matters. It is assumed, further, that with disease of the liver cells or of the organism in general, the hepatic activity may be so disturbed that bile may be passed into the blood together with the products normally furnished, being directed not only into the bile capillaries, but also into the blood, thus causing a general icterus without any retention.

Bilirubin infarcts occur as crystalline or granular masses in the renal tubules in *icterus neonatorum*. (See Chapter XI., A.)

The dark pigment of *melanotic tumors*, which is chiefly in the cells, is similar to that of the skin, choroid, and pia, and is commonly free from iron. It may be considered as an increase of the physiological melanin, for such tumors are usually found in pigment-bearing tissues, but a relation to blood-coloring matter is not excluded. Such melanin must be distinguished from pigment arising from bleeding into the substance of tumors. In Addison's disease there is a general discoloration of the skin, which may be regarded as an excess of the physiological pigment in a disease of autotoxic type.

Other pigments which have not been described are the green of *chloroma* (usually a sarcoma) and the coloring matter of *xanthelasma*, which is found in drops of fat. In cartilage and insertions of tendons, joint capsules, and other places there is an unusual discoloration of a dark and inky hue whose nature is not understood. Perhaps the increase of the pigment in cartilage is derived from the blood.

A final group of pigments is introduced from without, taken up by the skin or the respiratory channels, and either laid away in the organs or carried by the lymph as metastatic deposits. After tattooing of the skin the color appears in the nearest lymph nodes, and the black color of the lungs from coal-dust which is inhaled is passed from the alveoli through the lymphatics to the interstitial fibrous tissue, the bronchial nodes, and the pleura. From such places the coal-dust may be carried by the blood to the spleen, liver, and mesentery.

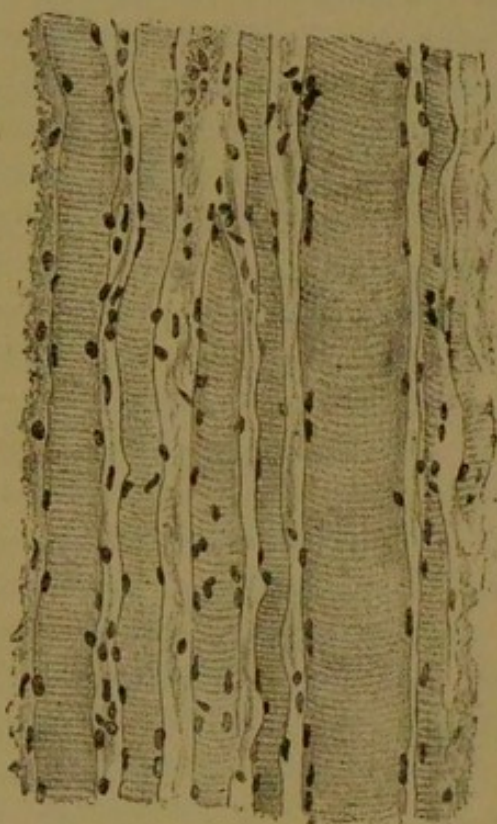
This transportation is in part accomplished by leucocytes, as has been mentioned under metastasis (p. 49). Other dust particles, as of stone, iron, and organic matters, may be taken in by the lungs and carried to other organs, where it may cause fibrosis and contraction. This dust infiltration is termed *koniosis*, and the various kinds have special names, as *anthracosis* for coal, *siderosis* for iron, and *chalicosis* for lime-dust. (See Chapter IX.)

Various pigments which are dissolved may precipitate and cause granular pigmentation of certain parts, as in the kidney, skin, and intestine after long internal use of silver nitrate, which is reduced at the site of deposit. Bacteria which produce pigment are not included here. (See Chapter V.)

C. ATROPHY.

The term *atrophy* indicates simply decrease in the volume of an organ, and is distinguished from all forms of degeneration by the fact that there is no pathological metamorphosis of tissue elements nor deposit of foreign substances. If these are considered as degenerative atrophy, then this form may be called simple atrophy. Its essential character is the quantitative loss of substance, and single tissue elements are usually affected, as in the muscles the contractile

FIG. 34.



Muscle fibres in simple atrophy.

elements, in glands the secreting epithelia, and in nervous tissues the fibres and ganglion cells.

The supposed decrease in the individual elements of an organ may be observed when the fibres of a muscle are slim but striated, and seemingly normal in structure. With loss of many fibres a numerical atrophy occurs, and in atrophy of the skin there is a thinning of the epidermis and a flattening of the papillæ; in atrophy of nerve tissue there is decrease in fibres and ganglion cells, and both are of lessened dimensions.

In a pure form atrophy is found in but few cases. As a general rule it accompanies changes which exceed the definition of atrophy alone, as when, with quantitative decrease, there is also a deposit of pigment as mentioned above (p. 75). Beside pigmentation, vacuolation, fission, and rupture of the fibres may be found in atrophied muscles, and also an increase in the size of the nuclei. (Fig. 34.) In epithelial tissue, as in liver, pigmentation and atrophy are often seen together, and in bone the process causes small round depressions in the bone lamellæ (Howship's lacunæ) which excavate the trabeculæ till they are broken through. The same process occurs in the walls of the Haversian canals, so that they widen, and also in the marrow spaces of the spongy bone. (See Chapter XIII.)

These qualitative processes which in various tissues accompany atrophy prevent the fixing of a sharp limit between degeneration and atrophy, for at times atrophic processes are merely the repetition of physiological changes. In atrophy of bone there is the same resorption which occurs during the period of growth of normal osseous tissue. In other cases atrophy more nearly approaches metaplasia, as in the peculiar senile transformation of fatty marrow to mucoid tissue.

Other cases of atrophy are strictly degenerative, although the tissue destruction may proceed in a very gradual manner, and the products of decay being at once removed, the impression is given of pure quantitative decrease. When a nerve is cut through the two portions, peripheral and central, do not behave alike. In the peripheral stump there is a rapid fatty degeneration of axis-cylinder and medullary substance, the neurilemma being filled with their remains, which are finally taken up and removed by granular cells. This is termed Wallerian degeneration. In the central stump there is also a degeneration, but it is less evident, the loss of fibres is much smaller, and accumulation of destroyed tissue is but temporary, for it is rapidly carried away. If the cut ends do not unite the central stump becomes atrophic, its fibres become more slender than normal, and perhaps many of them are wholly lost, but the process is really an extremely slow degeneration.

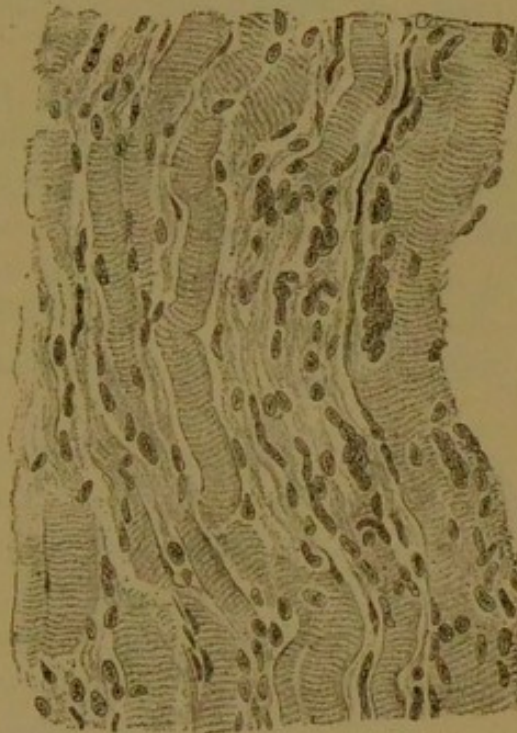
Finally, parts in which a rapid degeneration has taken place may assume the atrophic appearance when the degenerative process ceases and when no more products of tissue destruction remain to indicate the nature of the lesion. Hence a column in the spinal cord in which the fibres are entirely lost appears, from the glia stroma remaining,

as an example of gray sclerosis, in which an occasional fatty fibre may still suggest the original structure.

Hence the idea of atrophy is not so simple as the gross appearances of atrophied organs may indicate, and it must not be understood as mere decrease in volume without any accompanying qualitative features.

With the loss of the distinctive parenchyma of an organ the interstitial tissue may not be decreased; in many cases there is even a compensatory increase of the stroma, and if this precedes it may be the cause of the parenchymatous atrophy. (See Hypertrophy, Chapter III., C.)

FIG. 35.

Atrophy of a muscle with increase of nuclei. $\times 250$.

From its various causes we may divide atrophy as:

Senile atrophy affecting the skin, brain, heart, bones, and cartilages, and appearing in the vessels as arterio-sclerosis. Closely related is *marantic atrophy*, as in cachexia, fever with heightened catabolism, and following exhaustion of a gland from over-production. These may all be called *cellular atrophy*, because primarily affecting cells, although with the anemic forms lessened nutritive supply also plays a part. General diminution of nutrition may also produce atrophy of organs, as starvation, imperfect absorption of nourishment in chronic diseases of the alimentary tract. Here the fat, body muscles, liver, and blood suffer, less markedly the heart and central nervous tissues, which may be nourished from the products of destruction of other organs.

With sclerotic and other affections of limited portions of the vascular system, scattered areas of atrophy may appear in certain organs or parts of organs, as when sunken and atrophic regions are found on the surface of a kidney when its vessels are atheromatous, and in the cortex when the glomeruli and tubules are destroyed. Similar localized atrophy occurs in the brain. A cyanotic atrophy may accompany chronic passive congestion in parenchymatous organs.

It is probable that certain nerves have a trophic influence upon certain organs, for, with lesions of the cord and nerves, atrophies of the skin and muscles supplied by these nerves are often observed. Although vasomotor disorders also act in these cases, they are not alone sufficient to cause the atrophy. Among the neurotic atrophies may be mentioned unilateral atrophy of the face with affections of the trigeminus, and hemiatrophy of the face with cerebral lesions, the latter being a crossed paralysis and accompanied by changes in the opposite limbs. In lepra of the nerves there are usually atrophic disorders in the skin, as loss of hair, destruction of the skin about lepra tubercles, ulcers, and abnormal pigmentation.

In bones and muscles of paralyzed limbs, in amputation stumps, and in the muscles of mastication after loss of the teeth, there is a form of *atrophy* from *disuse*.

Pressure atrophy follows long-continued moderate pressure, which if stronger might cause necrosis. Examples are found in the depressions in the skull corresponding to the Pacchionian bodies, in the thinning of the bones with hydrocephalus, in the atrophy produced by hard and cystic tumors of various organs, and in hydronephrosis with loss of renal tissue. It is notable that soft organs, as the brain, are less influenced by slight pressure than are denser tissues, perhaps because they have more power of adaptation.

Lastly, certain chemicals have the power of causing atrophic changes of some organs, as seen in the action of iodine on glandular tissues.

Within glandular organs the secreting epithelia may lose their characteristic appearance and become more like the cells lining the ducts. Thus the cells of the convoluted tubes in the kidney may resemble those of the straight collecting tubes, and those of the liver the cells lining the biliary channels. This change is interpreted as a return to a less differentiated form (Ribbert).

CHAPTER III.

PROGRESSIVE PROCESSES.

IN contrast to the processes already described, we come now to a series in which the vital activity of the body is actually increased, and which we consequently term progressive disorders of the cells. The most important among these are grouped together as vegetative or formative, implying an increase in number or size of the elements. The original stimulus of a cell to produce another of its own kind we observe in the first cell of the organism, in the ovum after impregnation. Such possibilities of increase are not wholly lost, even in the cells of the fully developed body, but slumber in them to be awakened at need. The factors in such reproduction may be external or internal, and in the latter case may be inherited or acquired. Even the first class of factors are but occasional in their influence. According to the type of stimulus the new tissue may be of various forms, and its development may be directed by many influences in different directions. We are unable to separate the various forms sharply from each other, for only the external characteristics may be offered for our consideration. Even if we should succeed in separating the various types of these tissues, we may expect that numerous transitions bind them all together as the links in a steadily unfolding series, with lateral offshoots, according to the etiological factors involved.

In every part of the organism during the stage of development there exists the power to advance to a certain size, and, when this is attained, the power to replace elements which may have been lost. This formation of new tissue we recognize as *repair*, and it is generally in very close connection with physiological growth.

A second variety of tissue growth leads to an increase in number and size of the parts, with retention of the normal structure of the organ, occurring either without previous discoverable loss or after part of the organ has disappeared. This process receives the name *hypertrophy*. In some cases it follows heightened functional activity of an organ, in other cases the stimulus is some unknown internal cause, and many of its phases have close relations with the following group.

In another class of cases the cell growth follows external influences, which either directly excite to new formation or cause injuries and modify the reparative processes which then arise. With these, more or less definite vascular phenomena are observed. This variety of progressive activity belongs with the phenomena of *inflammation*.

A fourth group of new formations includes processes in which from a single or many localities, commonly without apparent causation, a growth of young tissue elements takes place, often marked by persistent power of self-multiplication and corresponding destruction of the adjacent tissues and of the site of origin, so that, as parasites in the organism, they attain a more or less circumscribed or diffuse development. Thus are formed the true *neoplasms*, *tumors*, or *new-growths*. In them the vegetative powers have not only an increased, but also a metamorphosed development.

All progressive changes are subject to certain laws, both physiological and pathological. Thus the general principle holds that a tissue once differentiated never is transformed into one of a different kind; epithelium never makes connective tissue, or *vice versa*, muscle and nerve tissue proceed from their own kind, never from each other. Among the derivatives of the mesenchyme only a few present transformations, such as occur physiologically in the group of connective tissues. Bone may develop from connective tissue or cartilage, and connective tissue may become mucous or fat tissue. Such changes, affecting chiefly the intercellular substances, are known as *metaplasia*. This may occur in preformed and in new tissue. In this way fat tissue and mucous tissue develop physiologically, and fatty marrow replaces the lymphoid in the long bones, and in old age mucoid marrow replaces fatty. In pathological conditions this metaplasia occurs as either a regressive change, as in mucous degeneration of bone and cartilage, or a progressive process, especially in tumors. In epithelial structures metaplasia may transform the cells from one kind to another, as cylindrical cells to squamous. Whether there is a true metaplasia of cylindrical epithelia into corneous, or only a substitution of one for the other, is much disputed. On the other hand, a metaplasia of epithelial tissue occurs in repair, as when lining cells of gland ducts become actual secreting epithelia, or buds from the bile capillaries become hepatic cells, while similar changes are seen in the alimentary tract.

Pathological growth, like the normal type, occurs by karyokinesis, a characteristic transformation of the nucleus involving, first, division of the nucleus, later of the protoplasm.

In spite of many variations, a generally correct description of mitosis may be thus epitomized: The nucleus consists of many substances (Fig. 36), threads of *linin* in a network forming the stroma of the nucleus. This reticulum carries a peculiar substance which has an affinity for basic stains, and is hence called *chromatin*. The chromatin is arranged in threads or at the nodes of the reticulum in masses. Between these, in the meshes, there is a nuclear fluid, the *karyolymph*. In the nucleus there is also a rounded *nucleolus*, similar to chromatin, but somewhat different in staining qualities. A membrane, more or less chromatic, surrounds the whole nucleus.

The quantity and arrangement of the chromatin are not uniform for all cells, and vary in the same cell according to its age. If the chromatin is scanty the nucleus appears light, and the membrane, nucleolus, and chromatin particles are distinctly seen. This appearance is expressed by the term *vesicular nucleus*, and is common in young connective tissue, epithelial, endothelial, and wandering cells. Other nuclei in fresh preparations are very dark, as in ordinary connective-tissue cells, because the chromatin is copious or lies closely packed.

The form of the nucleus of the leucocyte requires special mention. Lymphocytes have a single large nucleus, simple and round, and darkly staining. The majority of the leucocytes possess a nucleus which is irregular, polymorphous, more or less lobulated, and these lobules may be connected with each other by delicate strands of pedicle. (Figs. 38 and 39.) In this way horseshoe, clover-leaf, and ring-shaped nuclei may appear, and in many cells the portions of the nucleus are separate, and the cell is polynuclear. These cells are said to have fragmented nuclei, and usually they stain very dark and uniformly.

Typical cell division is called *karyokinesis* or *indirect mitosis*.

At first the polar body, or *centrosome*, lying near the nucleus divides and the two halves retreat from each other, connected by a number of light strands which make the *achromatic spindle* which develops as the halves reach the opposite poles of the nucleus. About each centrosome there forms a radiating figure called the *polar radiation* or *attraction sphere*. During this change the chromatin of the nucleus increases and becomes rearranged. A tangled mass of chromatin occupies the site of the reticulum, made of a number of chromatin threads, and called the *primary skein* or *spireme*. Nucleolus and nuclear membrane disappear, probably forming part of the spireme. The chromatin threads become bent into loops, which are then arranged

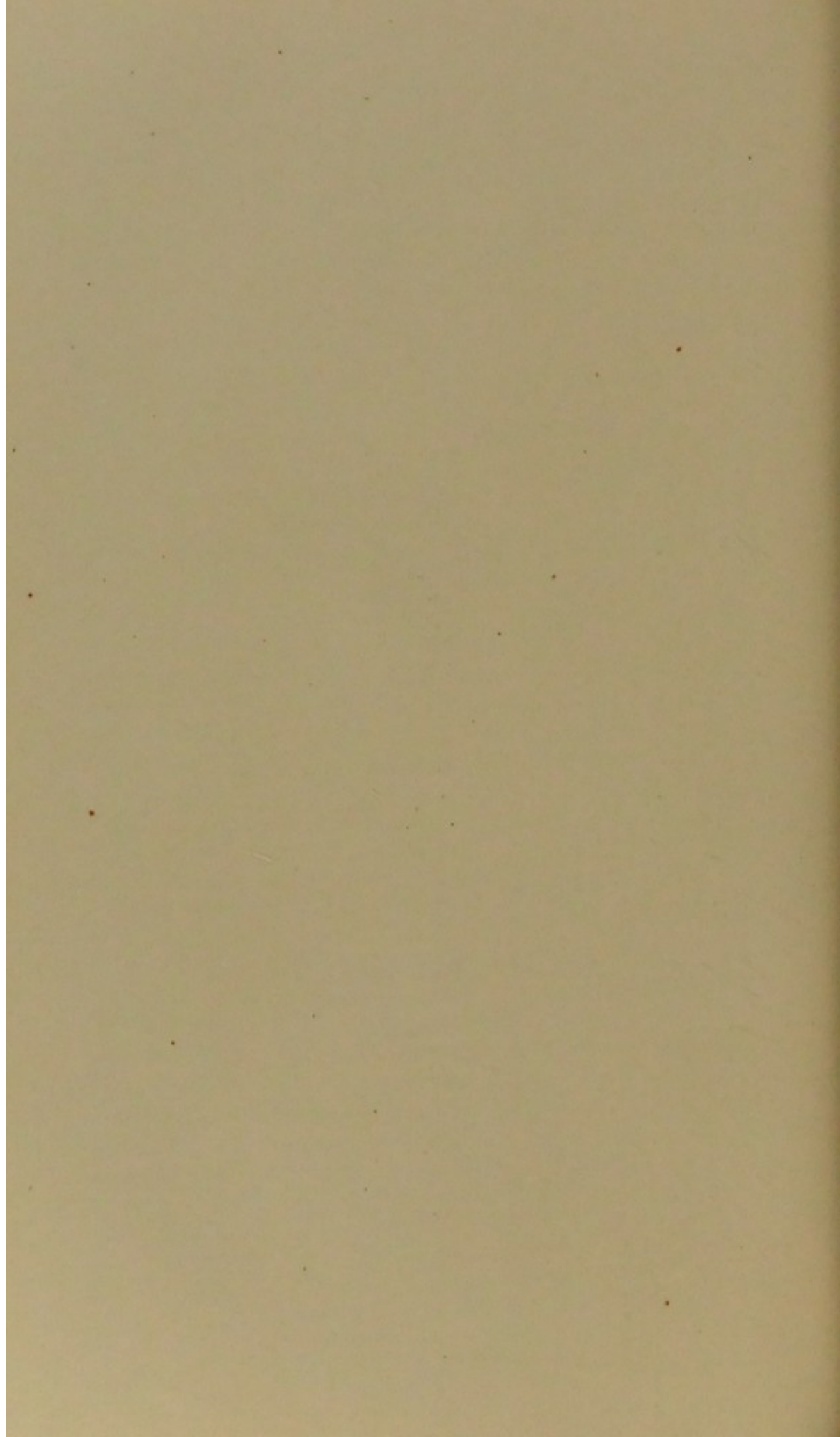
PLATE VI.

FIG. 36.



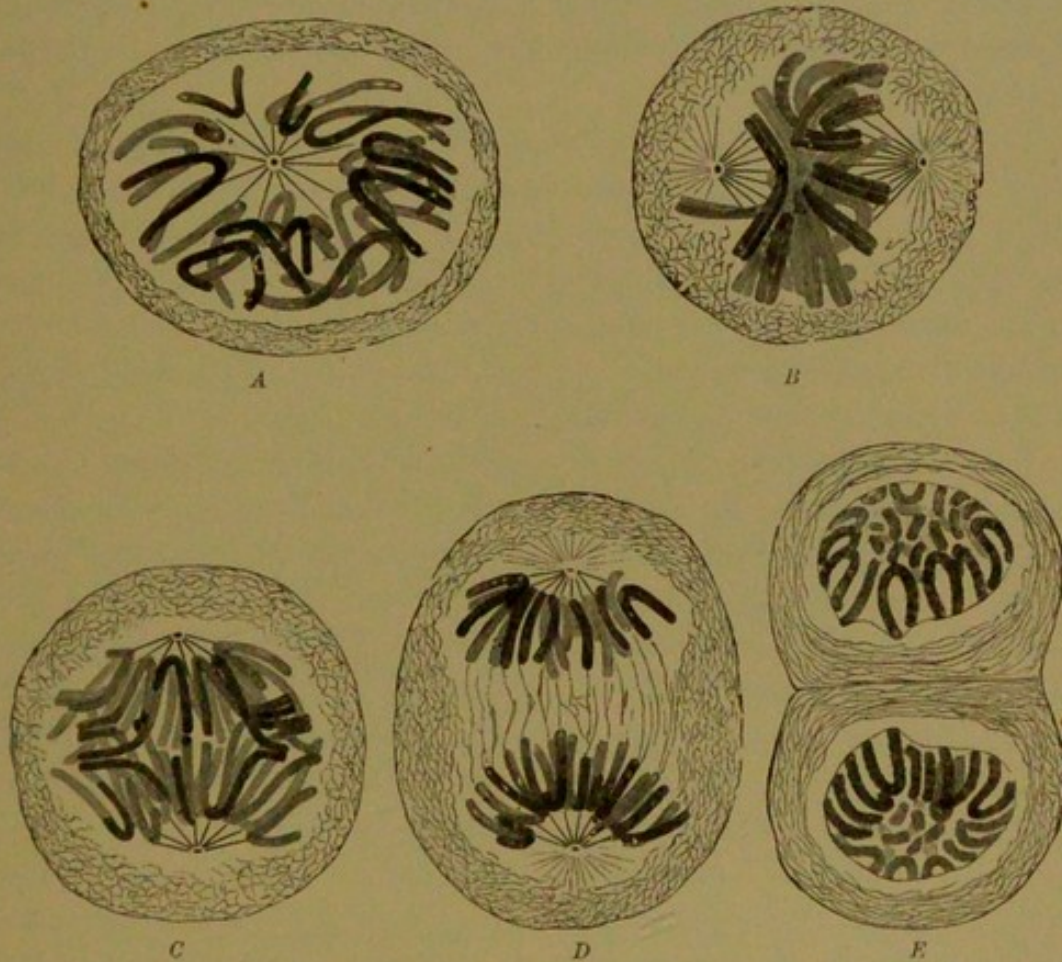
Diagram of Nuclear Structure.

Chromatin red, in granules and threads, lying on the nuclear membrane and the karyolinin reticulum; the latter is black. In the middle of the nucleus a red round nucleolus. Nuclear fluid unstained. $\times 800$.



about the equator of the achromatic spindle, making the *monaster*, or mother star. (Fig. 37.) These loops are then split lengthwise, so that each makes two more slender figures. The halves then separate, each going toward its adjacent pole, angle first. Thus half of each loop is contained in half of the entire figure, and the entire chromatin

FIG. 37.



Five stages of indirect mitosis in the land salamander (Bergh, Lectures on the Cell, Wiesbaden, 1894). A. Beginning mother star. B. Transition stage, splitting of the chromosomes. C, D. Wandering of centrosomes to the poles. E. Daughter stars. A. Shows the achromatic spindle, polar body, and polar view of the loops. B. The equatorial plate, the same picture from the side. C, D. Also from the side. (Modified from RABL.)

is equally divided between the two. The arrangement about the mid-plane of the spindle is called the *equatorial plate*, the movements of the end phase are called the *metakinesis*. The two halves separate from each other and form the daughter stars, *diasters*, which develop secondary skeins, later exhibit nuclei and nucleoli enclosed in membranes, and so attain the resting stage, while the spindle disappears.

A. REPARATIVE PROCESSES.

1. Regeneration and Healing.

The power of regeneration which many lower vertebrates have, replacing even entire organs, is lacking in the higher vertebrates and man, although small defects in tissue may be repaired, to a varying extent in different tissues. Thus in epithelium and connective tissue reparative faculty is fairly high, but in nervous tissue it is hardly observed.

In general the process of repair involves mitotic division of cells of corresponding tissue, epithelium from epithelium, etc. Often a larger mass of young tissue is formed for repair than is actually needed, or will remain permanently, as in the case of large callus after fractures of bones, which disappears when the bones become firm enough. Similar over-production marks the early stages of repair in epithelium, in glands, and in connective tissue.

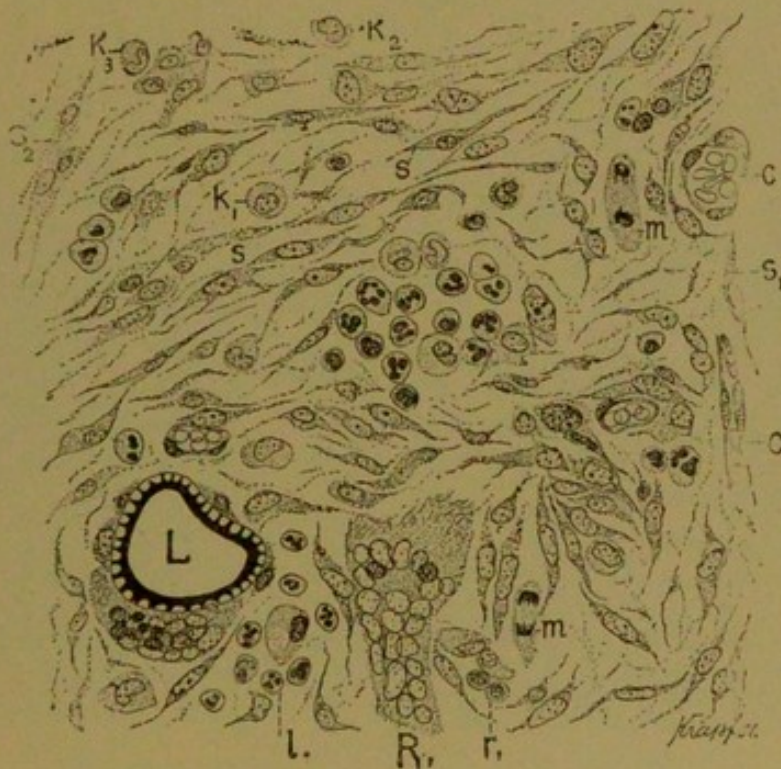
Necessary conditions for repair are that disturbing influences do not interfere in the process, so that sufficient nutrition is supplied to the young cells, and that the general state of the organism be correspondingly good. Constitutional weakness of the organism, as in age, diminishes reparative power. As a matter of fact, in higher vertebrates repair of lost substance and closure of wounds do occur, but the process belongs only in part to regeneration and far more to repair by increase of the supporting stroma. It is the general law that where regenerative power in a tissue does not suffice to restore a loss by specific tissue, an indifferent interstitial repair covers the defect, just as in the embryo the derivatives of the mesenchyme enter the space between two germinal layers. In the majority of organs the replacing material is connective tissue, in the central nervous system it is glia tissue. In most cases, then, there is the formation of a scar in which the specific elements of the part may be represented, but do not occur in the normal arrangement or function. Connective-tissue new-growth in scar formation is exactly like the same formation in repair of connective tissue, and begins as an active growth and increase of the connective-tissue cells in the neighborhood of the edges of the wound.

The new young connective-tissue cells are mostly long, spindle-shaped, with long processes in the direction of their main axis, or with numerous processes which give the cell a star shape. These cells are called fibroblasts or granulation-tissue cells. (Figs. 38 and 39.) The

largest resemble epithelia by their relatively large bodies, and hence are called epithelioid cells.

Beside the long cells, others are found in granulation tissue, with a large nucleus, often indented, which are called *wandering cells*. (Fig. 38.) Their origin is not certain, the old idea being that they came from the blood, the present view being that they are derived from the fixed connective-tissue cells, especially that they are originally wandering cells which have become attached to the adventitia of vessels, so-called *clasmatocytes*, but which then become motile again,

FIG. 38.



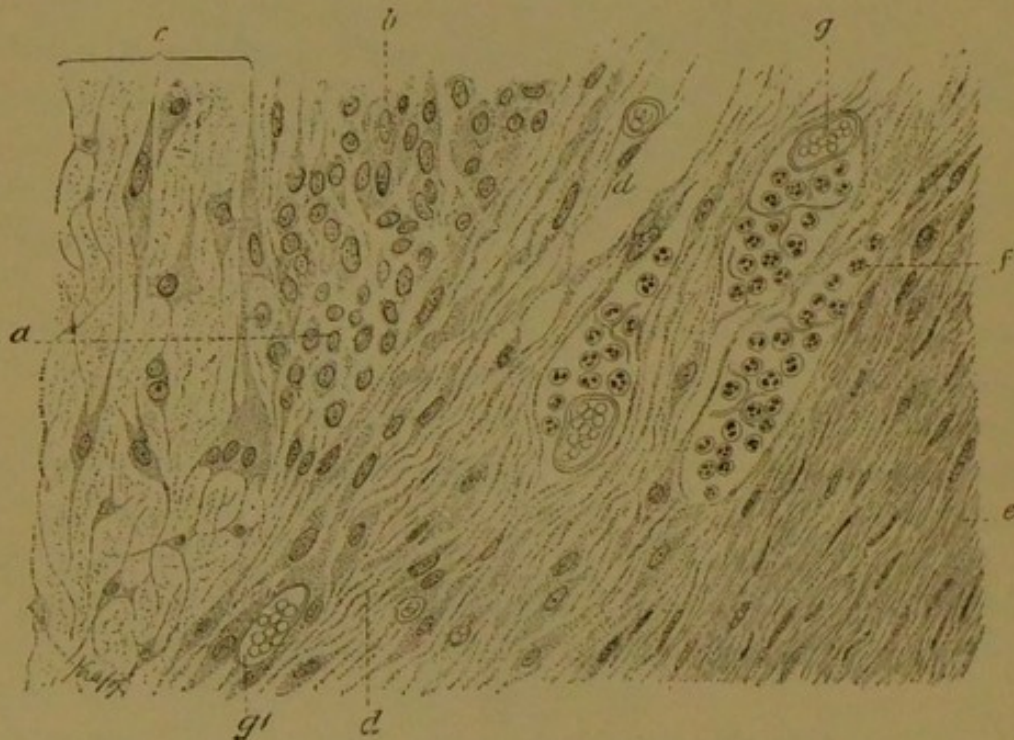
Granulation tissue from the peritoneum of a guinea-pig after injection of lycopodium spores. S. Spindle cell. m. The same with mitotic figure. $k_1 k_2 k_3$. Wandering cells with large nuclei. l. Leucocyte with polymorphous or fragmented nuclei. r. Mononuclear cells. R. Giant cells. c. Young capillary. L. Lycopodium spore with adherent giant cell.

multiply, and take part in forming young connective tissue. The young tissue contains also a varying number of small round cells which are mononuclear or polynuclear *leucocytes*. (Figs. 38 and 39.) The first leucocytes surely come from the blood, the last may come from neighboring lymph follicles and lymphadenoid tissue in various organs, others may be derivatives of the adventitia cells. We apply the name *round cells* to all these varieties.

Between the granulation cells there are yet other varieties known as *mast cells*, leucocytes which include in their protoplasm small granules

staining deeply with basic aniline dyes, and *plasma cells*, large lymphoid elements which take methylene blue especially. Lastly a cell appears, and hence called *giant cell*, possessing, as in marrow, a very large single nucleus with many polymorphous subdivisions, often found in thin sections and giving the impression of a polynuclear cell, or actually containing as many as one hundred nuclei, often disposed about the margin of the cell. (Figs. 38 and 10, *r*.) In pathological conditions giant cells appear where foreign bodies occur, or where there is active resorption of tissue, and they may be provided with many branching processes.

FIG. 39.



Older stage of granulation tissue. *a*. Lymphoid cells. *b*, *c*. Granulation cells connected by processes, with ground substance between which has become granular by hardening. *d*. Fibres forming near spindle cells. *e*. Fibrous tissue. *f*. Infiltrating round cells with polymorphous nuclei. *g*, *g'*. Vessels. $\times 350$.

The essential elements of young connective tissue are the round, spindle, or stellate cells mentioned, and because they form the new tissue they are called *fibroblasts*. In properly prepared sections the mitotic figures demonstrate the lively multiplication in which they are engaged. For this an increased supply of blood must be furnished, and this vascularization of the tissue may proceed from the immediate neighborhood. Adjacent capillaries form buds which push their way between the young cells (Figs. 38 and 41), at first in the form of solid projections from the endothelium, which then become hollow with

independent nuclei. These come from the nuclei of the budding portions, or else a multiplying cell divides into two in such a way that between two young cells there is a space connected with the lumen of the capillary, which then joins such a vessel. From the young capillaries the arteries and veins develop by the formation of muscle fibres and elastic elements in the capillary walls, sprouting from older vessels. As the capillary buds join, develop a lumen, and join with blood-carrying vessels, the circulation is established through them, and the new tissue has a system of young and delicately walled capillaries.

FIG. 40.



FIG. 41.

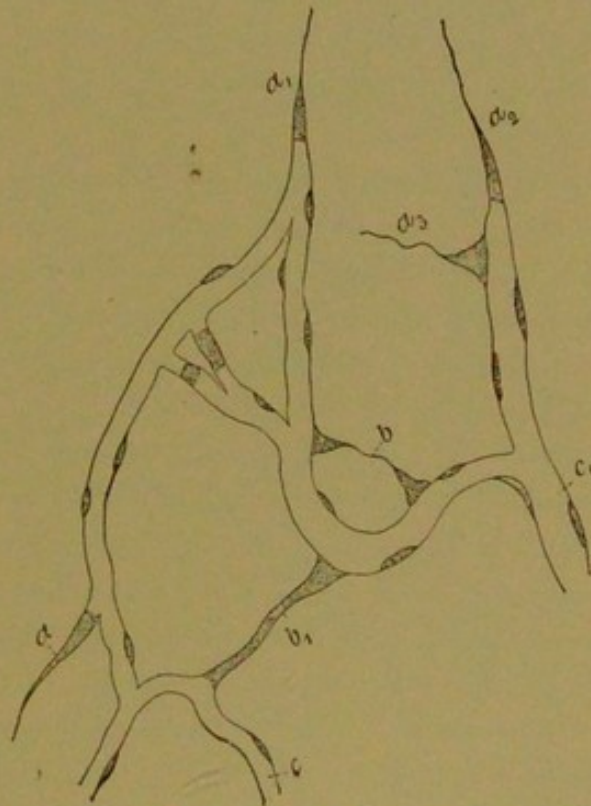


FIG. 40.—Fibrillary connective tissue with cells and fibres. The single fibrillæ are seen with spaces between the bundles. (After LEYDIG. Histology.)

FIG. 41.—Formation of capillary vessels. $a-a_3$. Buds. bb_1 . Buds joining. cc_1 . Complete young capillary. $\times 320$. (After ARNOLD. Virchow's Archiv, Band lili. and liv.)

Such young and vascularized connective tissue is called *granulation tissue*. At first its structure is not fibrous, but at last fibres form, either by change of cell bodies into fibres while a portion still remains protoplasmic, or by the extrusion from the cells of a homogeneous substance which differentiates into fibrillæ. It is not certain which is the right view; perhaps both methods are followed. The fibrillæ form the chief mass of the connective fibres, but some of them become elastic fibres. With the increase of the fibres some of the cells disap-

pear altogether, others remain lying on the fibres as flat, fixed connective-tissue cells. Then they appear as small spindle or linear figures parallel with the long axis of the fibre, their protoplasm so reduced that but a minute remnant can be seen at the poles of the nuclei. Some others persist as stellate cells or homogeneous and flattened cells, both with reduced protoplasm.

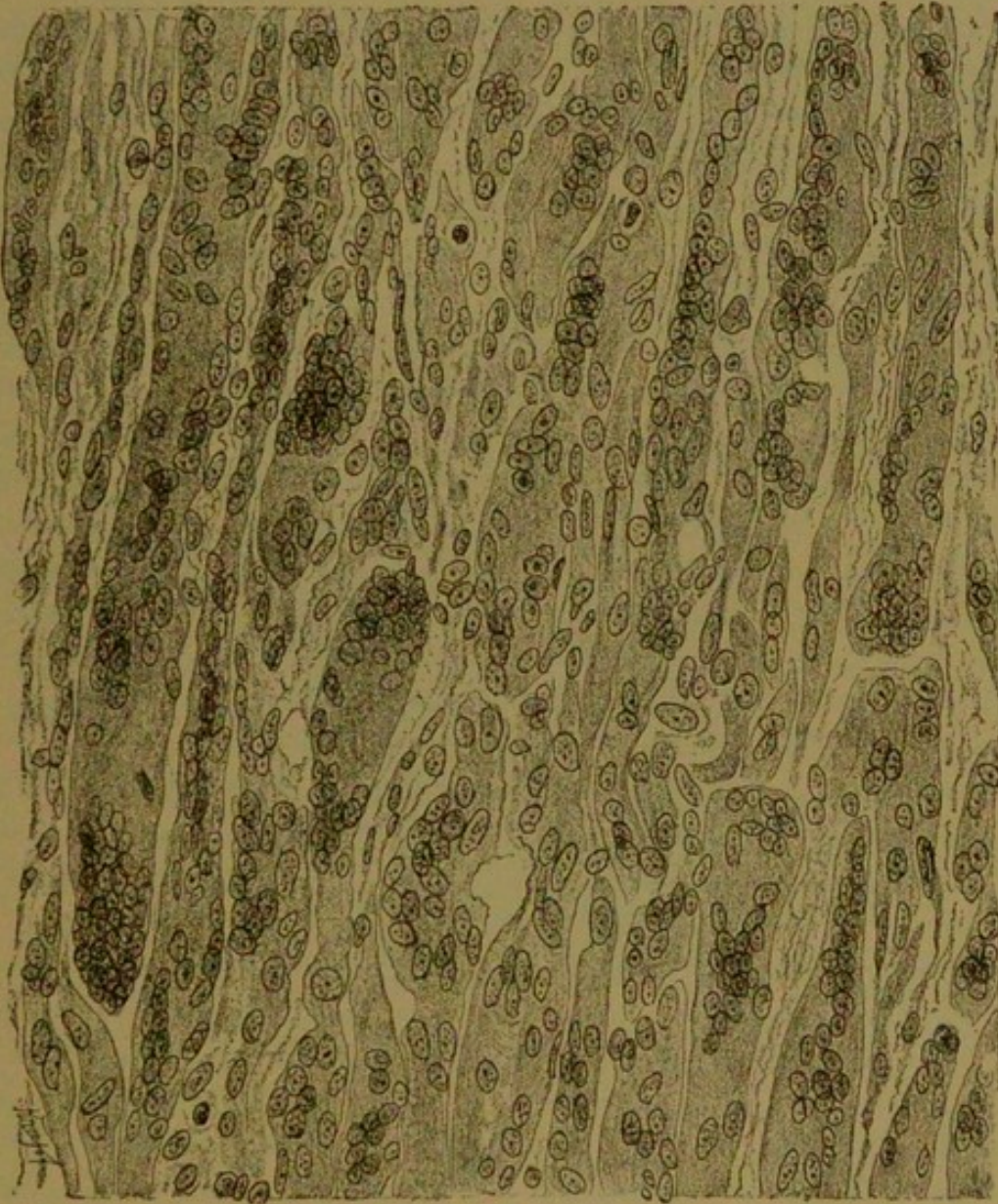
In ordinary connective tissue the fibres are arranged as thick and interwoven bundles, with a system of spaces between in which the tissue fluids circulate and which are the beginnings of the lymph system. In these spaces there are found in small number both lymphoid and mast cells. Cicatricial tissue formed as described undergoes a contraction of its young fibres, so that its bulk is often much reduced, and in time there is a partial, regressive diminution of the vascular network.

The best conditions for regeneration are given when single cells or groups of cells are lost without injury to the other structures. This may be called physiological regeneration—*i. e.*, the restoration of cells lost under physiological influences. Thus there is a continual new-growth of investing cells of skin and mucous surfaces and also of hair and nails. Similar observations may be made on the Lieberkühn follicles of the intestines, sebaceous glands, and the functioning breast, in all of which the secretion implies partial destruction of the cells. There is a continuous loss and regeneration of blood cells, for the life of a red cell is brief, and hence the need of new supplies, which are furnished, at least in the adult, solely from the bone marrow. The white cells are lost by exit upon mucous surfaces and are renewed in the germinal centres of lymph nodes, the follicles of the spleen and intestine, and the marrow. Somewhat similar is the formation of spermatozoa in the testis from spermatoblasts, and the regeneration of epithelium in the uterus after menstruation and pregnancy.

Pathological losses where the entire structure of the part is not lost are also easily repaired, especially if the connective-tissue stroma is not severely injured, and thus relatively large defects in certain organs may be repaired. After catarrhal inflammation of mucous membranes we see a rapid regeneration of the epithelium, and observation and experiment prove that in the kidney a complete regeneration of the epithelia is also possible if the loss is not too great. In the liver the possibilities are even more favorable, for new liver cells may be made from bile capillaries, buds forming which make close connections with the remaining liver tissue, and even become transformed into hepatic

cells. In a similar manner in the alimentary canal tubular glands develop from remnants of former ones or from the epithelial cells of the ducts. In striated muscle a renewal of the fibres may occur, as after waxy degeneration with loss of single fibres, and also

FIG. 42.



Regeneration of muscle after waxy degeneration in typhoid fever; myoblasts and giant cells.
× 250.

after the trophic disorders which follow section of peripheral nerves. (See Chapter XII.) The muscle forms from large cellular bodies which grow, divide by mitosis, and surround themselves with much protoplasm, then fuse to granular plates, and differentiate by taking on cross and longitudinal striation. Smooth muscle cells multiply by

ordinary mitosis. In the nervous system when the vessels and the stroma are not much affected, regeneration of nerve fibres and their function may occur. The peripheral nerves will be treated later.

Wounds in which the tissues have been divided by a clean stab or cut, without bruising or other change in the edges, heal like losses of simple cell complexes, especially if immediately closed by suture. In the absence of infection healing proceeds without complications, and is called *primary union*, or *first intention*. Thus in the skin freshly sutured uninfected incisions show adhesion of the edges, the adjacent fibrillary tissue loses its fibrous structure, swells, and becomes more gelatinous, and any blood or exudate present aids in the adhesion. From connective and endothelial cells of the margins a narrow line of granulation tissue forms and at last a linear scar, while lost epithelium is restored from adjacent cells. Incised wounds of mucous membranes and glands heal similarly, and the cicatrix may show the glands growing through it. The central nervous organs show slight variations from this process, since incised wounds cause traumatic degeneration about them. (See Chapter XII.) In the peripheral nerves, as mentioned above, a complete power of regeneration exists, the peripheral end being destroyed after section, while numerous axis-cylinders grow from the central stump into the peripheral, unless the parts are too widely separated or a tough connective-tissue scar forms between. (See Chapter XII.)

In muscle the conditions are less favorable. Immediate reunion of muscle demands approximation, which is difficult to secure on account of the retraction; hence there forms a narrow scar, which is equivalent to a new tendinous growth of pathological origin, but does not hinder the function. Cut tendons reunite, after careful fastening of the ends, by a connective-tissue scar, and even long spaces may be filled by such fibrous cords. Cartilage heals by connective tissue which later may contain cartilage. Healing in bone is discussed in Chapter XIII., A.

When the loss of substance is too large for simple scar formation the defect is closed by new connective tissue, of an extent corresponding to the wound. Few tissues have marked regenerative power of their own. Where a wound is not healed by immediate junction of the edges, but by a large amount of young connective tissue, it is called *union by second intention*, or *secondary union*. The regeneration is then imperfect, for the original tissue may not be restored.

With large and gaping wounds, granulation tissue repairs the defect,

starting at the bottom and sides of the injured portion. From about the third day there are visible fine, red, projecting granulations, which bleed easily, and as these granulations gradually fill the wound space there is a contemporary restoration of the integument between the scab and the granulating surface, which pushes the former off and at last covers in the new tissue. As long as the epithelial covering is not complete it is possible for the superficial epithelium to take on an abnormal and excessive growth, in the form of pegs and nests which reach down into the young connective tissue for a short distance. This is called atypical epithelial proliferation, and its differentiation

FIG. 43.



Atypical epithelial growth. *e*. Superficial epithelium. *c*. Corium, infiltrated with cells.
e'. Epithelia growing down into the deeper tissue.

from carcinoma is given in Chapter III., E. Fig. 43 presents such a case. From sebaceous glands an analogous overgrowth may occur and result in atypical gland proliferation in the spaces of the young tissue.

Before the time of antiseptics, healing of wounds was accompanied by profuse suppuration, but the inflammatory symptoms are reduced to a minimum since exclusion of infectious agents has been practised. Still, at times, there are slight degrees of this feature in healing of wounds, which may be referred to the irritant action of the antiseptic fluids used or to other unavoidable external influences, and it is worthy

of note that wounds heal more favorably with aseptic treatment than with antiseptic. In sharp contrast with the union by first intention, free from all symptoms of irritation, the wound secretes a reddish, serous, or seropurulent fluid in slight amount and without danger for the organism.

When injury has been attended with bruising of the edges of the wound, or other causes of necrosis enter, there is a profuse emigration of white cells and a demarcation of the dead tissue from the living. As the dead tissue sloughs off the wound cleanses itself. The strong irritation which accompanies union by second intention is evident in the excessive granulation and delayed formation of fibrous tissue, a condition called *proud flesh*, or *caro luxurians*.

With the completion of the epithelial covering the granulating process reaches its end, and its transformation into fibrous tissue is finished. Then occurs a strong contraction of the cicatrix, with decrease in its size and increase in its density. This *scar* is not wholly like the original tissue; the epithelial investment is reproduced, but sweat and sebaceous glands and hair follicles are replaced only when portions of these structures remain. Elastic fibres form later, lymph vessels are imperfect or lacking, the numerous vessels are slowly reduced in number, nerves are not found, and the papillæ are rudimentary. Hence the surface of the scar is smooth, glistening, and tense, and of a pale color; the new fibres of connective tissue are tightly woven, inelastic, and of dense-white character.

In a similar manner defects of the mucous membranes are healed, with regenerated investing epithelium, scar formation, and new-growth of glands into the cicatricial tissue from remnants in the edges of the wound. Later contraction of the scar disposes the mucosa in folds which radiate from the site of injury. If the cicatrix reaches into the deeper parts, marked changes of form may follow its contraction, as stenosis of hollow organs. Ulcerating surfaces in mucous membranes are partly reduced in size by the lapping over of the edges.

Since in all tissues where the wound is at once united there is a small scar, it follows that there will be larger scars, with large defects in muscle, cartilage, and other tissues. In the large glands a marked proliferation of glandular structures may occur into the young connective tissue and persist in the scar, the different organs varying somewhat in this respect, but restoration of specific functioning tissue may hardly be said to occur. The testis and ovary are peculiarly lacking in regenerative power. In lymph nodes and bones (see Chapter VIII.)

there may be remarkable regeneration. In the central nervous organs small defects may be repaired by glia tissue, the larger either by connective tissue or by the formation of cysts. (See Chapter XII.)

2. Transplantation.

The experience that small pieces of tissue retain their vitality for a time outside of the body has been used to aid in the repair of wounds, and this practice is called *transplantation*. Such transplanted fragments become part of the site to which they are removed, in favorable circumstances, and materially aid in covering granulating wounds. The best results are obtained when a piece of integument, still held by a pedicle, is turned and fastened to another portion, as in rhinoplasty. The portion so used is not wholly severed from its source of nutrition until firmly grown in the new place. Small bits of epidermis with or without attached connective tissue, or a suspension of epithelial cells in fluid, have been used, and in certain cases favorable results have been secured, the cells multiplying, though the connective-tissue portions are lost. Transplantation of bone has been tried for the repair of defects in osseous tissue, and, though the bone is destroyed after a time, the accompanying periosteum and marrow are the starting points for new osteoid tissue.

Implantation of portions of organs in the subcutaneous tissues, in other organs, or in serous cavities, has been often tried experimentally, and the foreign tissues may heal and persist for a time where planted, but after a longer or shorter period they disappear. Only when a transplanted part can retain its function does it remain. Thus ovaries implanted upon the peritoneum of the guinea-pig produce matured ova, and after removal of the thyroid a substitute by implantation of a portion of that gland in the peritoneum prevents the development of the tetany otherwise commonly seen. (See Chapter VI.)

In the subcutaneous tissue, transplanted bits of epidermis with fragments of connective tissue may develop epithelial cysts, by growth of the cells in the cavity in which the new tissue lies.

A necessary condition for transplantation is that the tissue shall be living; but many elements, as skin and cornea, may retain the power of growth in the new site even for weeks after removal from the original organism, and be transplanted with success if extremes of temperature, suppuration, etc., be avoided. Transplantation from one part of an individual to another part is most successful, to another of the same species less so, to a foreign species least. In the case of

lower animals regeneration and transplantation are far more successful than among higher species.

3. Inclusion of Foreign Bodies with Healing. Organization and Resorption. Cyst Formation.

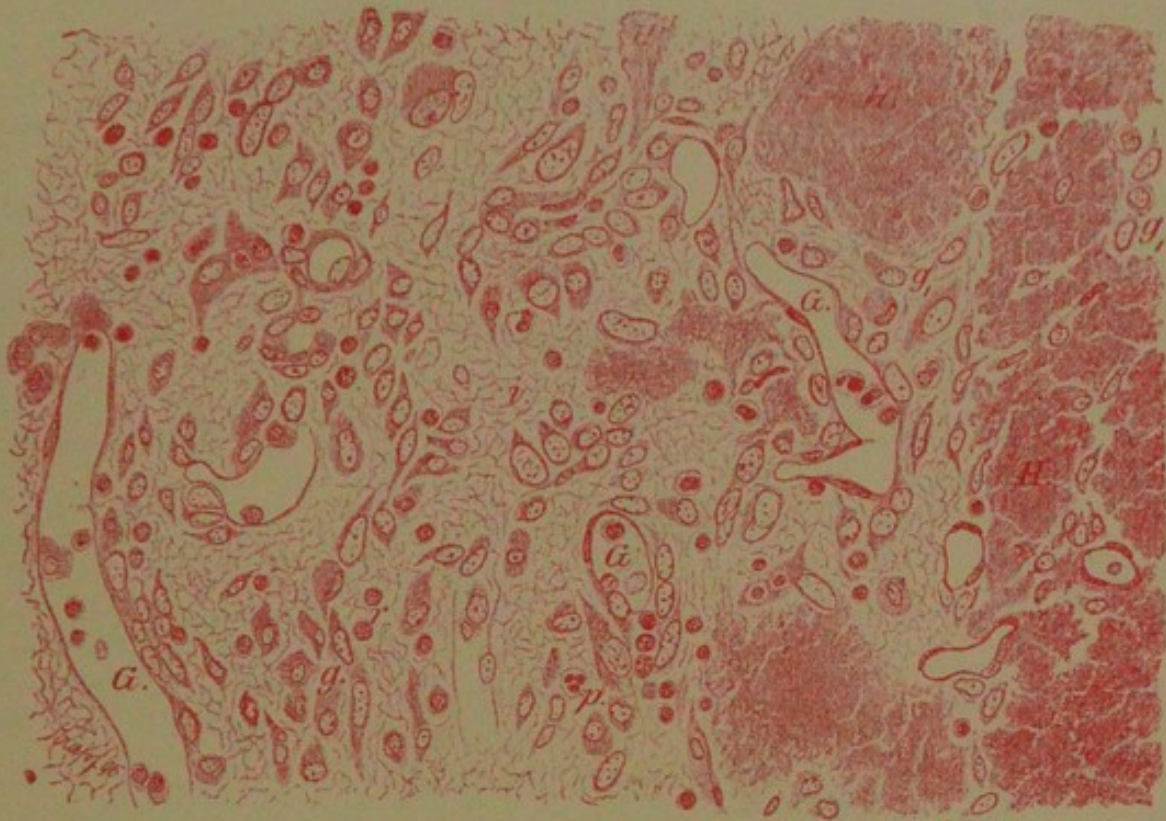
The smooth healing of a freshly sutured uninfected wound proves that the body has the power to reunite separated parts, without further complication, by means of cell growth. Modern aseptic surgery has demonstrated that unirritating substances may be included in a healing wound without inflammatory reaction if there be no infectious material carried in with them. About the *foreign body* there is a proliferation of connective tissue, and since the space they occupy cannot be taken by it, they are simply encapsulated. Needles, pieces of instruments, bits of glass, bullets, etc., may thus be enclosed in the tissues without any other damage than was produced by their entrance by injury to tissue elements, or than by the mechanical pressure and stimulation to growth. If the foreign body is porous, as a piece of aseptic sponge or pith, the leucocytes wander into its spaces, then ameboid young connective-tissue cells join these, and fibrils are formed in it (p. 87). Where there is a continual supply of small particles, as dust of various kinds, the tissue reacts by chronic progressive inflammation.

Many concretions act as foreign bodies, usually made by precipitation of material from the organism. Lime calculi, biliary and urinary precipitates, may act thus if deposited in tissue. With continuous processes of this kind the tissue may react as to dust particles, with chronic induration as the result (p. 67). Related to these are the connective-tissue reactions observed about foci of chronic suppuration, tuberculosis, etc., which enclose and limit the advance of such lesions. (Part II., Endarteritis obliterans.)

When portions of tissue necrose from any cause, or dense extravascular or intravascular products have been formed, these act like foreign bodies and are gradually eliminated and replaced by connective tissue. This process includes *resorption* and *organization*. The procedure has been touched upon in speaking of the organization of thrombi, emboli, and infarcts, resorption of necrotic cells, with wounds, hemorrhages, and softenings. It is essentially the removal of altered cells or exudates and the substitution of young connective tissue. The same is true of old inflammatory exudates after cessation of the irritation, for they lie in the body as lifeless material. The first step is collateral congestion about such foci, usually with transudation of slight degree; but there

PLATE VII.

FIG. 44.



Granulating Tissue from a Case of Fibrous Pericarditis.

g, g1. Granulation cells. *r.* Lymphocytes. *p.* Polynuclear leucocytes. *i.* Intercellular substance.
G. Bloodvessel. *H.* Hyaline fibrin. $\times 350$.

FIG. 45.



Section from a Focus of Softening, about Fourteen Days Old.

a. Connective tissue persisting. *b.* Granular bodies minus their fat. *c.* Detritus. $\times 250$.

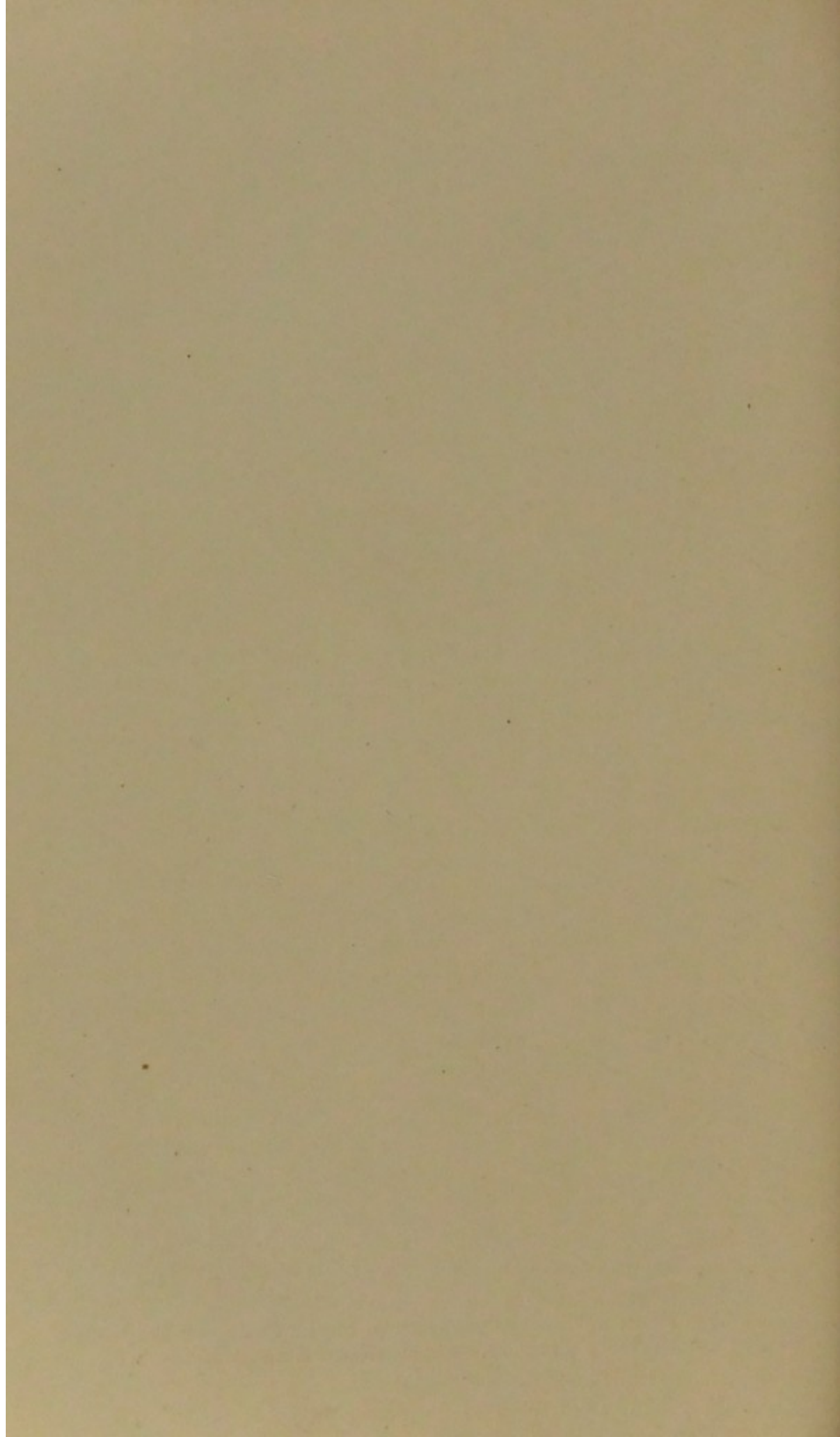
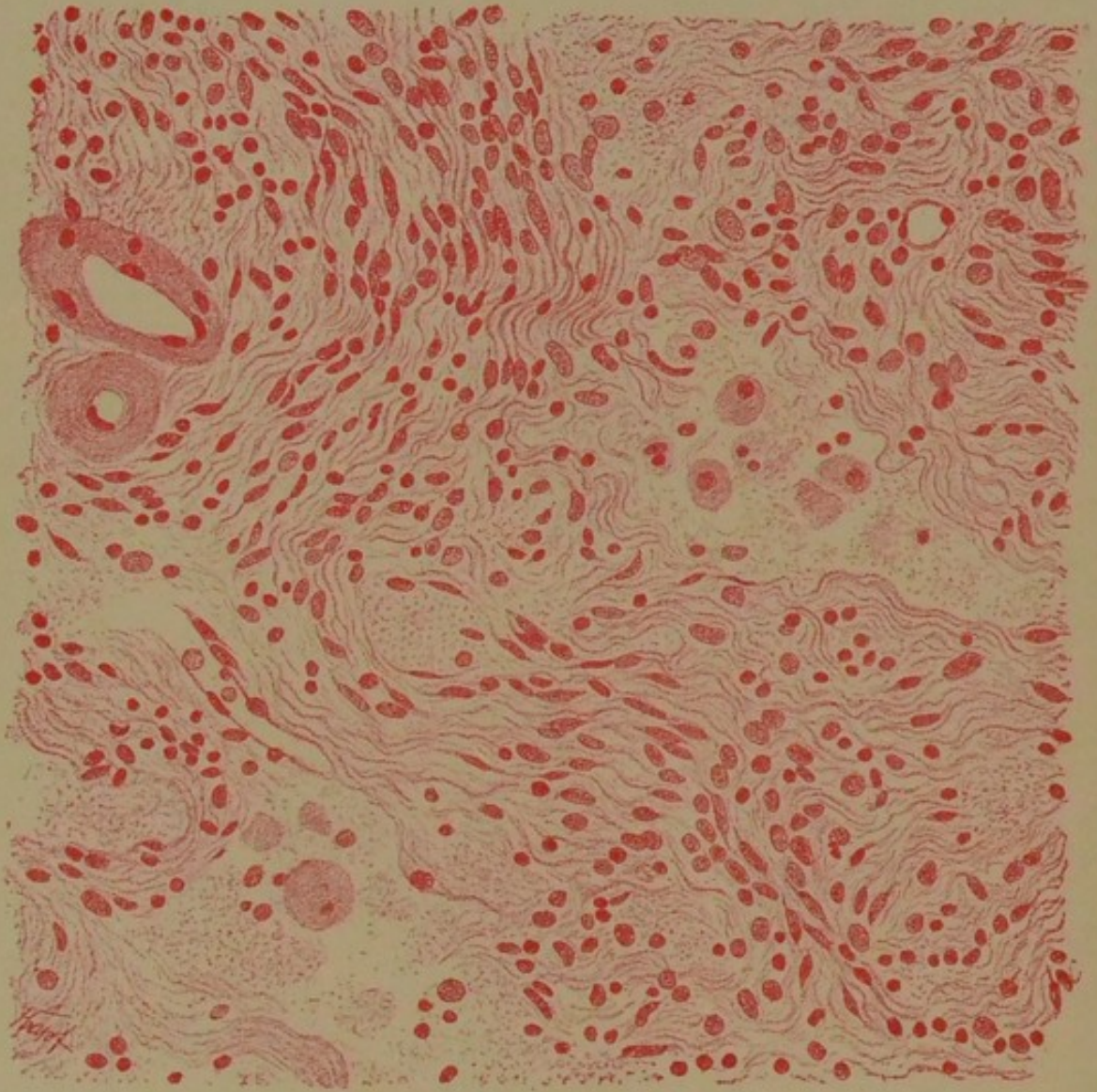




PLATE VIII.

FIG. 46.



Old Focus of Softening from the Cord, partly Cicatrized.

Here and there are areas with granular bodies and detritus; elsewhere fibrous tissue with spindle-shaped nuclei; above, to the left, two vessels with thick hyaline walls. $\times 250$.

is also a condition which is mainly inflammatory that leads to the healing of the part, and is also to be explained by the qualities of the substance to be absorbed. All dead tissues have a *chemotactic* influence, that is, they attract white cells, and in a short time the part may be richly provided with leucocytes which have wandered into it. These are the first contractile cells which one finds in the dead tissue, and they display phagocytic activity. All varieties of the products of tissue destruction may be taken up by these cells, and hence, according to the nature of the focus, we find them enclosing fat, pigment, medullary substance, albumin granules, and red cells. Thus granular fatty bodies, pigmented cells, and other varieties are found. The granular bodies are almost constant, and often countless, and appear as large, cloudy, grayish elements which with high powers are seen to contain fat in granules and droplets.

Frequently the fat is so excessive that the cells break up and add themselves to the necrotic elements. Pigment may also cause the death of the cells carrying it. As a rule, there is a steady decrease in the dead elements, which are carried away by the leucocytes and absorbed.

In the neighborhood there has developed a proliferation of connective tissue, and another variety of ameboid cells enters the focus. These are the wandering cells with large nuclei and the fibroblasts, and from them a granulation tissue develops which ends, as usual, in scar formation. New vessels also enter the part early in the process.

Wherever resorption of dead or foreign masses occurs, many large giant cells may be found clinging to the surface of the foreign body or gradually dissolving it. Very small materials of this sort, as bacteria and dust, may enter the giant cell, and then the nuclei of the giant cell are apt to assume a position along its margin. These giant cells are derived from the fixed connective-tissue cells, formed in great part by multiplication of the nuclei without division of the protoplasm, or in other cases by fusion of smaller cells.

The progressive formation of fibrous tissue gradually supplies the place of the absorbed material. Hence there is strictly not so much an organization as a substitution of a dead material by a tissue which has a vascular supply and can continue its existence, having all the characters of young connective tissue and later undergoing shrinkage like a scar. Thus there is found a dense, fibrous, grayish-white area on the surface of the organ with perhaps marked depression in it.

With large masses or imperfect power of resorption the dead material may remain a long while, and in the granular detritus fat needles and crystals of tyrosin and cholesterin often form. By loss of water and condensation the mass may become dry and caseous, or lime salts may infiltrate the strands of connective tissue in and about it. Special conditions may lead to liquefaction of the part, with increased facility of resorption, and when such a fluid mass is encapsulated the gradual removal of its turbid contents may leave a cyst with clear fluid contents. With extravasations of blood, when the cells and their pigment are not removed, the coloring matter undergoes the changes mentioned above (p. 74), and gives the scar a more or less intense brown tint; cysts formed as above may also contain brown fluid with pigmentation of the surrounding parts.

The entrance of ameboid leucocytes into the part is not altogether the result of chemotaxis, for porous substances which may be assumed not to be irritating are penetrated by leucocytes, and small amounts of non-irritant dust are taken up by phagocytes and the lymph stream and carried away. The power of resorption belongs to the organism and may be stimulated by foreign substances, but hardly caused by them.

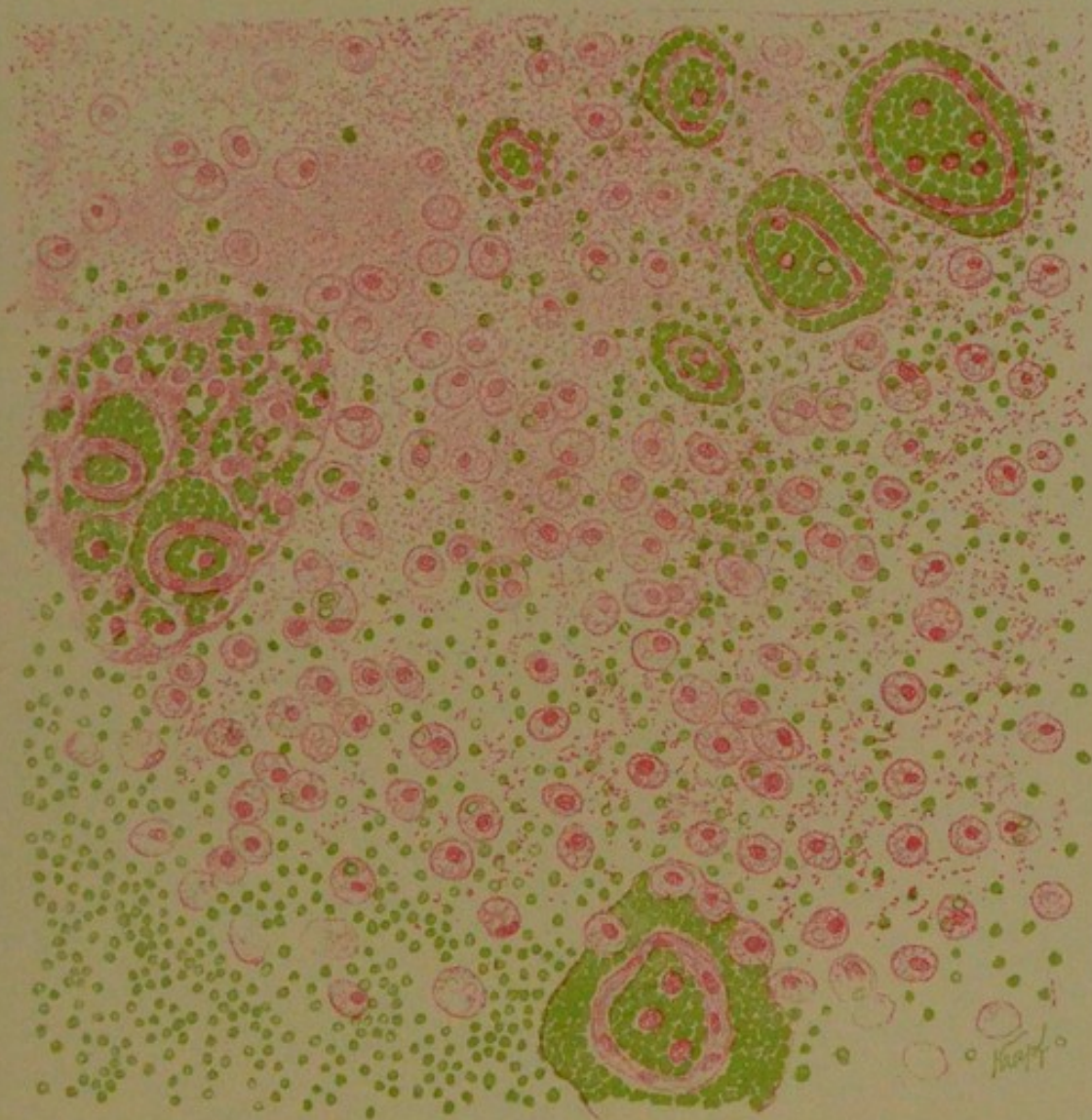
All the processes described so far have this in common, that they tend toward healing, and that they do not transgress the limits of resorption requisite for the removal of dead material or restoration of defects. Hence they may be regarded as part of the reparative process. On the other hand, we may often find, as in wound-healing, severe complications, irritative in nature, which we term inflammatory, such as the profuse emigration of white cells, with hyperemia and transudation. Since these phenomena do not include the prevention of healing, in some cases even assist it, their proper relation is formulated as reparative processes accompanied with slight inflammatory complications.

B. HYPERTROPHY.

When a tissue exceeds its normal dimensions it is said to be *hypertrophied*. The extra growth may affect single tissues or entire organs, and in the latter case it is understood that the specific cells of the part are increased. If the enlargement depends upon other than the specific cells, as on connective-tissue increase, or fat, it is called false or pseudohypertrophy. An example of the latter occurs when muscular tissues reach a large size from excessive development of the interstitial

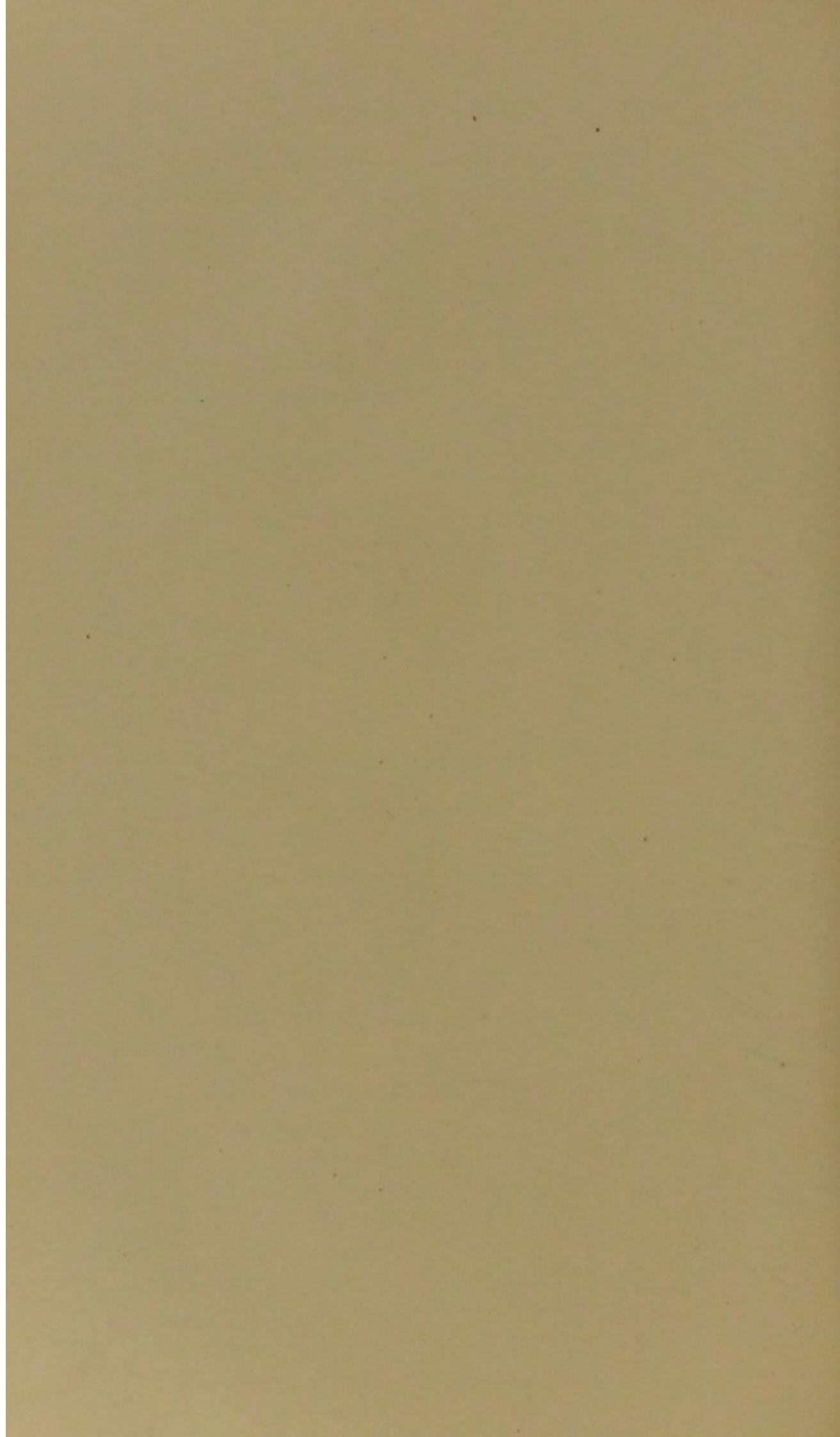
PLATE IX.

FIG. 47.



Red Softening with Capillary Apoplexies.

From the neighborhood of a traumatic hemorrhage of the cord. Numerous red cells (green) free in the tissue or enclosed in (red) wandering cells, and in the distended lymph sheaths of the vessels. $\times 250$.



fat. When the extra size is due to increase in the volume of single cells or other elements, it is a hypertrophy in the limited sense of the word. When there is a numerical increase of these elements it is termed *hyperplasia*. The distinction cannot always be made in practice.

Like other pathological conditions, hypertrophy is not essentially foreign to the physiological standard, for many of its forms are observed normally, as when the uterus hypertrophies during pregnancy, its fibres increasing fivefold in breadth and from seven to eleven times in length.

Many forms of hypertrophy succeed loss of tissue, and may be considered as reparative processes, for, though regeneration is but partial, there is a functional recovery. The elements remaining either increase in size or multiply in number, as when a large portion of the liver is destroyed and hypertrophy of the rest makes good the loss. In the rabbit four-fifths of the entire organ may be removed without permanent injury, the residue growing to nearly the original dimensions. The same thing in less degree may be observed in the kidney and thyroid. Such a compensatory hypertrophy may almost completely replace the lost tissue.

Where one of a pair of organs suffers in size or function, the other undergoes compensatory hypertrophy, and this may be partly a work hypertrophy from increased function as in the kidney, for aplasia or loss of one kidney may be replaced by the other. Loss of one testis or breast in the young may be compensated by the other, and the same rule may be shown experimentally in animals. Organs with similar functions may also take up the work of each other, and thus removal of the spleen may be followed by compensatory hypertrophy of the marrow and lymphatic tissues.

Compensatory or functional hypertrophy may occur in organs apart from any loss of tissue, when the physiologically functioning mass is relatively too small for the increased demand made upon it, and this form is the true hypertrophy of work or activity. Many such cases belong to physiology, as the increase in size of much exercised muscles. In pathological cases hypertrophy from work is typically seen in the heart. When the aortic ostium is too narrow from fusion of its cusps, the usual work of the heart drives too little blood into the aorta and to the organs. In favorable conditions there is a compensatory hypertrophy of the ventricular muscle, its fibres increasing in size and probably also in number, so that more blood is forced through the stenosed orifice. The weight of the heart may reach 500 to 1000 grammes,

and the auricle may share in the increase. According to the valve affected the hypertrophy appears in the corresponding chamber, and when the work of two or more sections of the heart is increased the whole organ may enlarge. The same is true of idiopathic hypertrophy of the heart, but many cases of this form are compensatory in their origin. It often happens that the hypertrophy follows suddenly upon unusual bodily exertion, as in military campaigns, or there is a true plethora, as seen in the effect of alcohol in the hearts of beer-drinkers, less markedly in chronic alcoholism. Plethora in beer-drinkers depends on the excessive nutrition, for with the enormous volume of the consumed beer there is much nutriment ingested.

Hypertrophy of the heart is almost constant in chronic renal diseases, and may be due in part to mechanical influences, as vascular lesions and retention of water, and partly to the chemical action of retained excreta. (See Chapter VI.)

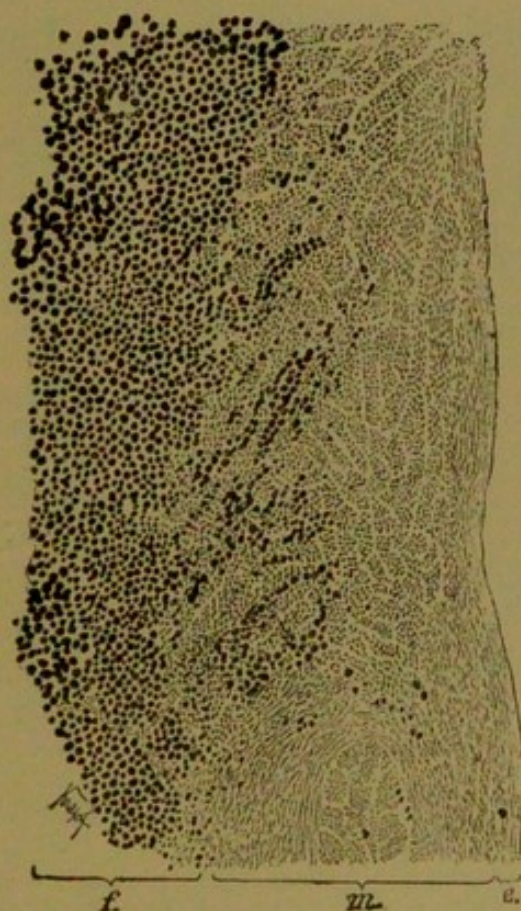
In organs containing smooth muscle, compensatory hypertrophy and increased work may correspond, as when with pyloric stenosis the muscle coat of the stomach increases, or with narrowing of the intestines hypertrophy is found in the muscles proximal to the constriction. Urethral stricture and urinary calculi cause hypertrophy of the vesical muscle fibres, as may be noticed even with chronic cystitis. (See Chapter XI.) Chronic disorders of circulation cause hypertrophy of the smooth muscle of the vessels and also of the intima of large and small vessels, which tends to prevent dilatation. The connective tissue surrounding these vessels is also increased, probably because of the increased arterial pressure, or the passive venous congestion, and this, with the thickened, dilated, and tortuous vessels, characterizes cyanotic induration (p. 28).

Increased work may not always produce hypertrophy, for in the lungs when one part assumes the duty of another a vicarious emphysema, or dilatation of the vesicles, occurs, in which the interalveolar septa and vessels may perish. (See Chapter VIII.)

Compensatory hypertrophy may include further the increased formation of single tissues which replace lost portions of organs, as when with diminished kidney tissue there is an increase of the fat in the hilum and about the organ, even when fat elsewhere is scanty. This form may also follow the removal of an opposing tissue, as when a joint cartilage grows after the antagonism of another is removed, and similar effects are observed in some disorders of growth and contractions of joints. (See Chapter XIII., B.)

While hyperplasia may be due to external causes there are forms which depend upon internal disposition, and are hence called idiopathic. Some of these are congenital, appearing before birth, just after it, or at some time during adolescence. Among them may be mentioned excessive development in height, giant growth, which may be general or confined to a portion of the body, as to the bones of the face (*leontiasis*) or to a finger or toe (*macroactylia*). These cases approach malformation very closely, especially when occurring during fetal life.

FIG. 48.



Section of the right ventricle wall in *adipositas cordis*. *f.* Subepicardial fat, at *m* growing into the muscle. *e.* Endocardium. Fat stained black with osmic acid. $\times 12$.

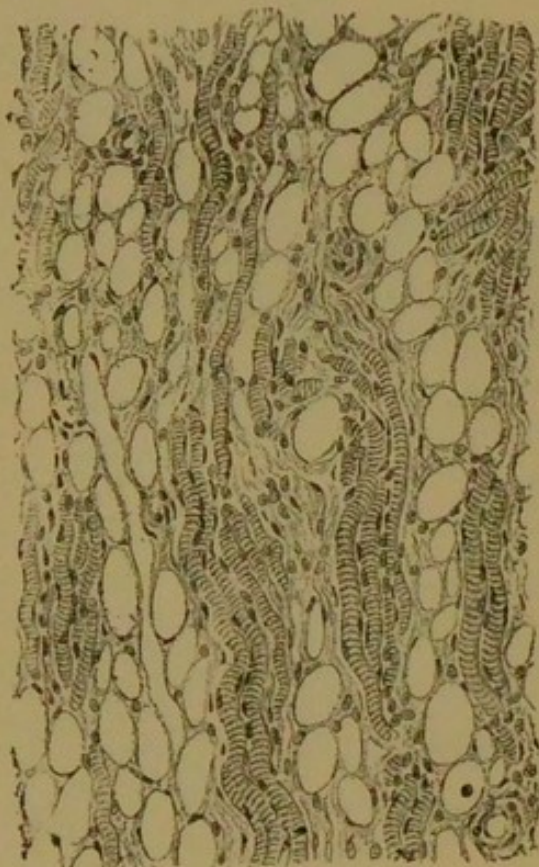
Developing later in life, they may depend upon accidental causes, as a slight trauma. In the congenital form they are of either the true or the false variety.

Idiopathic hypertrophy of entire organs is noticed in certain glands, as the breast and thyroid, and is apt to occur on both sides of the body at once. Hypertrophy of the epidermis as a congenital lesion covers the entire surface with thickened plates of corneous integument. *Cornu cutaneum*, or a horn, arises from elongation and growth of the

papillæ and the investing epidermis. Callosities or corns develop as the result of pressure, and the papillæ under them atrophy. *Hypertrichosis* is an excess of persistent lanugo hairs or great excess of the normal hair. *Onychogryphosis* is the claw-like elongation and distortion of the hypertrophied nails.

Elephantiasis is essentially a hypertrophy of the cutaneous and subcutaneous tissues, either in a diffuse form (fibromatosis), or with enormous development of the lymphatics (*E. lymphatica*), or with large,

FIG. 49.



Atrophy of muscle with lipomatosis. The muscle fibres have become very slender, and between them is an excess of fat. Hardening fluids have removed the fat, leaving vacuoles in its place. $\times 250$.

dilated blood spaces (*E. hemangiomatosa*), or lastly with fibrous hypertrophy of the nerve sheaths (*E. neuromatosa*). At times it follows chronic inflammation as a complication of varicose, syphilitic, and other ulcers, and may include hypertrophy of bone (exostosis or hyperostosis). Elephantiasis with dilated lymph vessels and stasis of the lymph is found in the tropics from the presence of a parasite, the *filaria sanguinis*. (See Chapter V.)

Many of the hypertrophies depend upon disorders of nutrition, and hence belong to the regressive processes. Great increase of the fat in

the body, *lipomatosis*, is an example of such processes. In part this is a replacement of lost tissue; in other cases there is a general tendency to the deposit of fat all through the body, especially marked in certain parts, as in the mesentery, the heart, and the renal pelvis and fatty capsule. In *adipositas cordis* the change is progressive, destroying the normal tissue by pressure atrophy. (Part II., Heart.) In pseudohypertrophy of the muscles a similar lesion exists, which may be hereditary, appearing in many members of a family. Even bone may be absorbed by excess of fat in the marrow. This tendency is both congenital and hereditary.

Two explanations have been offered for lipomatosis, either excess of blood supply, a supernutrition, or nervous influences.

All cases of hypertrophy depend upon blood supply or nutrition, for in its absence the growth cannot occur. Thus in valvular cardiac disease the compensatory hypertrophy fails to appear if there is cachexia or general amyloid disease, and hypertrophy of the right ventricle in pulmonary tuberculosis may not develop if the subject is emaciated. Hence we must suppose that the blood supply is but a secondary factor and that with it there must be other causes to produce hypertrophy.

The nerves have a certain influence upon the increase and energy of development; thus affections of the cord or the peripheral nerves may be followed by hypertrophy and also by trophic disorders, such as ulcers, local loss of hair, and pigmentation. Many authors ascribe the hypertrophy in acromegaly to a nervous disorder, the diseases being marked by thickening and enlargement of all peripheral tissues, as the fingers, toes, nose, facial prominences, both in the soft parts and in the bones of these regions. In contrast to giant growth it occurs only after the normal period of development. The occurrence of acromegaly with persistent thymus (see Chapter VI.) and with lesions of the hypophysis has led to the supposition that abnormal products of these glands may be its causal factor; according to others it is a congenital anomaly of constitutional origin.

A relation between some forms of hypertrophy and actual inflammatory processes cannot be denied, as in the elephantiasis mentioned above, hyperplasia of bone with exostoses, increase of glands in mucous membranes, and especially in hyperplasia of lymph nodes after chronic irritations. In many cases a clear line cannot be drawn in these chronic cases between simple and inflammatory hyperplasia. Tissue growth as the result of chemical irritation is also related to the inflam-

matory form. In animals certain poisons induce hyperplasia of special tissues, as arsenic in small doses, which increases the connective tissue of the liver.

Hypertrophy which results from incomplete involution may also be included here, as in the uterus after pregnancy and in the thymus gland. (See Chapter VI.)

C. INFLAMMATION.

The first meaning of inflammation was the purely clinical appearance of the four cardinal symptoms of Galen, *rubor*, *tumor*, *calor*, and *dolor*. By analogy we assume that these appearances characterize internal inflammations also, but in the cadaver only the redness and the swelling may remain. Deeper insight into the nature of diseases leads us to prefer an anatomical basis for our concepts rather than a group of external symptoms, and we realize that the four symptoms mentioned depend upon phenomena connected with the vascular system which are included under the head of inflammatory disorders of the circulation.

In most inflammations the first sign observed is the active hyperemia, with dilatation of the vessels and increased rapidity of the blood stream, giving the part increased flow of blood and a bright-red color, and making the vessels and their pulsation very evident. This active congestion may be connected with vasodilatation or passive exhaustion of the muscular fibre. Probably the conditions in the vessels are not uniform, but liable to marked alterations. Inflammatory hyperemia differs from simple congestion by its persistence, for while the irritation may continue to affect the vessels, the stream may not remain rapid. Most experimental observations detect a slowing of the current while the vessels continue dilated, leading to an accumulation of blood in the region. At times such slowing may be present from the first, as when venous stasis occurs before the inflammation, for instance in strangulation of the gut, or when the irritating agent produces stasis (p. 42). In these cases the stasis aids the vascular changes in prolonging the hyperemia, and with stasis the leucocytes gather along the wall, for the conditions of dilatation and slowing of current without increase of pressure specially favor this accumulation of white cells.

The *transudation* noticed with simple hyperemia becomes far more abundant in inflammation and the transuded fluids more nearly resemble plasma. The exit of the fluid rich in albumin is explained by a sup-

posed alteration in the walls of the vessels, which either become more permeable or are excited to active excretion (p. 35). The inflammatory exudate is more liable to coagulate, the fibrin masses appearing as flocculi or as larger, swollen, and gelatinous collections.

A third essential feature of inflammation is the free *emigration of leucocytes*, and at times this is so prominent that it is considered as the single element in the process, though it is but one of many. It is strongly influenced by the nature of the exciting agent, for the substances called chemotactic produce a large emigration.

The leucocytes gather on the wall of the vessel, then they flatten, and from each a process makes its way through and appears on the outer side of the wall, the rest of the cell follows the projecting "pseudopod," and the cells may be observed at times in transit, half in and half out of the vessel, with a narrow thread through the wall joining the two portions. Once beyond the vessel ameboid movements carry them through the tissues. Emigration is marked only in the case of small veins and capillaries, and through the latter there is a diapedesis of red cells also. Studied experimentally, as in the mesentery, this emigration may be so marked that the entire tissue is infiltrated by white cells, and the normal structure of the part may not be recognized. The particular white cells which are found are the polynuclear, in all recent inflammations, easily recognized from their nuclei. When the emigration takes place on a surface or in a cavity, as in one formed by solution of tissue, we have an enormous exudate of pus, the chief mass of which consists of emigrated leucocytes.

Thus we see that inflammation is but a pathological exaltation of normal processes which serve to explain the redness, swelling, and heat of the inflamed part. But the vascular changes are not the only ones. Where certain bacteria are present, or certain chemicals call forth large emigration, there may be also a multiplication of the cells of the part which mingle with the leucocytes, while the connective tissue becomes altered and at last dissolved in the pus. In catarrhal inflammation from inhalation of irritating substances there is an excess of local secretion and a desquamation of epithelial cells. In the organs there may be the granular change which is called cloudy swelling, or in chronic cases a fibrous hyperplasia with gland proliferation. Inflammatory symptoms may complicate physiological reparative processes, as in healing by second intention, where marked redness and exuberant granulations are observed and perhaps a purulent flow from the wound surface. With stronger irritation the more evident is the

inflammatory element, and with infection the suppuration delays healing or even prevents it.

Hence it is evident from the examples mentioned that with inflammation we study many and various processes affecting not only the vascular tissues but also those about them. In parts where there are no vessels, as in the cornea and cartilages, the circulatory changes occur at the edge of the region, and even where the vascular supply is large the circulatory phenomena may not be prominent in certain chronic inflammations. Hence we must regard inflammation not so much as an external symptom-complex, but rather as an anatomical condition in the entire region affected. Neither the circulatory nor the tissue changes are essentially foreign to the normal organism, but merely exaggerations of the physiological.

We observe in living tissues three main processes, namely, those of assimilation, function, and reproduction; and in conditions of inflammation corresponding disorders occur, those of nutrition, of function, and of cell multiplication.

The *disorder of nutrition* is especially marked in epithelial cells and muscle fibres, as in cloudy swellings (p. 59). This may disappear as the cell returns to the normal, or lead to further regressive changes, as fatty degeneration. Since these regressive lesions occur by themselves at times, we regard them as inflammatory only when accompanied by vascular and cellular disorders.

With the *functional inflammatory changes* there is often a tendency to cell destruction, as when on a mucous membrane the secretion is much increased and the producing cells give their entire protoplasm to mucin formation, and degenerate. The young cells also take part in this process and undergo a premature death. The transudation is increased, and, with the above changes, aids in altering the nature of the secretion.

While the third group of inflammatory disorders, the *multiplication of cells*, is especially marked in chronic inflammations, it is not absent from the acute forms. With acute catarrh the epithelial cells of the mucous membranes are rapidly multiplied, as also the cells of the renal tubes and glomeruli in nephritis, and the cells appear either in the mucous or urinary secretion. Acute inflammation of connective tissue is accompanied by swelling of the cell bodies and a more vesicular condition in the nuclei of the part, the latter resembling nuclei of young connective-tissue cells. An albuminous or fatty degeneration affects these cells, and new ones are continually developed by mitosis.

The new cells are ameboid. The endothelia of the lymph spaces, and in part also of lymph and bloodvessels, show similar effects. Where vessels are not present, as in cornea, cartilage, and cardiac valves, the changes in the fixed cells are at first the only expression of inflammation observed.

According to the result we can divide such proliferation into two forms. In one the young cells lose their relation with each other, mix with the exudate, and degenerate. In catarrhal inflammations the epithelia desquamate and form part of the exudate; with suppuration the connective-tissue cells mingle with the pus. In the other variety the new cells retain both their connection and their power to make tissue. So in chronic catarrh there is proliferation of glands and of stroma, the latter change being prominent in many chronic cases. In these cases the connective tissue is infiltrated with many round cells, either diffusely or in groups, each with a single round nucleus which takes up most of the cell and stains deeply. The small proportion of protoplasm makes these cells appear with low magnification as simple nuclei. The formation of new tissue is accompanied by new-growth of vessels also, and hence non-vascular portions may become vascular.

Essentially, then, the elements entering into the changing picture of inflammation are but life expressions of normal tissue when physiological, but here a reaction against an external stimulus. This irritation determines both the intensity and the quality of the inflammatory reaction. We observe then not only an exaggerated but also an altered vital activity, disordered by the lack of physiological co-ordination. We may, therefore, define *inflammation* as a condition of reaction, exalted above the physiological normal, pathologically altered, and called forth by an external irritation.

According to the main element in inflammatory process we distinguish three groups: *parenchymatous*, or degenerative inflammation, is the name given to cases in which the nutritive disorder is most prominent, as in cloudy swelling with parenchymatous nephritis.

In a second series of cases the circulatory apparatus is specially involved, and from the fluid and cellular elements of the part there forms an inflammatory exudate, gathered in body cavities, flowing from a surface or infiltrating the tissue and causing the symptom of swelling. All such inflammations receive the name *exudative*, and the kind of exudate is specified as below. The third form, *productive* inflammation, occurs in all processes where the cell proliferation leads

to the formation of new tissue. All these varieties may be combined, or one passes into the other by insensible gradations.

The form of inflammation depends upon the agent and the conditions, both local and general, for both intensity and quality vary according to circumstances. The mildest grade of inflammation is that in which the exudate is simply serum, the more severe leads to the death of the elements, or necrosis. Mechanical, thermic, and many chemical agents cause a serous or necrotic inflammation, but never a suppurative, while other chemicals, and especially certain bacteria, produce exudation, necrosis, and suppuration.

The reaction and the quantitative action of the stimulus determine the course and the result of the inflammation. According to the duration we distinguish acute and chronic, and, from practical reasons, also a subacute inflammation. The chronic irritations cause a chronic reaction, and such inflammation is also due to a series of acute irritations. Thus a single inhalation of dust may cause an acute catarrh of the respiratory passages; while people who work in a dusty atmosphere, as in many trades, suffer from chronic bronchitis. Again, a single acute attack may be followed by such tissue changes that a chronic inflammation remains as the result of a peculiar sensitiveness (erethism) for stimuli which the healthy organism will not notice. Many catarrhal inflammations belong in this group, characterized by acute attacks, imperfect recovery, and return of the lesion on slight irritation (as catching cold). The reactive powers of the body or of certain tissues will play an important part in these cases, as is evident with many obstinate catarrhal inflammations of the female genitals and of other mucous membranes in cachectic patients. With proper diet these tend more rapidly toward recovery. It is plain that the individual disposition in these cases is even more important than the external irritation in determining the course of the disease.

Nervous influences are connected with the rise and course of inflammations. The neurotic element may be either a diminution of sensibility, so that injurious agents are not avoided or removed, as in ophthalmia after section of the trigeminus and pneumonia after section of the vagus, or there may be vasomotor and trophic disorders, as in the joint lesions of locomotor ataxia.

The results of inflammation may vary. Inflammation is not a healing process, but a reaction to an agent which is called inflammation because it is pathological. After the irritation has ceased to work the pathological character may disappear, and the process returns

to a physiological or reparative stage. In this the single symptoms lose their intensity, the tissue formation is limited to that required to replace losses, and remaining inflammatory products are removed.

FORMS OF INFLAMMATION.

1. Parenchymatous Inflammation.

Albuminous or cloudy swelling of the parenchyma of organs, with possible resulting fatty degeneration of the cells, is called parenchymatous inflammation. The specific cells of the part are involved, as muscle fibres, epithelia, and nerve fibres, rather than the stroma. But as cloudy swelling is a regressive change, and may occur alone, we should call it inflammatory only when there is also exudation or proliferation of cells. Thus in parenchymatous nephritis, together with the cloudiness of the epithelia we find congestion, cell multiplication in the glomeruli, tubules, or stroma, with emigration of white cells, or, in chronic cases, round-celled infiltration and connective-tissue growth. (See Chapter XI.) The distinction between the simple degeneration and the inflammation with cloudy swelling may be very difficult.

Exudative Forms of Inflammation. In the following varieties the exudate is one of the most prominent elements in the pathological process, at least in certain stages. It may finally disappear without damage to the tissue structure, with complete *restitutio ad integrum*; or it is removed by softening and resorption, as other necrotic masses; or in addition to these latter processes there may be an independent cell proliferation and tissue growth, and then the inflammation is called productive.

2. Serous and Fibrinous Inflammation.

Inflammations accompanied by exudation of large amounts of serous fluids, with varying numbers of leucocytes, are called *serous* or *fibrinous*. The serous exudate may occur as an inflammatory edema which infiltrates the tissue, or as a collection in a body cavity, or it may pour from a surface. As a rule, it contains far more albumin than the normal blood plasma (1 to 5.5 per cent.). Because of the proportion of albumins it is not clear, but contains flocculi of fibrin. With much albumin and many leucocytes there may be coagulation, and the exudate receives the name of fibrinous or serofibrinous. This coagulum may lie in a film over serous surfaces, easily pulled off and leaving

the membrane opaque, of a gray or yellow color, and often disposed in coarse meshes or with tassels and projections. Microscopically there is a fine or coarse network, perhaps partly hyalin and entangling leucocytes. Pure fibrin may form the exudate, as in dry pleurisy, pericarditis, etc., or with the fibrin there is more or less serum. Floating in this fluid there are flocculi of swollen fibrin.

Pure serous exudate may be completely absorbed. With much fibrin the organization and resorption are similar to those processes

FIG. 50.



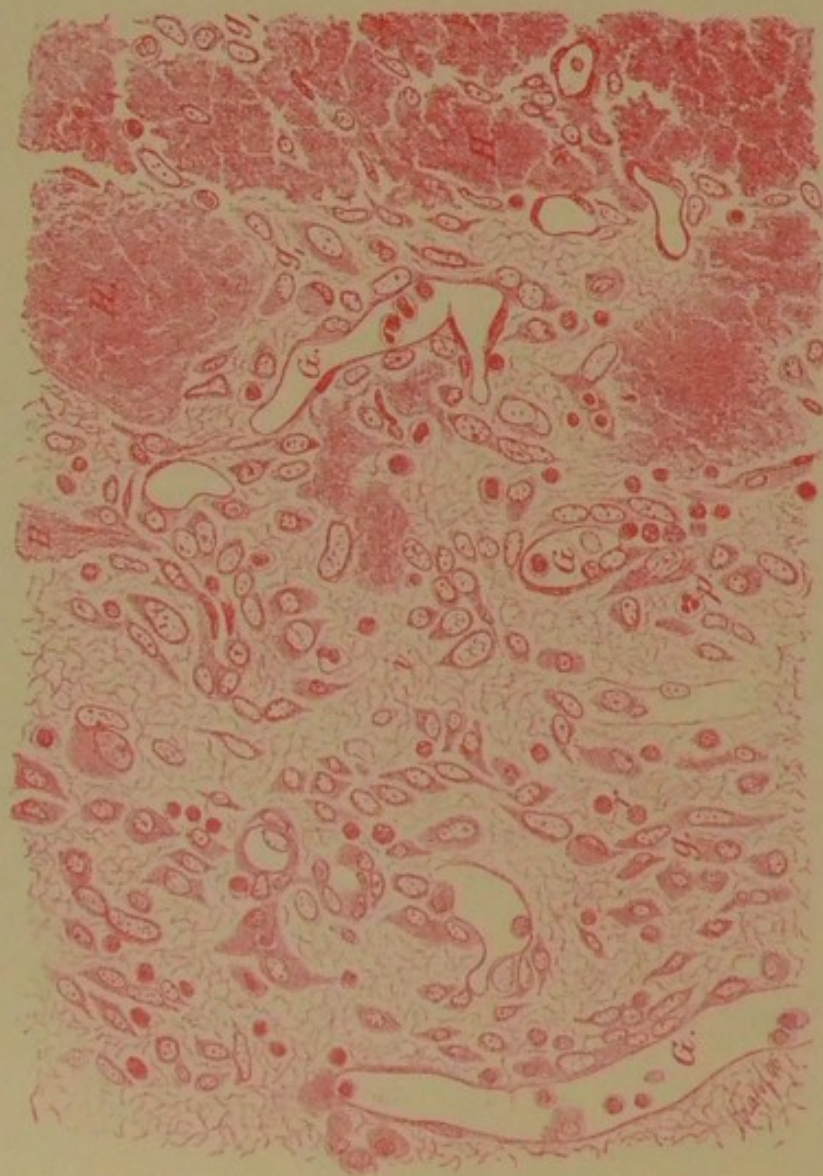
Fibrinous pericarditis. *a*. Subepicardial fat. *b*. Inflammatory granulation tissue with many cells and vessels. *c*. Fibrocellular layer. *d*. Collections of white cells. *e*. Capillaries entering the fibrin. $\times 250$.

with thrombi and infarcts. There develops under the fibrinous layer a zone of granulation tissue (Figs. 38, 39, 51), from which many vessels grow between the strands of fibrin. The fibrin is gradually converted into masses of granules, fat, and detritus, and removed principally by white cells. Young connective-tissue cells wander into the dead exudate and in its spaces form foci of granulation tissue, which later on become cicatricial fibrous tissue. Thus occur the



PLATE X.

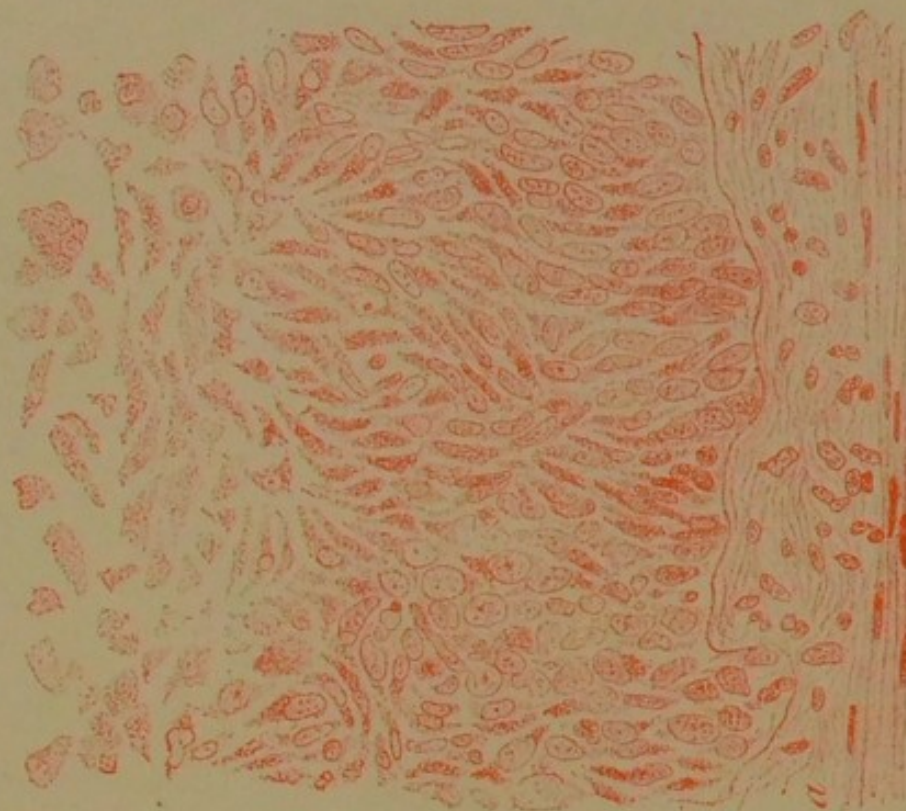
FIG. 51.



Granulating Tissue from a Case of Fibrous Pericarditis.

g *l*. Granulation cells. *r*. Lymphocytic leucocytes. *i*. Intercellular substance.
G. Blood vessel. *H*. Hyaline fibrin. $\times 350$.

FIG. 52.



Catarrhal Bronchitis.

a. Connective tissue of the mucosa; the epithelia above are proliferating and desquamating; in many cells the dark nucleus appears; in the lumen of the bronchus, above, many loose and degenerated cells, some without nuclei. $\times 350$.

callous fibrous spots on serous surfaces which in the heart are known as *maculae albae*, or milk spots.

Where two serous surfaces are in apposition they may become united by adhesive inflammation. Where such an adhesion is exposed to traction, as from the movement of lungs or heart, the fibrous bands may be drawn out as a false ligament or synechia. With profuse exudate the surface may be much thickened by tough masses, which later may become calcified. Where the exudate cannot be absorbed a detritus results which contains cholesterin and tyrosin, or becomes dry and caseous or infiltrated with lime salts.

In other cases the serofibrinous exudate occurs in more chronic form, persisting during the growth of granulation tissue, and the latter has a more independent character, serving less for the resorption and organization of the exudate, but becoming more progressive, even where the amount of original exudate was small. By this transition from a reparative process to a progressive tissue formation the serofibrinous inflammation becomes productive.

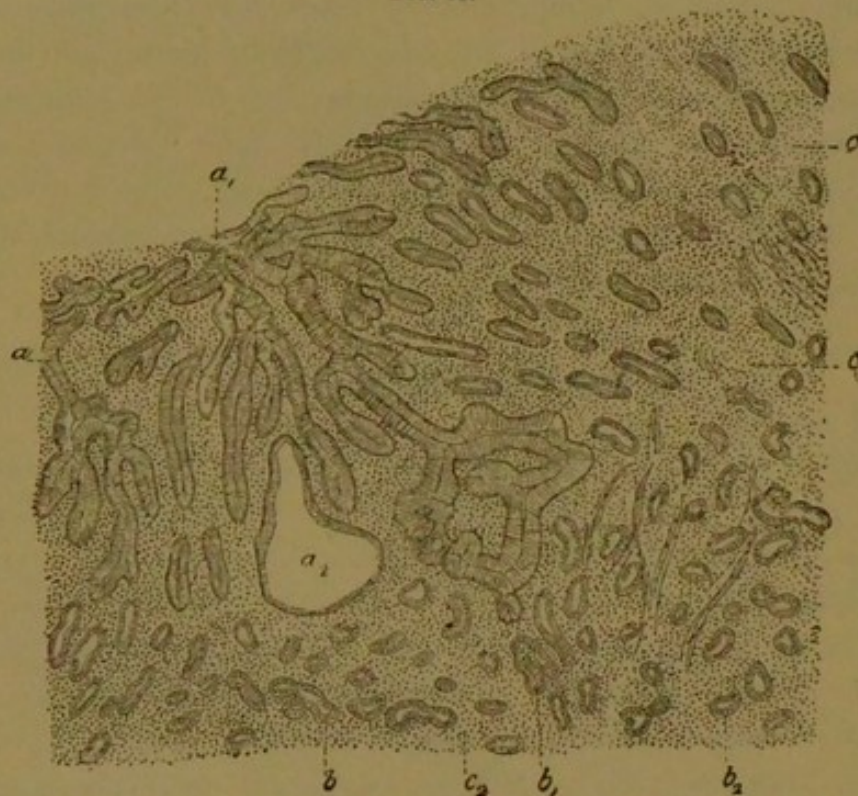
3. Catarrhal Inflammation.

Catarrh is an inflammatory reaction which is typically seen upon mucous surfaces. From the vessels there is a profuse transudation, with few or many white cells included. This catarrhal secretion is soon mixed with products from the irritated mucosa. Among these are the mucus which makes the exudate mucoserous, and the epithelia, which are found in a condition of active proliferation. (Fig. 51.) The transudate does not lead to thickening of the membrane, at least in acute cases, but the epithelial cells are imperfectly developed and suffer a speedy mucous degeneration. The form of the epithelial cells varies with the locality, but they may be much altered and hard to recognize. Thus with many round cells provided with cilia the site of origin is evidently where ciliated epithelia are found. (Fig. 19.) In certain catarrhal inflammations there appear also mucous corpuscles, round mononuclear cells, swollen and mucoid.

Commonly the exudate is at first serous, after a stage of redness and swelling in the membrane, and then mucous, and lastly more cellular. Other cases occur in which for a long time but one of these stages appears. Inflammation with specially marked production of epithelia is called desquamative; where the exudate chiefly contains leucocytes it is called purulent catarrh or blennorrhœa.

Catarrhal inflammation in the majority of cases is a benign process, limited to the surface and causing no deep changes of the mucosa, or ulceration. It heals by decrease of transudate and secretion and regeneration of the epithelium. Only when the catarrh becomes chronic, or is of this type from the first, is the mucosa involved in both connective and glandular tissue, and the exudative merges into the productive form. The secretion may remain excessive, and its constitution may vary from the normal in chronic catarrh, and with it there may be capillary hemorrhages which leave a brownish discolora-

FIG. 53.



Chronic gastritis. *a, a₁*. Glands proliferating, partly dilated. *b, b₁*. Non-proliferating glands pressed apart by new connective tissue, *c, c₁*. $\times 40$.

tion of the region. Areas where the epithelium, or even the mucous membrane entire, has been lost are called erosions. The peculiarity of the process is given by the proliferation of new gland tubules which vary in form from the physiological type of the locality, and also by the cellular infiltration of the connective tissue, which leads to new fibrillary connective-tissue formation. Hence the mucosa presents diffuse or circumscribed thickenings, at times pedicled and polypoid. If these polyps contain all the tissue elements of the part they are called mucous, if made chiefly of gland tubules they are called glandular polyps. Single glands may be distended by mucus and project

as polyps. Such hyperplasias form a transition to tumor formation. In other cases the growth is diffuse with fungous areas. These may diminish by shrinking, the glands becoming atrophied, and the place is smooth, glistening, dense, pale, and perhaps marked by a few prominent veins and small pigmented spots.

In a similar way desquamative lesions occur in the lung, on the skin, and in other organs, as will be shown in Part II. In the lungs with such inflammations there may be thickening of the interlobular septa.

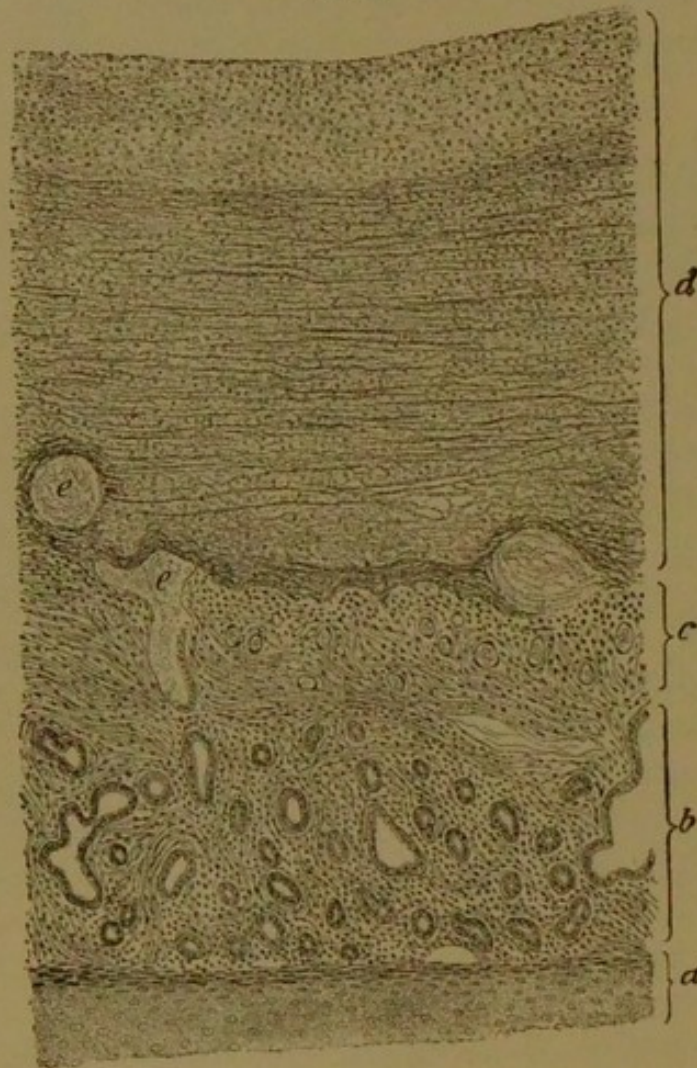
4. Diphtheritic Inflammation.

Like the former variety, **diphtheritic inflammation** is seen especially on mucous membranes. Its characteristic peculiarity is the formation of false membranes, which are yellowish-white, somewhat elastic investments of the surface, consisting of coagulated albumin, and due to a combined exudation and necrosis. Superficial and deep forms are distinguished. Among the former may be included the common diphtherias of the fauces, pharynx, and upper air passages. They begin with the appearance of a thin film over the mucosa, but where the lumen of the passage is small, as in the infantile larynx, the membrane may occlude it as it increases. The film spreads laterally also and may be stripped up in large masses. The under surface may be reticulated and indented by the outflow of secretion from gland ducts which have been covered (Fig. 54, *e*), or even perforated and sieve-like. The surface of the membrane under the exudate may be moist and glistening, very red, often with small hemorrhages; in other words, a mucous membrane deprived of its epithelium but otherwise unchanged. In certain places, as the tonsil and vocal cord, the membrane is more tightly adherent.

The pseudomembrane presents microscopically a fine or coarse network of fibrin. (Fig. 54, *d*.) Those which come from the mouth and pharynx may be made of hyaline fibrin in large or slender trabeculae. (Fig. 23.) In the meshes of the fibrin are numerous white cells. The site of the membrane shows on microscopical examination complete loss of the epithelial cells, for the membrane lies not so much upon these cells as in place of them, and they are destroyed by necrosis. The close adhesion of the membrane to certain parts is explained by the fact that squamous epithelium clothes them, and below it there is no basal membrane, hence the exudate lies directly on the mucosa, while in the tonsils it penetrates the lacunae.

Deeper diphtheritic inflammations begin in the same way by the formation of small spots of white membrane which make the surface appear as if dusted with fibrinous exudate; but they are distinguished by the greater or less depth to which the necrotic process penetrates the mucous membrane, leading to the formation of eschar-like masses which are firm and contain no nuclei. The basis and the tissue

FIG. 54.

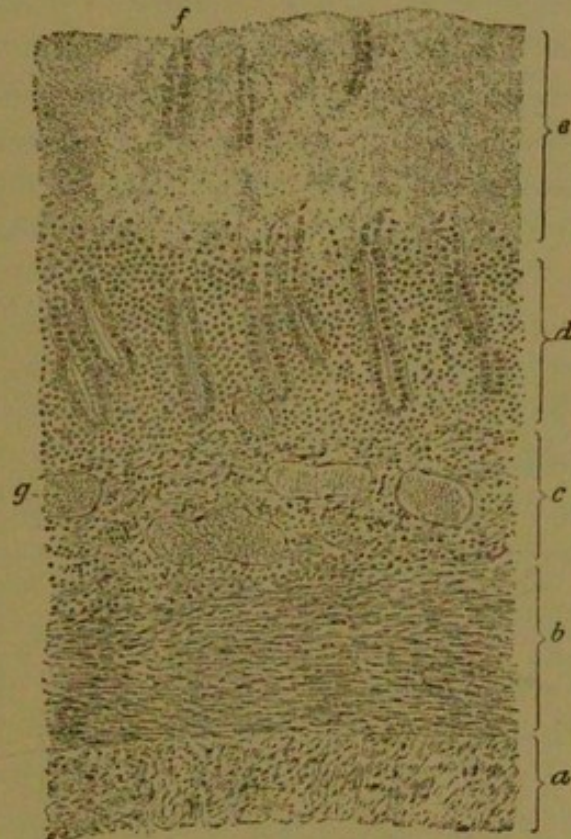


Laryngeal croup. *a.* Cartilage. *b.* Submucosa with many glands. *c.* Mucosa. *d.* Fibrin. *e.* Mucous plug in the gland duct. $\times 40$.

adjacent to such eschars present severe hyperemia and cellular, and at times hemorrhagic, infiltration. The slough corresponds, then, to a layer of dead mucous membrane. In such cases the pseudomembrane cannot be easily lifted off, and if torn away by force there must remain a defect in the membrane; and where the slough separates by itself, often with suppuration, an ulcer is left which heals with scar formation.

The superficial forms of pseudomembranous inflammation have been called croup, the deeper known as diphtheria. The distinction does not agree with clinical observations, and the grades between the two forms are numerous and merge into each other. (See Chapter X., A., 3).

FIG. 55.



Intestinal diphtheria (dysentery). *a, b.* Muscularis. *c.* Submucosa. *d.* Mucosa preserved. *e.* Mucosa necrosed. *f.* Remains of gland tubules. $\times 40$.

The deeper form is common in the intestine, less so in the pharynx. Both may arise from different bacteria, and with both the loss of the epithelial layer is the essential element.

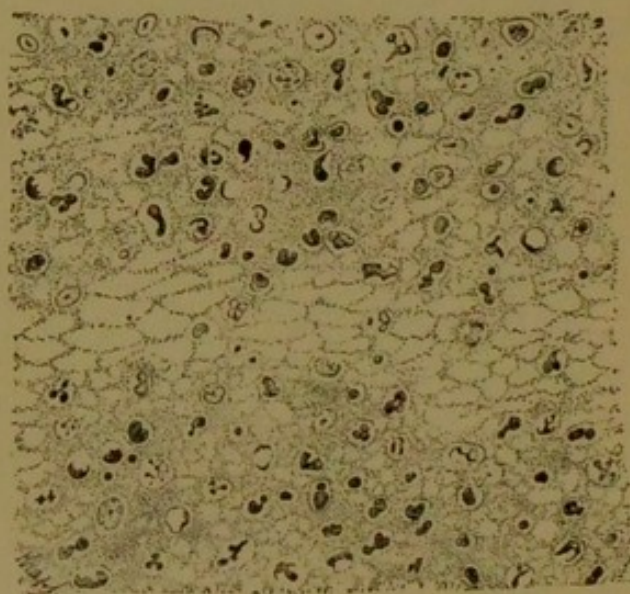
5. Suppurative or Purulent Inflammation.

In this form there is a peculiar exudate called *pus*, on surfaces or in cavities, which is a yellow fluid with at times a green tinge, creamy or viscous, alkaline when recent, and consists of serum and cells. The serum is albuminous and may contain flakes of fibrin and also mucus. The cells are round, ameboid when fresh, in part lymphocytes, but the vast majority are polynuclear leucocytes. (Figs. 38 and 39.) Many cells undergo a fatty degeneration which gives them the look of fatty granular corpuscles. In many catarrhal inflammations (as of the bladder) the pus cells suffer a mucous degeneration. Remaining for a

time as a collection, pus cells become dry and caseous. The pus cells come almost entirely from emigration of white cells from the blood. But the fixed cells may undergo multiplication, and their derivatives may be mixed with the pus cells.

A peculiarity of suppuration is that not every irritation suffices to produce it. Mechanical stimuli and chemicals which may lead to necrosis do not cause it, while many other chemicals and many bacteria do so constantly. Among the bacteria the commonest are the staphylococcus, streptococcus, pneumococcus, gonococcus, and the bacillus coli communis; but other forms may be found in pus. The cellular exudate is determined by the chemotactic influence of the irri-

FIG. 56.



Suppurating connective tissue. Section through a phlegmon of subcutaneous tissue. Pus cells with polymorphous nuclei; reticular basement substance softening. $\times 250$.

tant (p. 105). According to the influence of the exciting agent there are differences noticed in the pus, partly from substances mixed with it and partly from changes in itself. In severe cases the cause of the suppuration may lead to necrosis of the tissue. In many cases there is also an invasion by bacteria of putrefaction, so that there is both suppurative and gangrenous destruction of the part, with evolution of stinking gases and exudate of putrid fluid. Accumulation of gases in the tissue spaces may cause a gangrenous emphysema (p. 57). The pus from such gangrenous foci is thin, reddish-brown, and full of putrefactive bacteria. Healthy pus is, as described above, the *pus bonum et laudabile* of the surgeons. (See Chapter V.)

Of the purulent inflammations we distinguish two forms, the superficial and the deep or interstitial. To the first belongs purulent catarrh (blennorrhœa), where the exudate is mixed with pus cells and the membrane is not seriously injured, the proliferated epithelia also being contained in the fluid. Slight suppurations in the rete Malpighi, called pustules, make another variety; and the serous and serofibrinous collections in the body cavities also may contain numerous pus cells. Such purulent fluids in the pleura, joint cavities, and elsewhere are called empyema.

The interstitial suppuration may be diffuse or circumscribed; the former is called *phlegmon* and the latter an *abscess*. Both result from purulent softening and destruction of tissue, the proliferated cells becoming mixed with the pus instead of making new tissue.

When there is a pronounced serous infiltration of the region involved in suppuration it is termed acute purulent edema, and this often precedes the formation of a phlegmon. The latter has no sharp limits, but tends to spread in a diffuse manner. It occurs especially in the loose subcutaneous tissue, in the subperitoneal and submucous layers, and wherever connective tissue is present in large amount. Together with such suppuration there may be necrosis of large portions of tissue without purulent destruction of them. Hence in purulent phlegmons there may be masses of connective and elastic tissue, muscle, fascia, and tendons. Especially those tissues which resist the suppuration may die in large masses and float in the pus, and when bone and cartilage are attacked portions of these may also be found. Phlegmonous processes are often accompanied by gangrene.

Abscesses form purulent collections in the deeper parts of organs, the tissue softening and making a cavity filled with the pus, and sharply limited from the surrounding parts. Here also the tissue may necrose, and thus in pyemic abscesses of organs there may be a necrotic centre surrounded by a zone of purulent and hemorrhagic tissue, infiltrated with cells and breaking down.

The necrotic focus may tend to separate from the healthy parts by a line of demarcation, and in bone this leads to the formation of a sequestrum which may be extruded, and thus the process brought to healing. Similarly, infected emboli set up abscesses which in the organs seldom end with healing, because the pus cannot easily be emptied and the suppuration tends to invade other tissue.

Accumulations of pus are found at times which have not been formed *in situ*, but have been caused by the burrowing of pus from higher

parts. Thus with caries of the vertebræ the pus may work along the psoas muscle behind the peritoneum and appear below Poupart's ligament as a "psoas abscess." In retropharyngeal abscess the pus may invade the mediastinum in a similar manner.

Circumscribed abscess with necrosis in the hair follicles is known as a *furuncle*; when several follicles together are involved, as a *carbuncle*.

By deep suppuration, either of the surface or of deeper parts, an *ulcer* may result (p. 57). Different forms may be recognized according to the defect caused. They usually tend to increase in size, and necrotic changes are combined with the pus formation, as in bed-sores, where there are death and separation along the edges and on the bottom of the ulcer.

The base of an ulcer varies in appearance according to its cause. It may be covered with fresh pus, or by granulations, or by diphtheritic membrane or gangrenous sloughs. Its edges may be swollen and prominent, or sharply cut, or undermined and prolapsed. When its edges become necrotic and the ulcer spreads, it is called gangrenous, and if the gangrene is confined to the surface it is termed phagedenic. When one side advances as the other heals it forms a serpiginous ulcer, and with proliferation of cells without healing it is called hyperplastic. (See Chapter XV.) When deep abscesses burrow to the surface there may be a narrow canal leading into the pus focus; this is called a *fistula*.

Healing in superficial suppuration is simple, the secretion lessening and the lost cells being regenerated.

In the deeper processes the conditions are more complicated. If the pus is evacuated and the bacteria die, regenerative processes start in the walls leading to formation of young connective tissue, emigration of white cells stops, granulations form, and healing is completed by a cicatrix. Only small abscesses may be healed by simple resorption of the pus without scar formation.

When wounds are complicated by suppuration the healing follows in the same way (p. 92). Closed wounds present but little redness, swelling, and secretion; open ones may be covered with purulent secretion, which is copious according to the virulence of the infection, and if gangrenous may lead to large putrefactive lesions. The pus implies the loss of the sensitive granulations, the wound surface has become an ulcer which may spread. If progress is favorable a scar is gradually formed. It may often be observed that among the superficial layers, exposed to pus formation, a zone of strong granulations

develops, takes on a denser character, and withstands the suppuration by forming fibrous tissue. This is the secondary union mentioned above.

Infected wounds, which never heal by primary union, often present the proliferation of atypical epithelium and glands already described (p. 93). Before the area is covered by new epithelium the granulations are large and fungous, and are called *proud flesh*, or *caro luxurians*. The same is observed in all slow chronic suppurations of mucous, subserous, and intermuscular tissues, with continual proliferation of cells, softening and death of these, and no apparent tendency to repair. With abscesses which slowly increase the adjacent connective tissue may present granulations which partly are lost but partly engage in enclosing the focus. Such a limiting process forms an abscess membrane or *pyogenic membrane*. Pus foci which form slowly without external sign of reaction are called cold abscesses.

The pus of abscess and empyema which is not evacuated may undergo more or less complete absorption or become encapsuled, but danger of general infection is present until completely healed, or exacerbations and rapid spreading may occur. Between the two layers of serous membranes adhesions may form and later calcify. Chronic collections are sometimes observed which show a return of the suppuration even after they are encapsuled, and the limiting tissue may be broken through or simply new purulent exudate collects in the cavity. Examples of this are seen in the pleura and peritoneum.

Practically all severe suppurations are caused by bacteria, and from the self-propagating powers of these organisms the process tends to persist. (See Chapter V.) It may spread in spite of the power of repair in the surrounding tissues. By metastasis there may be a diffusion to distant portions of the body. This depends upon transport of bacteria through the lymph or bloodvessels; if through the lymphatics the bacteria may be arrested in a node, which then suppurates. Through the blood, masses of cocci and other bacteria may cause embolism and thrombosis in various capillaries. Under thrombosis and embolism only those forms were discussed which were free from infection. If they contain bacteria or are due to their presence the conditions vary. Thrombi form rapidly in inflamed tissue, especially when the vessel walls are affected by suppuration. These thrombi have a far stronger tendency than the others to soften, and hence there is opportunity for particles to become emboli. Wherever such particles lodge their contained bacteria develop and a metastatic abscess

results. As these emboli are apt to be small and are arrested by small vessels, the resulting infarcts are commonly smaller and less regular than the simple infarcts, and occur both in the depths of organs and on their surfaces.

Such a suppuration, generalized through the body, with metastatic abscesses in many parts, constitutes *pyemia*. (See Chapter V.)

6. Caseous Inflammation.

This form, in which the infiltrated tissue becomes caseous, belongs among inflammations which lead to necrosis (p. 55). It is chiefly observed as a part of tubercular or syphilitic lesions, and will be noticed with them.

7. Hemorrhagic Inflammation.

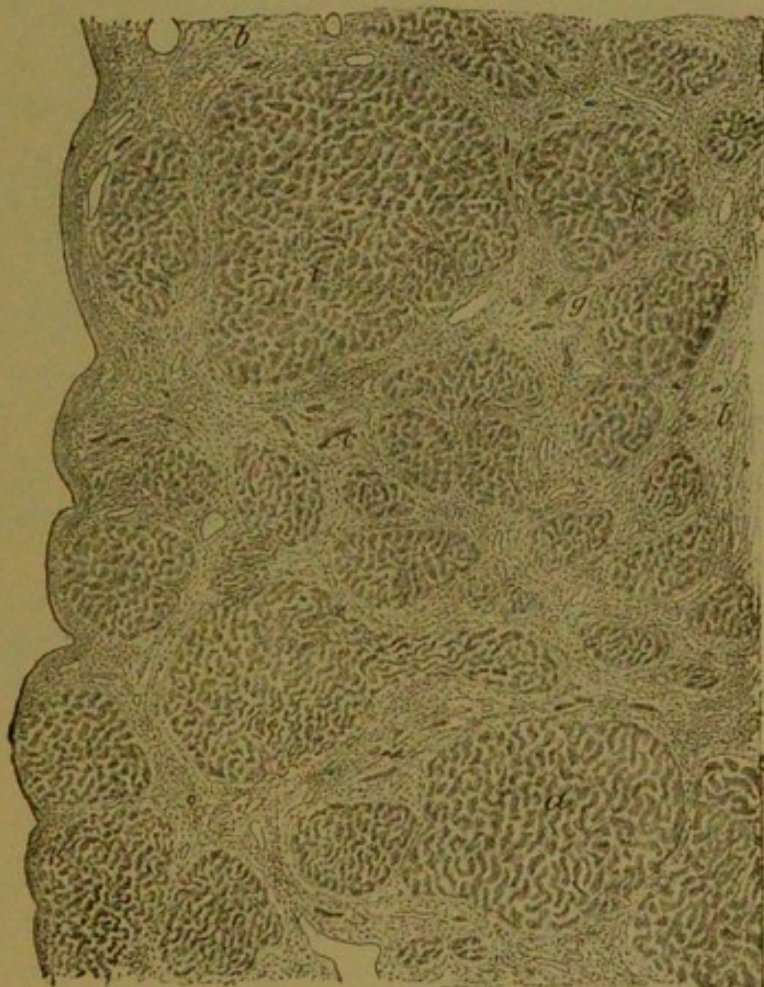
Any exudative inflammation may be accompanied by the exit of red cells from the vessels, and hence serous, fibrinous, and purulent inflammations may become hemorrhagic. It is often a sign of severity in the lesion. In the hemorrhagic diathesis the inflammatory exudate may have the same character.

8. Productive Inflammation.

Productive inflammation may be the result of an exudative form when the defects of the latter are restored by connective-tissue formation, but this process of healing may transcend the limits of a reparative change (p. 111). The same is observed in tissue which tends to limit destructive lesions, as when periostitis with osteomyelitis lasts beyond the duration of the latter and becomes an independent disease. (Fig. 9.) So also the connective tissue hyperplasia in tuberculous and syphilitic diseases, at first protective, may become progressive, as also endarteritis obliterans which occurs where destructive lesions surround vessels and tends to prevent the exit of blood from the vessels. (Part II., Vessels.) Such forms of productive inflammation are secondary. A *primary variety* is characterized from the first by a tendency to the growth of new tissue, while other features are unimportant. Thus in serous membranes there may be hyperplasia without marked exudation. In the lung, inhalation of dust may set up an interstitial inflammation, which is accompanied by catarrhal symptoms, but the fibrous stroma of the organ is specially affected. The interstitial tissue is infiltrated by round cells, often in groups. The connective-tissue nuclei multiply and lead to the formation of new connective fibres (p. 88), and,

becoming scar-like and contracting, the shrinkage leads to atrophy of the normal elements of the part. Typical instances of this are found in the liver and kidney. Such interstitial inflammation of the liver is called atrophic cirrhosis, the hepatic cells disappearing as the interstitial stroma increases. Similar forms in the kidney give an interstitial nephritis with loss of glomeruli and tubules. In the spleen the trabeculae and capsule become thickened. In the intima of vessels, in lymph nodes, and the genital organs similar changes occur.

FIG. 57.

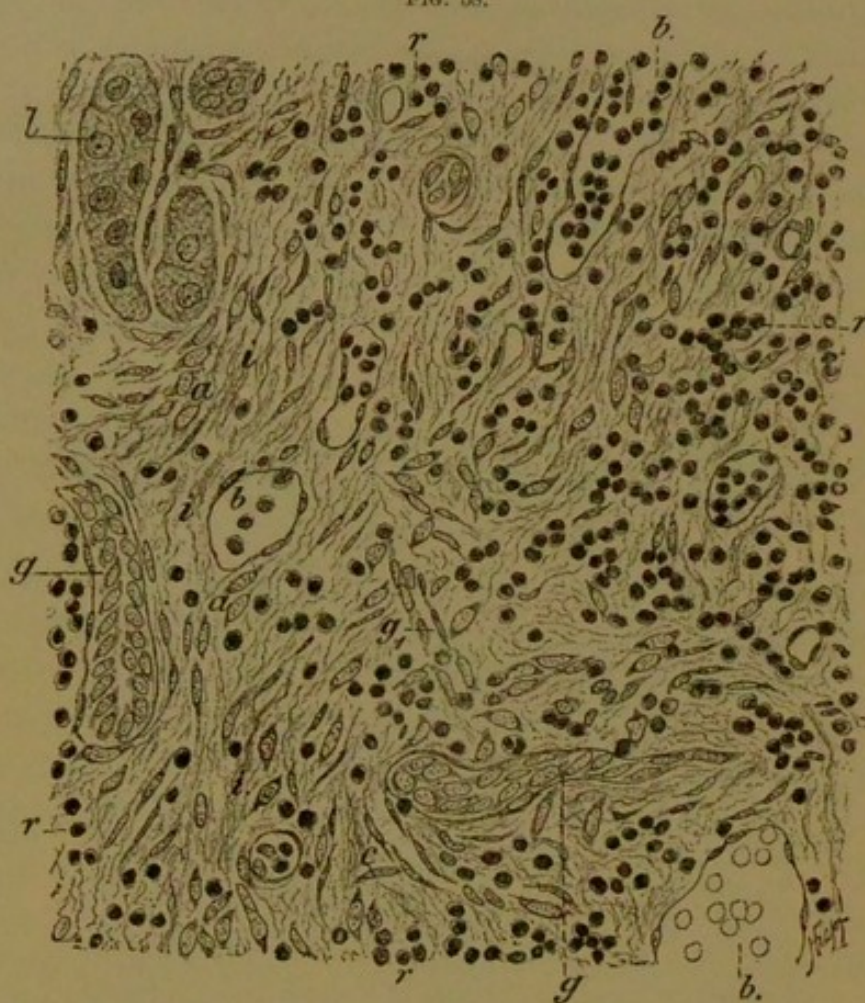


Interstitial hepatitis. Between the acini is greatly increased connective tissue. *b*. Strands of fibres between acini. *f*. The same within the acini. $\times 50$.

Primary productive inflammation is not limited to connective tissue, for it may involve cartilage, bone, and neuroglia. In the two former there may be circumscribed outgrowths or diffuse sclerosis; in the nervous system thickening of the stroma is followed by atrophy of the cells and fibres. (See Part II.)

Many local outgrowths in cartilage and bone form transitions to the strict neoplasms, and can at times be distinguished only by their

FIG. 58.



Interstitial hepatitis. *a*. Granulation cells. *r*. Lymphocytes. *l*. New fibrous tissue with spindle cells. *g*. Young gall ducts. *i*. Groups of liver cells surrounded by growing connective tissue. $\times 350$.

FIG. 59.



Papilloma (acuminate condyloma).

origin. On skin and mucous surfaces of certain regions, and especially where one adjoins the other, many inflammatory lesions are accompanied by elongation of the papillæ; these grow and divide, while their epithelial cells multiply, and thus a cauliflower excrescence results, called a fibrous papilloma. (See Chapter III., E.) Among such growths the pointed condyloma may be mentioned.

D. INFECTIOUS GRANULOMATA.

The name **infectious granulomata** is given to a group of diseases which are due to specific organisms and have the tendency to produce numerous small foci of granulation tissue throughout the body. This character and the resemblance to certain neoplasms justify the name, but they may also appear in diffuse forms.

1. Tuberculosis.

Since the discovery of the tubercle bacillus the signification of tuberculosis has become purely etiological, for it includes all the effects produced by the micro-organism. These may be of a vastly different nature, but the pathognomonic element is the appearance of more or less numerous, small, and circumscribed nodules, which tend to become caseous. These nodules are the site of inflammation, with fibrinous or cellular exudate and a varying proportion of cell proliferation in the neighborhood. It is an important fact that in these foci the blood-vessels disappear early, in part by caseous necrosis.

A **tubercle** is a small nodule, at first not visible in the gross, which increases to the size of a millet-seed, and is gray and non-vascular. It may lie in normal tissue and project slightly above the cut section, and it may be single, conglomerate, or regularly distributed in countless numbers.

Microscopically, the tubercle consists chiefly of cells, among which those of granulation tissue occur. The epithelioid cells are found with light nuclei and large, variously shaped bodies, at times with processes. The polynuclear giant cells occur with great regularity, and the nuclei are usually arranged about the margin of the cell. Small and large round cells are nearly constant, with single granular nuclei, and early or late the polymorphonuclear leucocytes appear. When the round cells are particularly numerous the tubercle is called lymphoid. Beside the cells there is usually a finely reticular fibrous tissue, which consists for the most part of coagulum whose appearance indicates the beginning

of caseation; but it includes also an actual reticulum whose fibres lie between the cells, and in its nodes there are single cells whose processes radiate into the reticulum.

The tubercle consists, then, essentially of cells of connective-tissue origin, between which leucocytes appear. Where epithelial cells occur there may be proliferation of these also, and of glands. About liver tubercles bile capillaries develop, whose lumen is filled with proliferating epithelia, and in tubercles of the kidney renal tubes multiply similarly.

Many small tubercles may fuse to a larger mass. It is characteristic of all tubercles that they lack vessels, which accounts for their short existence and rapid decay. By the time a tubercle has reached the size of a millet seed it presents regressive changes, the commonest being caseation. (Figs. 10 and 11.) This begins with a yellow change in the middle, while the periphery remains gray. The necrosis is noticeable early in the giant cells. Caseation progresses until the entire mass is converted into yellow, non-nucleated detritus.

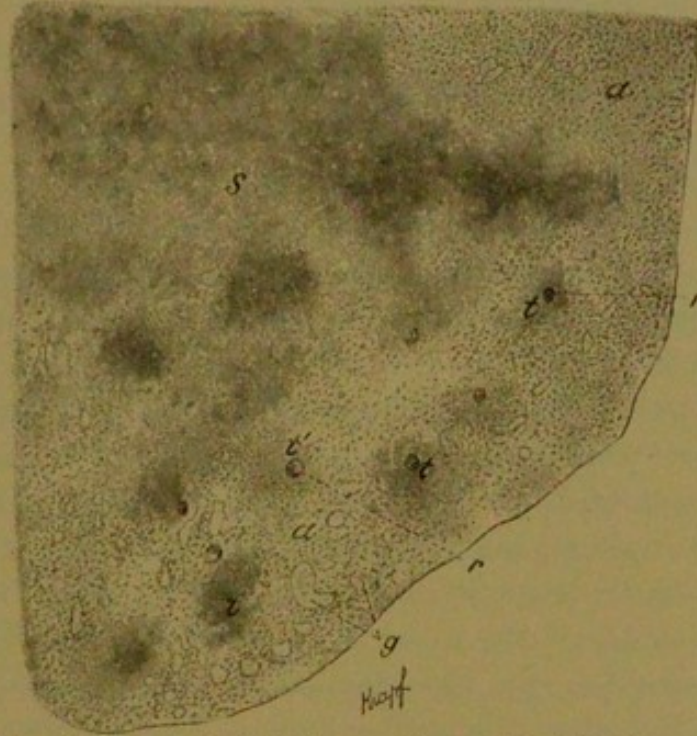
In many tubercles which grow slowly there is a fibro-hyaline change on the edge, by which slender and spindle-shaped cells are arranged, often concentrically, about the focus and form fibrous tissue. These cells, like the reticulum in the tubercle, undergo a hyaline thickening, as already described in lymph nodes (p. 70). This fibro-hyaline transformation extends inward concentrically toward the caseous parts, or even permeates the nodule before caseation. This is explained by the connective-tissue origin of the cells in tubercle and their power to form fibrous tissue.

When numerous tubercle bacilli enter the lymph or blood stream they are distributed to an organ or part of an organ, but entering the venous blood they may be scattered over the whole body. Hence we observe either partial or general dissemination of tubercle, and the latter is called general miliary tuberculosis. This is an acute condition which, with the symptoms of general infection, may end in death within a few weeks, and the bacilli may be found in the blood.

When but a small number of bacilli settle in an organ the general health is but little disturbed, and they have time to develop and infect the adjacent tissues. Thus large solitary or conglomerate tubercles may be found which have resulted from the formation of small secondary nodules about the primary focus and final fusion with it. Necrosis and caseation convert the whole into a uniform mass. The secondary nodules start by the entrance of bacilli into the lymph spaces about the

first nodule. Hence they are usually arranged in a ring about it. (Fig. 60.) The secondary are called resorption tubercles. The conglomerate forms occur in the liver, spleen, brain, kidneys, and else-

FIG. 60.



Conglomerate tubercle in the brain. *t, t'*. Many small resorption tubercles containing (*r*) giant cells. *a* Round-cell infiltration. *g*. Vessels.

where. Their growth is slow and they belong to the chronic variety of the disease.

Tubercle bacilli may cause diffuse inflammatory processes of various kinds. With nodule formation there may be serous, fibrinous, or

FIG. 61.



Tubercular ulcer of the intestine. *a*. Mucosa. *b* Submucosa. *c*. Muscularis. *g* Ulcer. *t*. Tubercle in the mucosa. *t'*. Focus caseating in the middle. $\times 12$.

purulent exudation, and between the tubercles a proliferation of connective tissue may occur. In such cases we speak of a tuberculous inflammation. Thus simple tuberculosis of the meninges is distinguished

from tuberculous meningitis in which there is an exudate, usually purulent. The same is true of serous membranes, and in the latter a cellular proliferation may take place, as already described (p. 110). With either exudative or productive tuberculous inflammation the exudate may be hemorrhagic.

On mucous membranes (Fig. 61), tuberculosis begins as a granulation beneath the epithelium, causing a marked infiltration of the mucosa and elevating the surface. Then the caseous mass breaks through on the mucous aspect and forms the tuberculous ulcer, in whose edges and base small tubercles and infiltrations are observed which break down and enlarge the ulcer. The edge is irregular and may be sinuously undermined.

Pure productive forms of tuberculosis are found in lymph nodes, bones, and joints. Caseous changes are apt to occur early in both tubercle and surrounding granulation tissue, at first in scattered areas and then spreading. Such processes, however, may heal, as is true also of mucous ulcers, healthy granulations forming about the area which end in cicatrization, absorption, or calcification. In some cases the young tissue about the tubercle shows a tendency from the first to make scar tissue, and in these favorable cases the caseation may be absent or unimportant; this applies to some cases of fungous joints.

The discovery of tubercle bacilli in certain exudates proves that they have the power of causing simple inflammations or those with but few tubercles, entirely resembling ordinary inflammations except that caseation of the tissue and exudate is liable to happen in time. Examples of this caseous inflammation are found in cheesy pneumonia and bronchitis, and in papillary caseous nephritis. (Part II., various organs.)

In cheesy pneumonia we find an exudate in the alveoli, as in other pulmonary inflammations, and this undergoes caseation.

In those cases where the tuberculous inflammation is purulent, as in meningitis, bronchitis, and arthritis, the pus consists of leucocytes in the main, like ordinary pus, and the tissues show necrotic tendencies, loss of nuclei, and fragmentation.

Special forms of tuberculosis are scrofula and the pearly disease of cattle.

Scrofula occurs especially in early childhood, between the ages of two and thirteen years, and affects the lymph nodes, especially of the neck. These nodes become swollen and hyperplastic in groups and undergo fibrous induration or suppuration, in the latter case with

obstinate fistulae remaining. By progressive involvement of many nodes there may be a transition to pseudoleukemia. (See Chapter III., E.) Together with the scrofulous lymphomata there are often affections of the skin, eczema or scrofuloderma, chronic catarrh of mucous membranes, especially of the head, scrofulous lips, phlyctenular conjunctivitis, adenoid vegetations in the pharynx, and enlargement of the tonsils. These diseased regions correspond to the point of entrance of the bacilli, but many infective agents may pass through these parts without injuring them, and reach the nodes. Thus in the cervical, bronchial, mediastinal, and mesenteric nodes, the port of entry is the mucosa of the throat, of the lung, or of the intestine, respectively.

The relation between scrofula and tuberculosis is viewed in different lights, but it is certain that there is a close relation between them. Some of the scrofulous invasions of the nodes are plainly tuberculous for they contain the bacilli, and with many scrofulous children tuberculosis of bones, joints, and lungs are observed, or miliary tuberculosis may complicate the case. Hence scrofula has been called the tuberculosis of childhood. It seems, however, as if the relation were more indirect. The various additional affections of cutaneous and mucous surfaces are not essentially tuberculous, and may show no anatomical or etiological relation to tuberculosis, though other bacteria, as the pyogenic, often appear. These facts suggest that scrofula is tuberculosis in only a portion of its phenomena, but is rather a congenital disposition with a peculiar sensitiveness to infections, especially to tubercle. Such a disposition is characteristic of early years and markedly so with scrofulous individuals. In many cases the skin and mucous lesions are the port of entry for the tubercle bacilli, and become tuberculous in common with the lymph nodes. This vulnerability may be explained by peculiarities in the anatomical construction of the patient, as looseness of the submucous tissue, lymph stasis, and ease of inception of bacterial products.

The *pearly disease of cattle* is accompanied by the formation of large conglomerate nodules resembling sarcoma, in various organs, having but little tendency to spread through the body, extending locally very slowly, and microscopically consisting of epithelioid, giant, and white cells, with some fibrous elements. They regularly caseate and calcify.

The further course and results of local tuberculosis are very manifold, depending upon whether the focus caseates or becomes hyaline and fibrous. By the latter change obsolete tubercles and scars are formed which bring no danger to the adjacent or distant tissues.

Small caseous foci may be absorbed when the bacilli present are dead, or lime salts deposit in them and a fibrous capsule forms.

With rapid increase and widespread caseation the softening and liquefaction lead to the formation of large cavities, in spite of some fibrous proliferation in adjacent parts. The wall of the cavity breaks down, and thus it enlarges; its contents are turbid, yellowish, and purulent. Small cavities may be encapsuled and even healed by resorption. (See Chapter IX.)

A small tubercular focus without infection of the immediate vicinity may remain a long time as a "latent" tubercle, but at any time a local or general invasion may proceed from such a focus. Generally the latent form lasts for years as a fibrous or calcified nodule and its bacilli die. In tissues entirely fibrous and scar-like or calcified, no living bacilli are found, and inoculations of animals with such material remain negative, while from caseous foci infection is always possible. Hence tuberculosis is curable, and at times heals spontaneously. The remains of tuberculous collections in the lungs are frequently an accidental find at autopsies after death from other causes. Tuberculous disease of nodes, bones, and joints, and lupus of the skin, may also heal without assistance. As a general rule, it may be stated that healing occurs in tuberculosis earliest in the organs most often affected.

Spread of the disease from a primary focus occurs by *contact* or *metastasis*. Contact infection is observed on the surface of hollow organs or cavities. Thus tubercles are disseminated over wide areas when a softening focus empties into the pleura or peritoneum, or when the renal pelvis is affected and the urine carries bacilli to the ureters and bladder, and very commonly in the bronchi when a cavity empties into one and the infected sputa are drawn into the fine twigs of other bronchi. Pulmonary tuberculosis often exactly follows along the distribution of bronchi. Similarly passage of infected sputa over the laryngeal surfaces or the intestinal mucous membrane infects these places.

Bacilli of tuberculosis may enter the blood directly through the vessel wall, when a nearby focus attacks it and the softened matter empties into its lumen. This may happen with caseous nodes and from other tissues. Frequently, with general miliary tuberculosis, large nodules or plaques of caseating tissue are found in the venous walls, which pour bacilli into the blood. The effect varies according to the vessel entered. If an artery, the bacilli are confined to its distribution, where they form new tubercles, or with detritus embolism

may be observed. If a vein, a much wider dissemination occurs, and tubercles are found in many organs, and general miliary tuberculosis develops with large numbers of bacilli. Tuberculous lesions of the cardiac valves, endocardium, or aorta cause similar invasions. When a focus empties into the thoracic duct the result is as with veins. Such lesions of the duct or of large veins may be found after careful search in most all cases of general miliary tuberculosis.

With local chronic and subchronic tuberculosis, as well as for general dissemination, the lymphatics play an important part. Spreading through these the resorption tubercles already mentioned are developed, as well as the discontinuous advance seen especially in the lymphatics of the mesentery, retroperitoneal tissue, pleura, and lungs. In the walls of the lymph vessels there form series of small nodules arranged like a string of beads.

All investigations agree in characterizing tuberculosis as an *infectious disease* exclusively produced by a *specific* and distinct *bacillus*. Inoculations in the anterior chamber of the eye, in the blood, a body cavity, under the skin, or into the intestine by feeding experiments, produce tuberculosis in various animals; and different tuberculous products, as from diffuse cheesy inflammation, or tubercles in the strict sense will cause such results when inoculated. This demonstrates that all the varied lesions belong to a single etiological factor. While the method of entry in all cases is not clear, it is certain that the lungs are the usual site of invasion.

The common observation that tuberculosis affects those whose parents were tuberculous has led to the supposition that the disease might be directly inherited, entering the ovum with the spermatozoön (*conceptional* or *germinative infection*), or coming through the blood of the mother and the placenta to the fetus (*intra-uterine* or *placental infection*). As tubercle bacilli have been found in the semen of patients with normal testes but suffering from phthisis, it was thought that such germinative transfer of the disease might occur as with syphilis, which can pass from father to child without infecting the mother. But it is still questionable whether tubercle bacilli may accompany the spermatozoön into the ovum, and also whether such an ovum could develop.

The idea of direct inheritance receives apparent support from the fact that parental disease can be discovered in one-third to two-thirds of all cases, and the possibility of bacilli passing from the placenta to the fetus cannot be denied. Congenital tuberculosis has been observed

in animals, and in the organs of a human fetus whose mother died with general miliary tuberculosis it was proved that tubercle bacilli existed. Cases in which tuberculosis developed a few weeks after birth have also been regarded as proof for inherited disease, their cogency as proof diminishing as the period after birth increased. But such early manifestation of the disease and proved congenital tuberculosis are very unusual in both men and animals. In the Berlin slaughter-house during a year it was found that 1.8 per cent. of cattle were tuberculous, but only 0.009 per cent. of the calves, which seems to prove an infection later than congenital; and statistics of human tuberculosis show that the disease begins more commonly in the second and later years, and that even in advanced age fresh infections are not uncommon. The opinion that most tuberculous infections are inherited can be accepted only if the additional hypothesis is correct that the bacillus may remain for an unlimited time in the body, unchanged and causing no lesions. It is true that a tubercle may be latent for years and at last heal, but that bacilli remain virulent in the body for one or two decades, causing no lesions, and after that produce tuberculous disorders, is a supposition contradicted by all experience, the fact being that a bacillus either causes pathological processes in the body or itself dies.

Granted that infection occurs in extra-uterine life, we must assume that the bacilli enter the body from the environment, inhaled in the air or swallowed with food or otherwise. The commonest source of infection is the sputum of patients, especially those with cavities, which lies where ejected and becomes a source of danger for others. The food most often introducing the bacilli is the milk of cattle with pearly disease, affecting the udder and other organs. The flesh of such cattle, usually eaten cooked, is far less dangerous, for inoculation with muscle from tuberculous cows reproduces the disease only when the muscle is extensively infected.

Not all tissues are equally sensitive to the bacillus. The skin may present lesions which usually remain local and tend to recover, as dissection tubercles, scrofuloderma, and lupus. Circumcision as practised by the unclean, the operation wound being sucked by the mohel, may be followed by general infection from his sputum, but the subcutaneous tissue is the point attacked. Tubercle bacilli cannot enter the uninjured skin, as many bacteria can. Probably the firmness of the skin and its variations in temperature explain its partial immunity.

The respiratory organs are the point of attack in the majority of cases, especially the apices of the lungs and afterward the lower lobes.

This does not prove that the lung is necessarily the point of entry, nor that the bacillus was inhaled, for in all cases the lungs show a disposition to tubercle formation. Latent or healed foci in the apices is a common lesion accompanying death from non-tuberculous disease. The location of the lesion in the apex of the lung may be due to the relatively slight movement and ventilation of this region during breathing, together with anemia and presence of dust particles. In animals the apex is not specially attacked, the posture and circulation of the animal differing from those in man.

Although the lungs are specially liable, the bacilli may pass through them and attack a bronchial node, and this is found in children as a focus of latent tuberculosis without lesion of the lung. Mediastinal and other nodes may be affected. By metastasis the lungs are frequently involved from other organs. The opposite is even more true, tuberculosis starting in the lungs and then invading other organs. The pleura is commonly involved, less often the vertebræ, ribs, and diaphragm, and by contact the larynx and trachea become tuberculous.

The mucous membranes of the upper respiratory and alimentary tracts have but little tendency to tuberculous disease, and the scrofulous affections met with here are not malignant. But these regions serve for the entry of bacilli into the lymphatics, especially the follicles of the tonsils, tongue, and pharynx, which may themselves remain unaffected.

The normal secreting stomach does not prevent the passing of bacilli to the intestine, but seldom itself becomes diseased. In the gut the lower portion of the ileum and the cecum are specially liable to be attacked, and the lymphoid tissue is commonly involved first. Intestinal tuberculosis may be primary or may follow swallowing of sputa. In adult patients intestinal lesions complicate tuberculosis in 70 to 80 per cent. of all cases; in children the figure is about 38 per cent. The mesenteric and retroperitoneal nodes may be involved without intestinal lesions. When all the abdominal nodes are tuberculous the disease is called *tabes mesaraica*. The peritoneum is invaded either from the intestine or pelvic organs, from the pleura, or through the blood.

In the kidney miliary tubercles from the blood are not unusual. A special form of renal tuberculosis results from extrusion of the bacilli through the tubules, the large collecting tubes in the pyramids being first involved, and then the whole pyramid and cortex. Bacilli in the urine may infect the bladder, epididymis, and other genital organs, and primary disease in them may secondarily invade the kidneys.

Bones and joints are infected through the blood.

Tuberculosis is one of the commonest diseases, about one-seventh of all deaths being due to it. Its morbidity is even higher, for statistics indicate that in large cities 40 to 50 per cent. of all cadavers show fatal or accompanying lesions of a tuberculous nature, excluding nursing children, and that 25 per cent. of patients dying from other diseases have healed or latent foci. Children's hospitals of large cities give 30 per cent. of deaths from scrofulous disorders and 18.8 per cent. of accidental tuberculous lesions. The disease is least common in the first year, occurs in high percentage from two to six years, diminishes from seven years to puberty, and of the later years from fifteen to thirty furnish the most cases. If macroscopical lesions alone be not considered, but all cases be subjected to a careful search for tuberculous processes, the figures are much higher; thus in one series of 500 cases 97 per cent. revealed signs of tuberculosis after diligent search. This means that practically every human being takes in the bacilli, but in most there is no further result. The percentage of lesions is less and the disposition is greater with the first years of life, and the disposition is less but the lesions more frequent as life advances.

As far as the various organs are concerned, a scale of liability to tuberculous lesions might be made as follows, the less immune first: lung, lymph nodes, intestinal mucosa, skin, central nervous system, muscles.

The general exposure to tuberculosis raises the question why everybody is not infected; for even among those specially occupied with the disease, as nurses and physicians, many escape, while certain trades are peculiarly attended by the danger. It is evident that mere juxtaposition of the bacilli and a human being is not enough; there must be conditions on the part of the patient and upon the part of the bacillus, for the human body does not act like a lifeless culture medium, but reacts to the presence of the germ, and may even control small infections.

The conditions affecting the development of the bacillus are, first, relatively large numbers; second, virulence; and third, a long enough stay in the body. Against the latter there are protective agencies. Bacilli in the inspired air may be arrested in the labyrinthine passages of the upper respiratory tract, so that but few actually reach the lung. The ciliated cells of the air passages keep up a movement which carries small particles outward. If the bacilli reach the lungs, unless virulent they may be destroyed. Inhalation experiments on animals, in

which countless numbers of bacilli are inspired and swallowed, do not in the least represent the actual conditions of human infection. Experiments with but few and weakened bacilli in the atomized fluid show that infection is less certain and takes longer to develop in proportion to the dilution, though the boundary beyond which it ceases to occur cannot be exactly determined. Bacilli may remain dried from six to nine months and still develop in the right conditions, but they have lost in virulence. Tuberculous material from different sources may act differently, and in any case the immunity of the subject must be considered. Thus it is clear why only a portion of the human race should be diseased by tubercle bacilli, in spite of their general distribution.

On the part of the receiving organism we notice in the majority of the cases an inherited disposition, or a weakness of body formation (phthisical habitus), or in later life there has been exposure to injuries of the lungs, as from inhalation of dust. The bodily formation which facilitates infection is known as individual disposition. With no such disposition a strong constitution may be overwhelmed by enormous numbers of bacilli; with it, however, fewer bacilli may cause some lesions.

Relative immunity of a portion of an organ is seen frequently in the lung, where we must assume that all parts are entered by bacilli, and yet only the apex may become diseased and the lower lobes escape. Apical healed lesions show the power of the organ to overcome the bacteria in favorable conditions.

Regarded from the point of view suggested above, we can refer all cases of tuberculosis to one of the four following groups:

1. **Infection without Individual Disposition.** A strong organism may be overwhelmed by numerous virulent bacilli, or with fewer and weaker germs the disease remains local and tends to heal.

2. **Infection of Individuals with Inherited Disposition.** In one-third to two-thirds of all cases a history of inheritance can be gathered or expresses itself in the phthisical habit of body—shallow and narrow thorax, sunken supraclavicular and infraclavicular fossæ, long, slender neck, imperfectly developed fat and muscular tissue. Children with this disposition who live with tuberculous parents are specially exposed.

3. **Infection with Acquired Disposition.** General body weakness from imperfect nutrition or connected with disease (as diabetes), together with unhygienic influences, as in certain trades.

4. Infection with the Disposition both Congenital and Acquired.

A weak body further weakened by various occupations and other injuries.

Lupus. This disease of the skin and certain mucous membranes is etiologically tuberculosis, but anatomically a peculiar variety of the disease. On the skin it begins with the appearance of small pinhead nodules of light or brownish-red color, but little prominent over the surface; later on they project more, and reach the size of a pea, or fuse over a wide area. Microscopically they consist of granulation tissue with giant cells, which has a stronger tendency to form fibrous tissue than to caseate, but they may contain products of necrosis. They begin with the gathering of round cells under the epidermis, then involving the latter, and ending in its desquamation. The epithelial cells soon show an active proliferation, as also the cells of the sweat and sebaceous glands, so that atypical collections of these cells may be found as in wound-healing (p. 93). New nodules form, and so the disease spreads.

The external appearance varies according to the excess of one or the other pathological changes, and hence we distinguish *lupus hypertrophicus*, with profuse granulation tissue and thickening of the skin, as in elephantiasis; *lupus exfoliatus*, with great desquamation; *lupus exulcerans*, accompanied by destruction of the nodules and sharply margined, shallow, roundish ulcers, commonly covered with crusts; and lastly, *lupus erythematosus*, broad, flat infiltrations without ulcers and of pronounced red color.

Ulcers in lupus have a chronic course and but little tendency to heal, and they may greatly distort the part attacked, as the face. The chief sites of the lesion are the cheek, nose, forehead, upper lip, and external ear; it may occur on other parts, and from the skin it may invade the mucous membranes, as of the lip, palate, and larynx.

Primary mucous affections are very rare. On the mucosa the lupus lesion is not so much a circumscribed nodule as a diffuse infiltration with uneven, gray granulations. Ulcers with large and deforming scars may be found also on mucous surfaces.

The course of lupus is always chronic, and changes with the appearance of new nodules, destruction of tissue, and scar formation. In 14 per cent. of the cases internal tuberculous lesions also occur. The skin disease probably has a hematogenic origin, for by inoculation of the skin its lesions can not be reproduced.

Scrofuloderma is a disease of the skin which also presents nodules, and these may break down and form ulcers. The nodules when confluent result in large ulcers, often with partial cicatrization.

2. Syphilis.

This disease, like tuberculosis, appears in various anatomical forms; as circumscribed new formations, as less sharply limited granulation tissue which has some neoplastic characters, or as diffuse processes, partly hyperplastic, partly inflammatory. The anatomical lesions are the effect of a specific virus not yet recognized, but probably a bacterium. It belongs among those parasites which exist only in the living body, and cannot last any time outside of it. The infection in the majority of cases occurs through sexual intercourse; it may, however, follow the use of infected surgical instruments and household utensils, vaccination, wound infection, and, on the nipple, suckling of a syphilitic child by a healthy woman.

At the point of infection there develops, after three or four weeks, a *primary lesion*. This is found on the prepuce, the frenum, coronary sulcus, or labia as a flat papule; on a mucous surface a herpes-like vesicle forms, and by its rupture reveals a small erosion. The papule on the skin shows a superficial ulceration without much secretion. The tissue about the primary sore becomes hard, making the *initial sclerosis*. As the induration increases with the ulceration there is formed a *hard* or *Hunterian chancre*. This may heal after a short time, with or without a scar. Almost always the initial lesion is single, and, as stated, may occur elsewhere than on the genitals. It consists of a granulation tissue, which is dense and shows collections of small round cells, especially about vessels.

Soon after the chancre forms the nearest lymph nodes, as the inguinal, swell, forming a *hard bubo*, due to the absorption of the virus through the lymphatics. The poison passes the nodes easily and is then distributed over the whole body, causing many skin eruptions, and ushering in the second stage of the disease, or *constitutional syphilis*. This happens six to seven weeks after the primary sore. The lesions of the secondary period are commonly of an exudative, inflammatory nature, with a macular, papular, or pustular exanthem on the skin and mucous surfaces. Bones which lie close under the skin, as those of the skull and legs, are apt to have an inflammation of their periosteum. All these lesions are relatively benign, and heal without deep injury to the tissues. Among the peculiarities of

secondary syphilis may be mentioned the broad condylomata and their appearance on the mucous surfaces as mucous patches. They are made of young granulation tissue, rich in cells, which causes localized infiltration and swelling of the papillary layer. Broad condylomata are usually found where two skin surfaces are in apposition, and are due to local infection by syphilitic secretions, and not, as the skin lesions are, to transport of the virus through the blood. They are especially common on the genitals, the labia, contiguous parts of the thighs, the anal furrow, the scrotum, and posterior aspect of the penis. The papillæ enlarge in groups, increase greatly in size, and so present broad, elevated surfaces whose epithelium is macerated and at last exfoliates; hence the condyloma is moist, with thin or purulent and very infectious secretion. They may also be destroyed by ulceration. The mucous plaques are common where skin and mucous membranes merge—on the inner side of the prepuce, the inner surface of the labia, the portio vaginalis, the mouth, and the larynx. They are made of swollen papillæ, with thickened and opaque epithelium of a gray or white color, often confluent to large, flat elevations; with loss of epithelium and erosion they become red.

The third stage, or *late syphilis*, follows the secondary after a varying time of latency, and is characterized by deeper lesions, which, if they heal, leave severe cicatricial deformities.

The *gumma* or *syphiloma* is a mass in the tissues, but little prominent, infiltrated with round cells, and either lobulated or flat. When fresh it is soft and gelatinous, gray to grayish-red, at times almost slimy. In size it varies from a size so small as hardly to be visible to that of a walnut or larger. Histologically it consists of granulation tissue in which the fixed and the endothelial cells proliferate and make for the most part large epithelioid cells, and among these are many round cells and leucocytes. When older the gumma is dense, dry, pale, and made up of fibrous strands, and in the middle portions there is apt to be yellow and firm caseous material in masses with irregular borders. The denser consistence of the caseating gumma, contrasted with the tubercular nodules, is due to the greater amount of fibrous tissue in the former. Even when the area is wholly caseous fibres may still be found in it. Surrounding the focus there is a zone of fresh granulation tissue. By the penetration of this and the resorption of the mass it may heal with large scars, which by contraction markedly diminish the original focus and appear as depressions with radiating fibrous strands on the surface of the organ. These are

typically seen in the liver and some other organs. In the central nervous organs the fibrous scars are not so often produced.

With incomplete resorption there remains in the middle a certain amount of caseous matter, and when this is superficial, so that its discharge occurs, there remains a deep ulcer, which may tend to rapid advance in all directions, or be serpiginous. Healing and scar contraction indent the surface. Gummata are found in the liver, brain, meninges, skin, mucous membrane, testes, bones, and periosteum, and the walls of vessels of large and middle calibre.

Beside the tumor-like growths of syphilis there may be diffuse forms.

The gummatous process may apparently infiltrate an organ or spread as a flat mass which has no sharp limits, but caseates here and there. This is called gummatous inflammation. It ends as a thick and dense scar, with great contraction. A process of this kind may combine with true gumma. An exudative inflammatory lesion, fibrinous or purulent, is rare in syphilis, but has been observed.

Diffuse syphilitic inflammations of indefinite form occur congenitally in the lung and the liver. They affect the stroma chiefly, and are productive, with accompanying exudative lesions in the lung.

The lesions of tertiary syphilis are not constant, but appear only in a certain number of the infected, and a sharp boundary between the two stages is not always possible to trace.

Although one attack of syphilis usually makes the patient immune against others, new infections do occur as great rarities.

Syphilis is both directly contagious and hereditary, and in the latter case both conceptional and intra-uterine inheritance are assumed to occur. Syphilis may affect the child of a syphilitic father without infecting the mother; but, curiously, such mothers commonly are immune against other syphilitic attacks. Placental infection is certainly common, the fetus being invaded from the maternal syphilitic blood through the placental vessels. Very often the result of this is death of the fetus—two-thirds of all abortions, premature and still births being referable to syphilis.

The heredity of syphilis is connected with the second stage; the lesions of tertiary syphilis are neither contagious nor transmissible. The virus apparently lessens in power spontaneously, and sooner in the man than in the woman. At first there is abortion, or a dead child is born, then a living but weak child, with the signs of congenital syphilis; later on healthy children may be born.

With congenitally syphilitic births there are no constant changes

in the placenta. There may be thickening of the villi, obliteration of the vessels, gummata, or sclerosis, or none of these. The child may show no symptoms until after the lapse of days, weeks, or, rarely, the first three months. In other cases it is syphilitic when born. This is manifested as a symmetrical pemphigus, often found on the hands and feet, paronychia, or coryza. In the liver there may be diffuse hyperplastic cirrhosis, gummata, and fatty infiltration. The kidneys show infiltration of the cortical vessels. The spleen is constantly large. The thymus may show multiple abscesses (Dubois' disease) or induration. Syphilitic osteochondritis (see Chapter XIII.) is commonly present in some degree. The umbilical vessels are usually thickened. *Syphilis tarda*, which appears much later, is either an exacerbation of an hereditary affection or the result of new infection.

3. Glanders. Farcy.

This disease is caused by a specific bacillus (see Chapter V.), and is characterized by rapidly ulcerating nodules or diffuse infiltrations. It occurs spontaneously in the horse, and may attack man. Its course may be acute or chronic, and there are two forms of the disease, the infiltrating and the nodular. In the latter there are nodules which rapidly break down in the mucosa of the nose, the lungs, and other organs, as also in the skin, muscles, and bones, and these are made up of granulation tissue; by their fusion and ulceration large defects may follow. Infiltrating glanders, of more chronic type, is accompanied by massing of round cells in the respiratory mucosa, in the skin, and subcutaneous tissue, and these imperfectly circumscribed areas break down, and either heal slowly, with scars, or change into a tissue which resembles sarcoma; pneumonic infiltrations may break down and enter the bronchi.

In man the disease occurs as a pyemic general infection, with development of nodules in the skin, which ulcerate after a pustular stage. Multiple hemorrhagic abscesses are found in the muscles, phlegmons in the subcutaneous tissue, and embolic foci in the lungs and other organs.

Formerly the lesions of the respiratory mucosa were grouped as *glanders*, those of the skin as *farcy*; both are due to the *bacillus mallei*.

4. Lepra. Elephantiasis Grecorum.

Leprosy is characterized by formation of nodules which are larger than those of lupus, more prominent and softer, and may be confluent.

They occur especially on the face, about the forehead and eyebrows, nose, ear, lip, and scalp. The skin of the face may thicken as in elephantiasis. The nodules break down and form ulcers, which leave scars when they heal.

Beside the skin lesions, the peripheral nerves may be affected, presenting nodes and spindle-shaped thickenings. Corresponding trophic disorders occur on the skin, as pigmentation, loss of hair, and ulcers.

Microscopically the lepra nodule is made of soft, cellular granulation tissue, without giant cells; within the cells the lepra bacillus is found. The nerve lesions start from the fibrous tissue of the trunk. Lymph nodes swell, and nodules are found in the testes, liver, bone marrow, and rarely on mucous surfaces.

The disease is endemic in regions of Spain, Italy, Turkey, Asia, and the Hawaiian Islands. It appears, as a rule, between the ages of twenty and forty years, and is slightly contagious.

5. **Actinomycosis.**

This disease is common in cattle, and is due to the ray fungus (see Chapter V., A.), which makes sarcoma-like foci of granulation tissue, especially about the mouth, as in the jaw or tongue, the lymph nodes of the neck, the lungs, vertebræ, and, less often, in other parts. In the jaw there may be tumor masses which are miliary, but by fusion make large nodules, consisting of fibrous or cellular granulation tissue, softening in the centre and then expressible. On section the tissue is spongy and eroded. In the nodules there are small granules, like sand, of a sulphur-yellow color, made up of the fungus. In man, where it is rare, the disease presents no such tumor-like masses, but a diffuse and quickly ulcerating infiltration, especially about the mouth, jaws, and mediastina. The foci may open externally by fistulæ. Among such cases some attacks of angina Ludovici may be included. Less often actinomyces foci are found in the lung, intestine, or brain. Metastases may occur. The infection results probably from food or through the air passages. In the ulcerated areas foreign bodies, such as portions of vegetable matter, may be found.

The rare disease called **rhinoscleroma** is an affection of the skin which may attack the mucous membranes of the head. It consists of a marked cellular infiltration of the cutis and papillæ, which results in cicatricial connective tissue.

There are, lastly, several **granulomata** which are mainly composed of lymphoid tissue, and affect the lymphatics. To the infectious

members of the group belong typhoid infiltration of the intestinal follicles and nodes, many infections occurring in animals (pseudotuberculosis), and probably leukemia and pseudoleukemia.

E. TUMORS.

The word *tumor* formerly meant any circumscribed swelling of a part, produced in various ways. Better knowledge of inflammation has led to the exclusion of swelling due to exudation, and now tumor or neoplasm refers to the local swellings of organs which are due to tissue newly formed *in loco*. Hypertrophy and retention of secretions are also excluded, though a neoplasm may become cystic.

The real *neoplasms* or proliferation tumors follow the laws of growth which apply to inflammatory and hyperplastic formations, increasing by cell multiplication, with the aid of increased blood supply, and transitional tissues between those already differentiated are found in the connective-tissue group. Tumors develop from the cells of the body, and are not foreign in that sense. There are no specific tumor elements—as, for instance, with carcinoma; here the cells are but proliferated epithelia—but there are several peculiarities which distinguish tumors from other tissues and justify their consideration by themselves.

When a proliferation of cells occurs at any place, ending in large quantities of young tissue, the immediate neighborhood of the primary focus may act similarly, and thus the new-growth increases over large regions by *apposition* of new and similar masses; or the proliferating cells of the primary focus increase without involving adjacent parts, and the growth enlarges by *central* or *expansive* development. The first is the rule with inflammatory tissue increase; both processes may be found with tumors, but the second is typical. Thus interstitial inflammation of the liver involves the stroma more and more, young connective tissue forming as new portions of the stroma are attacked. With chronic catarrh of mucous surfaces proliferation of glands occurs over large stretches, for the neighboring parts are more and more involved in the reaction.

With tumors the case is different. Carcinoma of a mucous membrane causes proliferation of the epithelia. On the edges we see adjoining glands in similar proliferation, and the process spreads in this way, the tissues lying nearest becoming like the tumor, and then part of it (appositional growth). But the carcinoma involves the sur-

face and makes prominences on it, and also attacks deeper parts under the mucous membrane. In the latter case it is not involving adjacent parts, but the original tumor elements make others out of themselves, and these penetrate other tissues (central or expansive growth). The near-by epithelial cells may not show any modification into cancer cells, but simply suffer death, so that the same tissue outside of the part attacked may remain free from the disease. This is true also of sarcoma. Thus with sarcoma of the dura which perforates the cranial bones, it is not the periosteal cells which proliferate externally, but sarcomatous cells from the dura which have made their way out. In certain ovarian tumors after the entire tissue of the ovary has been destroyed the growth continues until an enormous mass is attained, and the same is observed with polyps of myomatous nature which are attached to the site of origin only by a slender pedicle. Many tumors thus grow without apposition, but their immediate neighborhood suffers pressure atrophy. These principles apply, although from the first there may be multiple tumors, or large surfaces may be infiltrated, or the tumor may start in inflammatory and hyperplastic proliferations.

The power of unlimited growth implies great additional energy of proliferation acting continuously, of which inflammatory and hyperplastic lesions give no examples. Granulation tissue ends in a scar at last; a sarcoma persistently increases—that is, the physiological conclusion of the process is absent with the neoplasm. In addition, the tumor is peculiar in its ability to recur. When a tumor is removed, if but a small portion of it be left, this may reproduce it and reach the original size. This is called continuous recurrence.

Neoplasms behave as something foreign to the organism and to the tissues in which they start, and have apparently an independent existence. They present nodules in the tissues or projections from surfaces, sessile or polypoid, tuberous or fungous, and at times they are papillary or dendritic. The independence is less evident when the neoplasm is a diffuse thickening, except that it is apt to vary from normal tissue in color, structure, and density. Where the corresponding cells normally have a distinct function this is lost in the tumor formed from them; hence the young cells of an adenoma do not furnish a secretion, and muscle cells in a myoma are not contractile. There is at times a striking independence of the general bodily condition, for depressed vital powers do not lessen the growth of the tumor; it can increase as long as it remains in the body.

The independence is expressed also as an aggressive relation to the surroundings even in the case of benign tumors, which may penetrate and grow in adjoining tissue, their growth being at the cost of the healthy cells. Transplantation experiments of small pieces of tumor have shown the power of continuing and sometimes of growing in the new site; so epithelial tissue with a portion of connective tissue attached, and bits of glands, may take root and form cysts when transplanted. The elements of malignant neoplasms have a far greater power of existence. They send processes into the adjacent tissues, penetrate, and possess them, thus giving rise to what is called *infiltrating* growths. Hence a tumor may reach a tissue entirely foreign to itself, and lying in such a foreign place it is called *heterotopous*. Thus epithelial growths invade the muscularis of a mucous membrane.

The tumor invades also the neighboring lymph spaces and blood-vessels, and thus there is opportunity for *metastatic* transport of loosened portions. The further development of such particles follows the laws already noticed, and spreads along blood or lymph channels. Often the metastasis appears in the nearest nodes, or there may be a regional spread against the lymph stream.

The structure of tumors may correspond to that of the tissue from which they start, or be wholly atypical, with all transitions between. Two great divisions of neoplasms are made from this point of view. All tumors in which the original structure may still be recognized are called *homologous*, and those in which it has departed from normal structure are *heterologous*. Thus a fibroma is homologous, for it reproduces fibrous tissue; so also a myoma or an adenoma reproducing muscle or gland tissue.

Heterologous tumors may vary atypically in form, number, or arrangement of the cells. When the cells start from cylindrical epithelium and become irregular in shape, or from squamous epithelia, and lose this character, the variation is in the form of the cells. When the cells of a malignant tumor break through the *membrana propria* and grow into the connective tissue in an atypical place the variation is in the arrangement of the cells. When a connective-tissue tumor shows persistent cell proliferation far beyond the normal cell richness of the part, so that the picture is more nearly that of embryonal connective tissue, the variation is in the number of the cells. At times the heterologous growths vary in more than one of these directions.

Like other tissues, the neoplastic suffer regressive changes, but such metamorphosis seldom leads to the disappearance of the tumor. The

commonest of these changes are necrosis, fatty and hyaline degeneration, pigmentation, and calcification, while many tumors ulcerate, with putrid secretions.

According to the variety and energy of growth, recurrence, and metastasis we decide the practical question of a tumor's *malignancy*.

Benign tumors mechanically push aside the surrounding tissues and remain distinct from them; *malignant* growths infiltrate and destroy them. Extirpation of the latter is very difficult, for they permeate the vicinity in all directions, and bits of these processes may be left to cause a continuous recurrence. The growth-energy of a tumor coincides with its richness in cells, and hence the prognosis depends on the same feature. The richer a tumor is in cells the softer it usually is, and from its cut surface a fluid can be scraped, made up of fluid and cells. Soft tumors allow particles to break off and be carried elsewhere. Heterotopous tumors are malignant in so far as they invade tissues foreign to them. The worst effects of tumors are included under metastasis, for thus distant parts or perhaps the whole body may be invaded. When the tumor grows from adjacent nodes after extirpation of the primary, this is called recurrence by transplantation.

Many tumors have an apparent effect upon the general health, weakening it by taking its fluids for nourishment, as a parasite may. Tumors of the alimentary canal may lead to diminution or cessation of the supply of nourishment. If combined with ulceration and foul secretions, resorption symptoms may result. Thus in various ways a *cachexia* may arise.

The internal peculiarities of tumors, which presuppose an internal disposition and can not depend upon outside influences, make a third variety of recurrence possible. When, in spite of complete removal of a tumor from its site of development, after a period of time a new and similar tumor forms, without portions of the primary one being left in the scar, and hence only the local disposition to tumor formation has persisted, the new-growth illustrates regional recurrence.

All the expressions of malignancy appear earlier if the growth of the tumor is rapid, if the vicinity is involved, and if lymph nodes are attacked. As a rule, malignancy belongs to the heterologous neoplasms.

Beside the cachexia and the possible sepsis from ulceration, we must consider the reaction of the different organs and the disturbance of their functions. Tumors of the brain in all circumstances are of bad prognosis from their situation; those of the stomach interfere with

nutrition. Many tumors have a specially pronounced malignancy, as the pigmented sarcomata. Similar tumors vary in different places. Adenoma of the mucous membranes acts differently from adenoma of the large glands, because the former leads so often to carcinoma; and certain giant-celled sarcomas of the jaws (epulis) are usually benign, though elsewhere the same tumor may be malignant.

As members of the progressive group of lesions, tumors form the highest grade of the series, which includes chronic inflammations with persistent cell multiplication, and the idiopathic hyperplasias, like lipomatosis, with atrophy of other tissues (p. 103). The *characteristic qualities* which distinguish tumors are mainly two. In the first place, *the cells alter their form* and lose their normal characters more or less completely, so that they cannot be recognized as derivatives of special differentiated tissues. Thus a return to a more primitive type is seen when flat or cylindrical epithelia make the atypical cells of carcinoma, or cartilage cells become sarcomatous. Secondly, *the cells alter their nature* so much that they may penetrate tissues of other structures and increase in them, and thus epithelia may be found in connective tissue. This change in form or loss of differentiation, and the increased independence of the cells, are summed up by Hanse-mann in the term *anaplasia*.

The *etiology* of tumors is one of the darkest points in pathology, for the hypothesis of anaplasia does not explain why in a given case the altered cells develop into a tumor. Certain tumors are related to chronic irritations. Transitions between hyperplastic and inflammatory growths and tumors occur, and it may be difficult to say to which of the three a new formation belongs, as with many papillomata, condylomata, polypoid growths on mucous membranes, hyperplasias of lymphadenoid tissues, and others. Certain tumors—as, for instance, many carcinomata of mucous membranes—follow ulceration, and hence bear a relation to chronic external irritations.

The long-continued local effects of paraffin vapors, tar, and soot may lead to cancerous tumors of the skin, and a stage of chronic inflammation may precede them. Carcinoma shows a preference for certain parts which are exposed to mechanical injuries, as the breast, the penis with phimosis, the uterus (which is involved more in multipara than in nullipara), and the intestine at flexures in which feces may accumulate.

Such observations lead to the theory of irritation, which explains neoplasms as the result of stimuli whose exact nature is unknown.

The fact that in a tumor but one kind of tissue cells often predominates has led to the assumption of a preponderance of one over the other, and especially for carcinoma this loss of balance between tissues has been held to explain the growth. Thiersch's idea is that with the increase of age the epithelial tissues preponderate over the connective, and hence carcinoma is a disease of advanced life, because the epithelial cells conquer in the border warfare.

Congenital tumors and their appearance in organs which normally never contain their elements, as with rhabdomyoma in the kidney and chondroma in the testis and parotid, suggest the theory that such tumors are due to scattered portions of embryonal tissues which later on develop to heterotopous growths (Cohnheim's theory of fetal inclusions). Such cases can hardly be explained otherwise. Scattered remnants of adrenal tissue are fairly common in the kidney, and heredity speaks for the same view; but the supposition does not apply generally. Histogenesis, as with most carcinomas, contradicts it, for these tumors start in normal pre-existent epithelium. Moreover, it is not clear why a scattered embryonal remnant should suddenly take on the formation of a neoplasm in some cases and in others remain quiet during the entire life of the individual.

Tumors may be classified according to the tissue elements of which their cells are derivatives, and thus we obtain the four chief groups—tumors of connective tissue, tumors of nerve tissue, tumors of muscle tissue, and tumors of epithelial tissue.

This division is easily carried out for the homologous neoplasms, but for the heterologous there are difficulties, for they depart so much from the structure of the original tissue that their histogenesis is often hard to determine, while different tissues may produce similar tumors and morphological transitions are not uncommon.

The developmental principle is unsatisfactory as a plan of classification. The supposition that epithelial tumors occur from tissues derived from the outer or inner embryonal layer, and muscle and connective-tissue tumors from derivatives of the middle layer, leads to error. We know now that true epithelium, and hence its tumors, may develop from the middle layer, and that the external layer makes not only epithelium, but also the nervous tissues and their supporting glia. Hence the developmental plan would lead to classifying heterogeneous tumors together, as carcinoma and glioma, and also separate those of similar structure, as carcinoma of the mucous membranes from the same tumor of the kidney.

In all tumors there is a certain amount of connective-tissue stroma which carries the vessels. Tumors which consist of connective tissue thus appear to contain but one kind of tissue, and are called *histoid* tumors. When the chief element present is muscle or bone the stroma is more evident. In the epithelial tumors the connective tissue is most plainly distinguished, and hence this is called the stroma, and the cells make up the tumor parenchyma. Such tumors are called *organoid*.

Beside the true proliferation tumors there are those due to *dilatation* and *retention*, and among the congenital tumors there are those which contain several kinds of tissue, or even organs, such as skin, hair, teeth, and portions of nerve and muscle. These are termed *teratomata*. (See Chapter IV.)

A. HOMOLOGOUS TUMORS

I. Connective-tissue Tumors.

1. **Fibroma.** In its structure fibroma resembles other fibrous connective tissue, but presents many differences in its finer composition. Though always made of fibres, these may be loosely arranged, with wide spaces between, filled with serum or closely packed and with no apparent finer fibrillation. The former are called soft fibromas and the latter hard (p. 69). The cells are like those of connective tissue, but more numerous. Usually they are narrow and fusiform or linear, with a single nucleus and only a trace of protoplasm. Often there are larger cells, like those of granulation tissue, with more protoplasm (p. 87), and here and there are spaces filled with similar cells, which are probably endothelial. Collections of lymphoid cells are not uncommon, as also in ordinary connective tissue.

Dense fibromas are glistening and smooth on section, and have a fibrous structure of white or yellowish-white color. The soft fibromas often appear edematous and swollen, almost gelatinous and succulent. The tumor may be sharply marked off from the surrounding tissues or more infiltrating, and it grows by crowding other structures aside.

Fibroma occurs in many forms, which may be mentioned singly, as they are found with other tumors.

1. *Tuberous*, commonest; circumscribed nodular, inlaid, or projecting, as in skin, breast, and uterus.

2. *Polypoid*, round or long, pedicled; common on mucous membranes, as of nose and larynx; made up of mucous tissue, and called mucous polyps, or of gland tissue (see Adenoma); polypoid myomata occur in the uterus.

3. *Warts*, verrucæ and papillomata (see below).
4. *Diffuse*, without sharp edges, taking in large areas, as in elephantiasis, or affecting the fibrous tissue of a whole region as a fibromatosis, causing atrophy of parenchyma, as in breast and ovary.

FIG. 62.

Fibroma of the ovary. $\times 230$.

5. *Keloid*, linear, flat, or projecting, smooth or slightly uneven, on the skin and often starting in scars. Microscopically presents closely packed bundles of fibrous tissue, often hyaline, with but few cells.

6. *Plexiform*, from the connective-tissue parts of peripheral nerves, making long stretches or nodules of thickening; plexiform and cirroid neuromata.

7. *Fibroma* with cyst formation; by softening of tissue or dilatation of pre-formed or new gland spaces. (See Cystadenoma.)

8. *Combinations* of fibroma with many other tumors—chondrofibromata, osteofibromata, and myofibromata. Regressive changes also occur—softening, fatty changes, cysts, and calcification.

2. **Myxoma** corresponds to mucoid tissue, and contains stellate cells with processes (Fig. 63) in a mucinous

FIG 63.

Myxoma. $\times 250$.

ground substance. On section the greater part of the mucin is precipitated as fibrils between the cells. Macroscopically it is glistening, elastic, and gelatinous. It may be round or lobulated, and is found in the skin, marrow, breast, peripheral nerves, brain, and elsewhere. It is benign, and is often combined with fibroma, lipoma, chondroma, and sarcoma.

3. **Lipoma** consists of fat, is round or lobulated, often with a fibrous capsule which marks out lobes on the section. Such tumors are circumscribed, and occur in connective tissue of the back, neck, thighs, axilla, less often in joints, the peritoneum, and other sites. The size may be large. They are benign. When polypoid they are called lipoma pendulum. Often combined with fibroma, chondroma, and angioma; calcification fairly common.

4. **Chondroma** is a new formation of cartilage (Fig. 75), and may resemble hyaline, reticular, or fibrous cartilage. The cells often lose their capsules and take on a spindle or star form. Connective-tissue septa are always present on section and carry the vessels. Chondroma may be of large size, and start from cartilage, connective tissue, or bone; but are also found as heterotopous growths in parotid and testis, and then are considered as due to portions of mislaid embryonal tissue. Mucous degeneration, making myxochondroma, calcification, softening, and ossification, occurs.

5. **Osteoma**. Tumors of bone are either inflammatory or hyperplastic, and the two forms are not always easily separated. They are made of spongy or hard bone, and start in the periosteum, bone marrow, cartilage, and connective tissue. In many regions their growth is slow and their nature benign. (See Chapter VII.) Combined as osteochondroma, fibroma, and sarcoma.

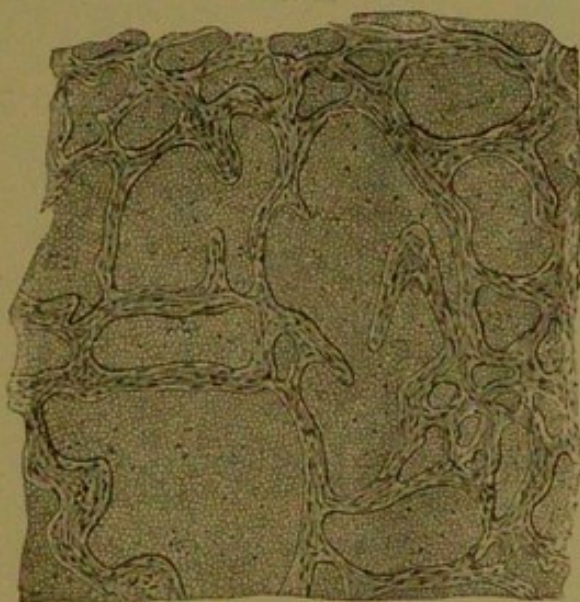
6. **Angioma and Lymphangioma**. These are tumors due to the new-growth of blood or lymph vessels; and since many are formed by dilatation of pre-existent vessels, they are not strictly tumors. The distinction between dilated and newly formed channels is not always practicable. Excluded from such tumors are varicose, cirroid, and racemose aneurisms. (See Part II., Diseases of Vessels.) Other forms are telangiectatic and cavernous angiomata.

Telangiectatic angiomata consist of wide and numerous capillaries, whose walls at first are thickened, and later stretched by dilatation; they may be arranged in a tangle, and then make a plexiform angioma. They occur as vascular nevi in flat, red spots in the skin, or warty projections. In the latter the hair and glands are increased (p. 152).

Nevi often spread over greater surfaces. Found especially on the skin of the head and neck and mucous surface of the lips. Often combined with fibrous, fatty, and sarcomatous growths.

Cavernous angioma (Fig. 64) is formed by closely packed and freely communicating blood spaces lined with endothelia and surrounded with fibrous tissue, like cavernous tissue in the penis. They are dark red, round or wedge-shaped, sharply marked off from other tissue, and reticular on section. They occur in the liver, spleen, kidney, bone, fibrous and fatty tissue of the orbit, and brain. If on a surface they may project, and after section they collapse. Occasionally they are erectile.

FIG. 64.



Cavernous angioma of the liver. $\times 40$.

Lymphangioma occurs in different forms. As a telangiectasis it occurs in the tongue or lip as a congenital anomaly, forming macroglossia or macrocheilia. Here it may contain cysts. On the skin it belongs with elephantiasis, affecting the scrotum, labia, and thighs. Sometimes such dilatations may be explained by lymph stasis (p. 102). Large dilatations may form hygromatous cysts, unilocular or multilocular, with clear or milky fluid contents mixed with cholesterin and detritus. These cysts, lined with endothelium, may occur in the neck congenitally.

7. Lymphoma and Myeloma. Lymphoid tissues and bone marrow undergo a series of progressive changes which are partly hyperplastic and inflammatory and partly like true tumors, but presenting such frequent transition forms that they constitute an almost unbroken series. Apart from acute and chronic inflammation with hyperplasia

(see Chapter VIII.), there are enlargements of one or a number of nodes which are simple lymphadenomata or lymphomata.

Malignant lymphoma resembles the benign form in its histology. Chronic hyperplasia and induration of the lymph tissue are found, but with this there is a tendency to involve continuously new groups of nodes, and after removal of the tumor recurrence is common. Fibrous induration, which often occurs, does not stop the process. The entire lymph system may at last become involved, and also the lymphoid tissue of the spleen and gut and the scattered follicles in the lungs.

With the appearance of such malignant lymphomata the blood is apt to undergo a peculiar change, but its exact relation to the tumors is not known. The blood changes are like those in leukemia, and hence leukemic and aleukemic lymphomata are recognized; the latter are called *pseudoleukemia*, *adenia*, or *Hodgkin's disease*.

These multiple hyperplasias of the lymph system vary toward true tumor formation in two directions. They may involve not only the nodes, but their capsules also, perforating them and invading the vicinity. In the second place they make similar nodules by metastasis in the liver, brain, and kidney, or diffuse lymphoid infiltrations in these organs. There are thus true metastases from primary tumors to organs which normally contain no lymphoid tissues. Such tumors are called lymphosarcomata.

The chief points of departure for lymphomas are the nodes, the thymus, and the intestinal follicles.

Changes are observed in the bone marrow analogous to the tumor formation. In leukemia, and often apart from blood lesions, there are hyperplasias which in certain circumstances take on the characters of tumors, pushing out the bony walls, with thinning and perforation, and then infiltrating the periosteum and adjacent tissues (myeloma, myelosarcoma). (See Chapter XIII.)

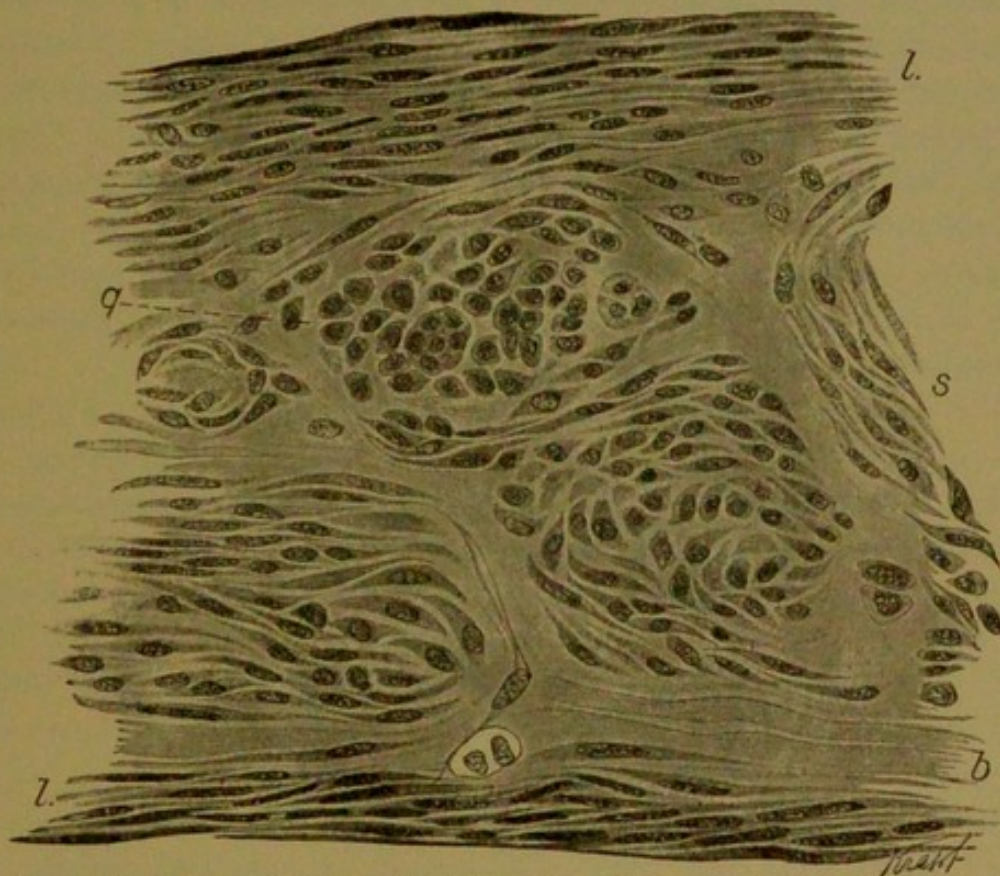
II. Tumors of Muscle Tissue.

These are divided into the leiomyomata and the rhabdomyomata.

Leiomyoma, or simply **myoma**, is a tumor made of smooth muscle fibres, making sharply limited dense tumors like fibromata, often lobulated and bounded by a capsule. They are dry, gray or whitish-red on section, and their composition of interlacing muscle bundles is apparent in the gross. Microscopically they are quickly distinguished

from fibroma. Instead of the single fibres irregularly disposed, there is a regular arrangement of fibres in bundles, with long, usually parallel and regularly spaced nuclei. The nuclei of fibroma are more spindle-shaped and less regularly placed. Characteristic appearances of cross-sections of muscle bundles are met with as polygonal spaces in which the long nucleus occurs as a round cross-section. (Fig. 65, *q*.) As the nuclei are not all at the same level, the section does not give one to each fibre. Focal necrosis, hyaline, calcareous, and

FIG. 65.



Myoma of the uterus. *l.* Fibres cut longitudinally. *q.* Cross-section of fibres. *b.* Necrotic fibres. $\times 500$.

softening changes are common in myomata. With a large proportion of connective tissue the tumor is called fibromyoma. At times the tumor may separate spontaneously and be cast off. The tumor is benign; in size it may be as large as a fist, and may produce local disturbances; combines with sarcoma, myxosarcoma, or changes into these. Common in the uterus, less so in the alimentary tract.

In many uterine myomata there is gland proliferation, which may come from portions of the Wolffian or Müllerian ducts which have been included (adenomyoma).

Rhabdomyoma is an unusual tumor, made of striated fibres. In many cases it combines as a myosarcoma, and the latter is the chief element, so that muscle fibres are found only here and there. This form occurs in the heart, kidney, bladder, uterus, testis, and sometimes in the ovary. It is often heterotopous.

III. Epithelial Tumors.

This name is given to tumors in which the proliferation of epithelia is the essential element; but epithelia by themselves never form tumors, so that in all a certain amount of connective tissue is to be found which carries the vessels and secures the nutrition of the tumor. Homologous tumors of this kind include those involving superficial epithelium and those involving glandular epithelium.

1. **Tumors Involving Superficial Epithelium.** These neoplasms include a number of small growths which appear on the skin or mucous surfaces, either entirely made up of connective tissue—the epithelium only elevated and not hyperplastic—or similar tumors in which the epithelium shows marked proliferation.

The *wart*, or *verruca*, of the skin is one such tumor. At times this is a pure fibroma, of slight and smooth or uneven projection, as is true of most congenital warts (*nævus verrucosus*). The pigmented nevus contains much coloring-matter, and is either flat or elevated. The hairy mole (*nævus pilosus*) and the birthmark (*nævus vasculosus*) are other forms.

These warts contain irregular nests and strands of large cells, which are probably endothelia, and when pigmented these cells contain the pigment.

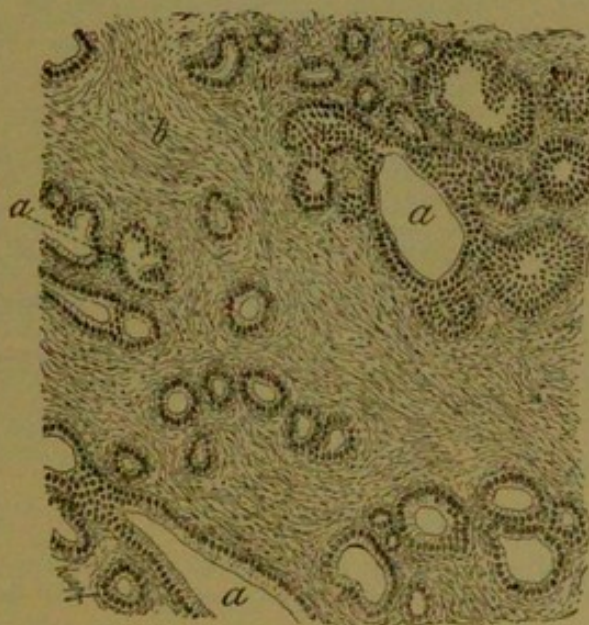
Many of the ordinary hard warts present hyperplastic papillæ, either with dilated ends, and hence club-shaped, or long and narrow and branching; these tumors are called *papillomata*. Their gross appearance depends on the form of the enlarged papillæ and also on the thickened layer of epithelial cells over them. The broader warts are of uneven surface; the forms with lengthened papillæ are smooth or full of fine crevices, in which the epithelial cells lie; or the crevices may penetrate the surface, so that the tumor looks as if covered with countless filiform projections.

On section both papillæ and cells may occur separate from their proper relations, and it is important to distinguish such cell nests from those of carcinoma by the fact that they never lie beneath the level of the epithelium.

Similar tumors of mucous membranes occur. *Acuminate condyloma* is a form connected with inflammation. (Fig. 59.) Larger tumors with long papillæ make *cauliflower growths*, as in the bladder, where the branching, twig-like papillæ may break off and escape with the urine. In the enlarged papillæ are many large vessels, and the epithelia may be much proliferated in many layers of transitional cells, as normally occurs in the urinary passages. These tumors may cause severe bleeding.

2. Tumors Involving Gland Epithelium: Adenomata. An adenoma is a homologous tumor containing glands which differ from the normal type by their irregular form and arrangement, but yet preserve the glandular structure and have a distinct lumen in their ducts. (Fig. 66, *a*.) Between the gland there is more or less fibrous stroma (*b*).

FIG. 66.



Adenoma of the breast. *a*. Glands with regular epithelia and clear lumen. *b*. Stroma. $\times 250$.

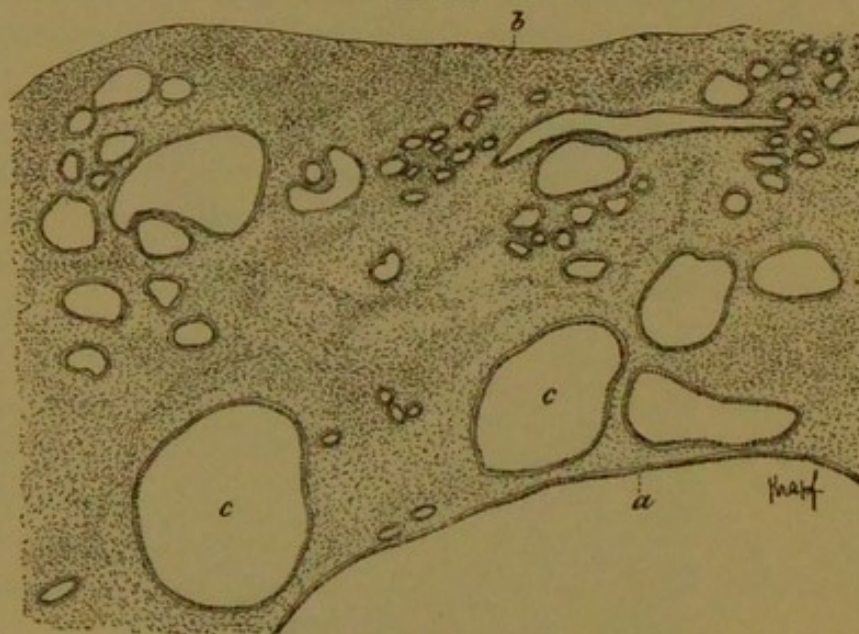
Adenoma of the skin may start in sebaceous glands, making *adenoma sebaceum*, or from sweat glands—*adenoma sudoriparum*—and both are unusual. They develop in the subcutaneous tissues, and may reach the size of a pigeon's egg.

Adenomata of the mucous membranes are common, especially in the alimentary canal and the uterus. They may be but little elevated, and merge imperceptibly into inflammatory hyperplasia (p. 123), or they are polypoid, with slender pedicles. The pedicle is usually made of submucosa drawn out from the site of the polyp's attachment. The glands in the tumor are apt to be dilated, branched, and irregular.

In the large glands, breast, liver, kidney, etc., adenomata occur as included nodules which present atypical glands that retain nothing of the acinous or tubular form. The more they preserve these characters the easier it is to recognize tubular and acinous forms. They are encapsulated or sharply marked off from the rest of the tissue. The epithelial investment is always regular, though it may exhibit many layers.

Many adenomata reach a large size, and their glands become cystic by retention of secretion after occlusion of the ducts or by rapid proliferation of the epithelial cells. Such forms are common in the follicles of the ovary. The *cystadenomata*, in spite of their size, do

FIG. 67.



Glandular ovarian cystadenoma. Section from the wall of a large cyst. *a*. Inner side with cylindrical epithelium. *b*. Outer side. *c*. Small cysts in the wall of the large one. $\times 40$.

not recur after removal, or make metastases. The contents of the cysts may be mucous, gelatinous, colloid, or thin and serous; paralbumin is constantly present (p. 63). With multilocular cysts of this kind the septa may atrophy, making large cavities, with projections on their walls which mark the site of septa. Two varieties are recognized—the glandular and the papillary.

In the glandular form there are observed on the internal surface, covered with cylindrical epithelium, small depressions, which increase in depth, constrict at the neck, and so make daughter cysts, which then widen out. These may also form new cysts from their walls. Hence multiple nodular groups of such cysts may be developed which

contain 40 to 50 kilogrammes of fluid. These are called *myxoid cystomas*. In the papillary form (Fig. 68) there is a proliferation of the investing epithelium, and a series of papillary, branching, tree-like projections reach into the cavity of the cyst. These contain vessels, are covered with epithelium, and by their growth and multiplication may entirely fill the cavity; then they perforate the wall and appear externally. The two forms may be combined. The papillary have more tendency toward malignancy, and attack the vicinity and make metastases (cancerous transformation).

FIG. 68.



Cystadenoma papilliferum of the ovary. p. Papilloma of the outer surface. a. Wall of cyst. $\times 50$.

The so-called polypous cystomas present papillary growths of the outer surface.

Combinations of adenoma and connective-tissue tumors are common.

Fibro-adenoma implies excess of stroma.

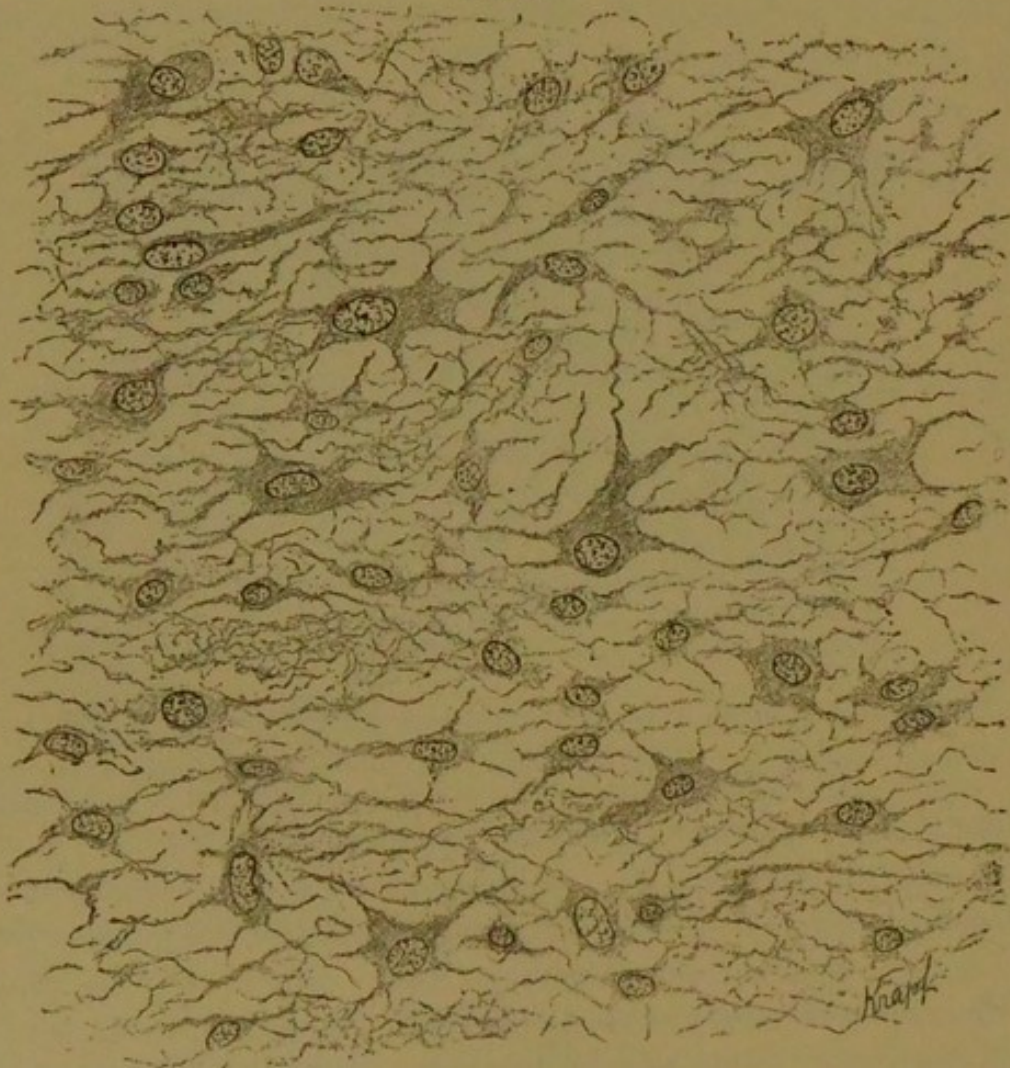
In the lumina there may be papillary outgrowths which lose their epithelium. The stroma in other cases becomes myxomatous, and hence arise myxadenoma and adenosarcoma. Lastly, adenomas may occur as heterotopous growths, as when tumors with the structure of the adrenal are found in the kidney, where they arise from aberrant portions of adrenal tissue, *struma lipomatodes aberrans renis* (Grawitz). They may be malignant and give metastases.

IV. Tumors of Nerve Tissue.

These tumors contain nerve fibres and ganglion cells, or they start from the fibrous elements of nervous tissue, the neuroglia. Among the former, those which imply a new formation of ganglion cells—ganglio-neuroma—are very rare; they occur with a slight increase of glia in different parts of the nervous system.

Glioma is the name of a tumor formed from glia tissue, and especially from glia cells. They are nodular or lobulated, and in the cord

FIG. 69.



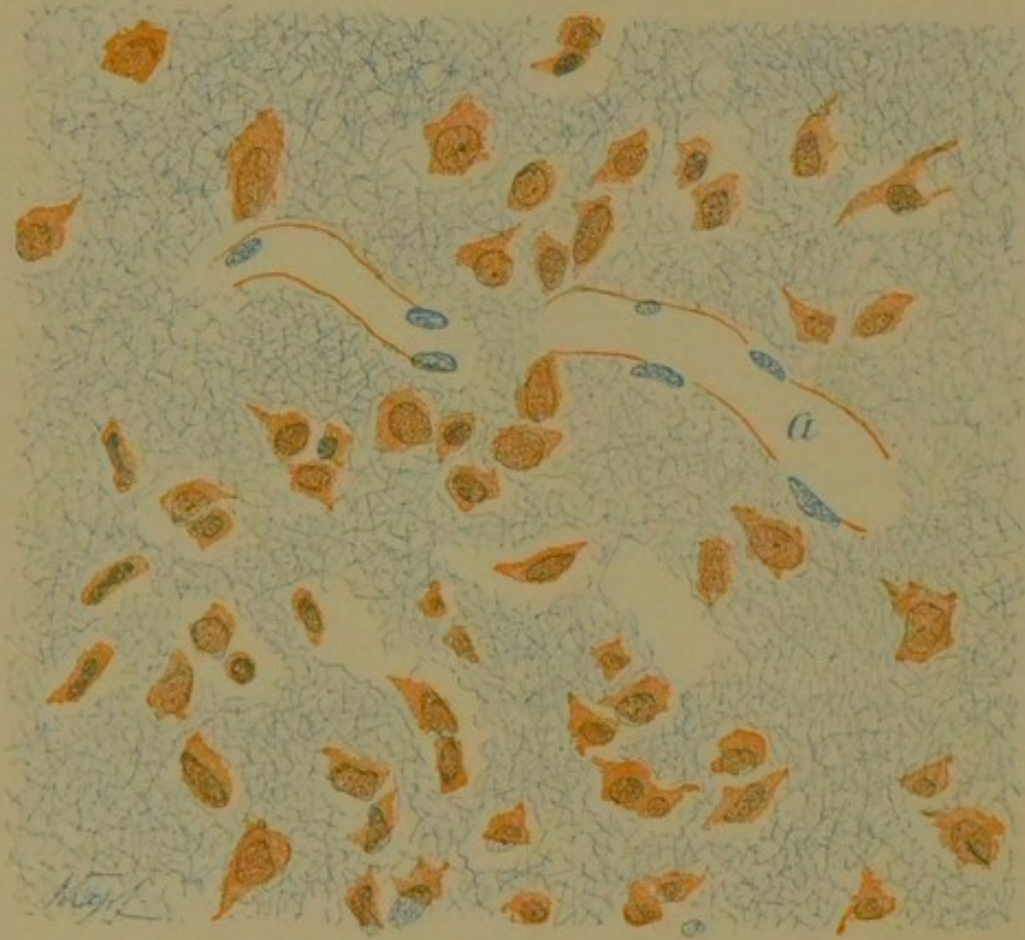
Glioma with stellate cells, their processes forming part of the fibrous elements. Stain, alum cochineal. $\times 500$.

run longitudinally. The tumor is usually denser than the normal tissue, but on section it is, as a rule, medullary, and swells up over the cut edge. Gliomata usually take origin from the gray substance, but penetrate the white later on as a local infiltration, so that the



PLATE XI.

FIG. 70.



Glioma. The cells without processes, the glia fibres differentiated from the cells. Weigert's glia stain. $\times 500$.

tumor has no clear limits. The pia is almost never invaded, but it may be pushed before the tumor. Many of these gliomas have a rich vascular supply, and in the gross there may be large, cavernous dilatations and hemorrhages into the tissue.

A further peculiarity of many gliomata is the tendency to regressive changes, either yellow and caseous or as softening of the substance and fluidification.

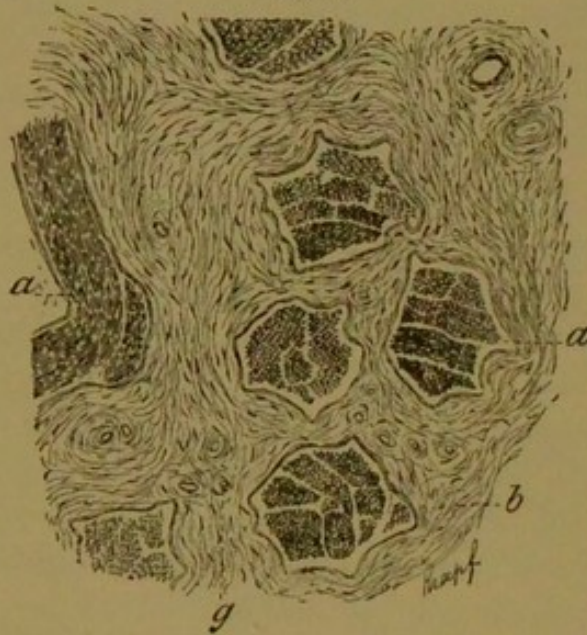
Microscopically a glioma consists of numerous cells and some fibrillary ground substance; but there are great variations in number, form, and arrangement of the elements. Some gliomas contain cells which are embryonal, like sarcoma cells; there may be astrocytes or spider cells with processes running out into the surrounding tissue. In the fibrous portion of the tumor may be distinguished large polynuclear or even giant cells, very small cells, some with long, bristle-like processes, and others with few and short ones. (Figs. 69, 70.)

In other gliomas the spider cells are absent or scanty. The cells are then round, without processes, having but little protoplasm and an eccentric nucleus; or the protoplasm may be reduced to a small remnant on the side of the nucleus or be apparently absent. These cells apparently have given their protoplasm to the construction of the ground substance. The latter is copious and finely fibrillated in some of these tumors, like ordinary glia (Fig. 70); we may perhaps connect them with sarcoma of connective tissue. Other gliomas have but few glia fibres or none at all, presenting instead an undifferentiated granular or homogeneous mass in which the nuclei are closely strown. This appearance of having no ground substance may depend upon hardening methods, which in material from the cadaver do not always preserve the delicate glia tissue either normal or degenerated; but in quickly growing tumors there may be no formation of intercellular substance, and the appearance is given of a tumor made wholly of cells. These tumors are the sarcomata of nerve tissue, and correspond to the same neoplasm in fibrous tissue. Like sarcoma, such a tumor infiltrates the vicinity, and beside permeating and supplanting it may cause an irritation which leads to proliferation of glia cells and growth of the tumor by both infiltration and apposition.

Combinations of glioma with fibroma, myoma, and sarcoma are frequent, and many of these have an angiomatous element; while hemorrhages, cysts, and softening are common. Glioma and mixed forms occur in the central nervous organs, the retina, and the optic nerve.

Peripheral nerves present both neuromata and fibromata. The latter start in either the perineurium or the endoneurium. Tumors of nerves, after amputation especially, consist of nerve fibres (Fig. 71), and appear as nodular swellings of the stumps of the nerves. They may grow into the scar and make plexiform groups. Occasionally there are multiple fibroneuromata, especially at points of branching along the nerves (p. 147), containing new medullated or non-medullated fibres. Myxoneuroma and neurosarcoma are combinations of neuroma with such tumors of the nerve stroma.

FIG. 71.



Amputation neuroma. *a*. Bundles of medullated fibres cut partly lengthwise and partly crosswise. *b*. Fibrous tissue. *g*. Vessels. $\times 40$.

B. HETEROLOGOUS TUMORS.

1. Sarcoma.

Sarcomata are heterologous tumors of connective tissue, and they may take origin from any tissue of the group—mucous, fatty, osseous, cartilaginous, bone marrow, and endothelium. Contrasted with tumors of the homologous division, sarcomata are peculiar in the numbers of the contained cells, the stroma being relatively at a minimum. On this account sarcoma has often been compared with the embryonal form of connective tissue, which is marked, as are the tumors, by a rich supply of vessels.

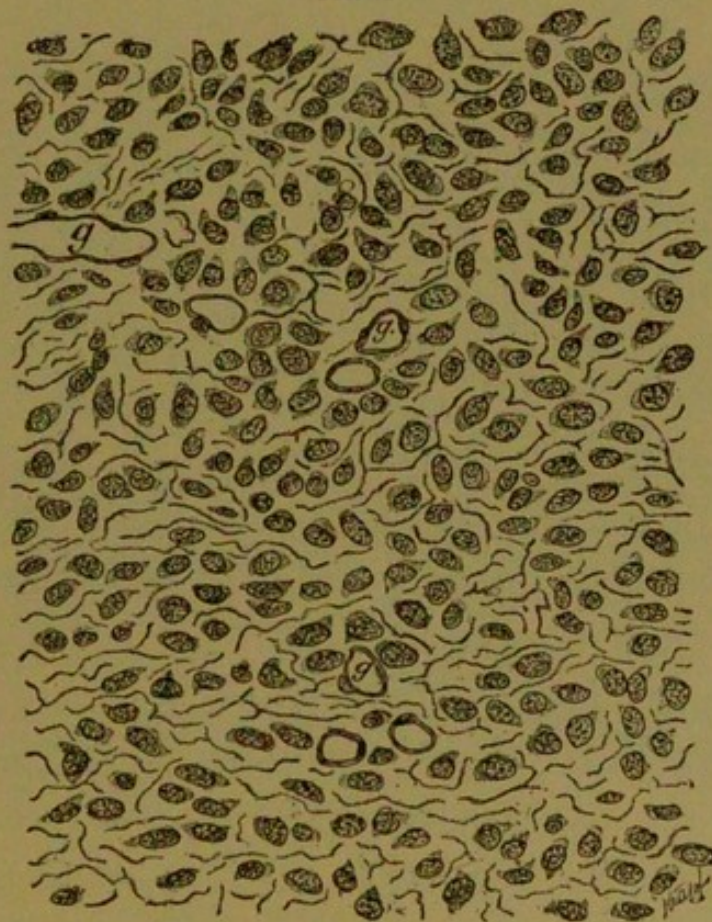
In their forms the cells of sarcoma vary greatly from those of developed connective tissue, but all the forms occur which we have

discussed in connection with granulation tissue (p. 87), namely, small and large round cells, spindle, stellate, and giant cells.

The ground substance of sarcomas is found in varying quantities. It may be so scant that the tumor appears made up entirely of cells, or between the cells there may be a fibrous element; and, lastly, there is often a large proportion of fibrous stroma, irregular in arrangement or reticular. (Fig. 72.)

An important element in these tumors is the free vascular supply. In young and rapidly growing tumors the cells appear distinctly related

FIG. 72.



Round-celled sarcoma. Between the cells there is a fine fibrous reticulum. $\times 350$.

to the new bloodvessels. Such vessels usually have a very thin wall, which is not made up of different layers, but is formed from endothelial cells which lie directly upon the sarcoma cells.

The gross appearances of sarcomata differ widely. They may be circumscribed inclusions, especially when dense, or very malignant infiltrations without clear definition. They may be soft, grayish-red, or whitish, and on scraping the section a turbid fluid may be obtained.

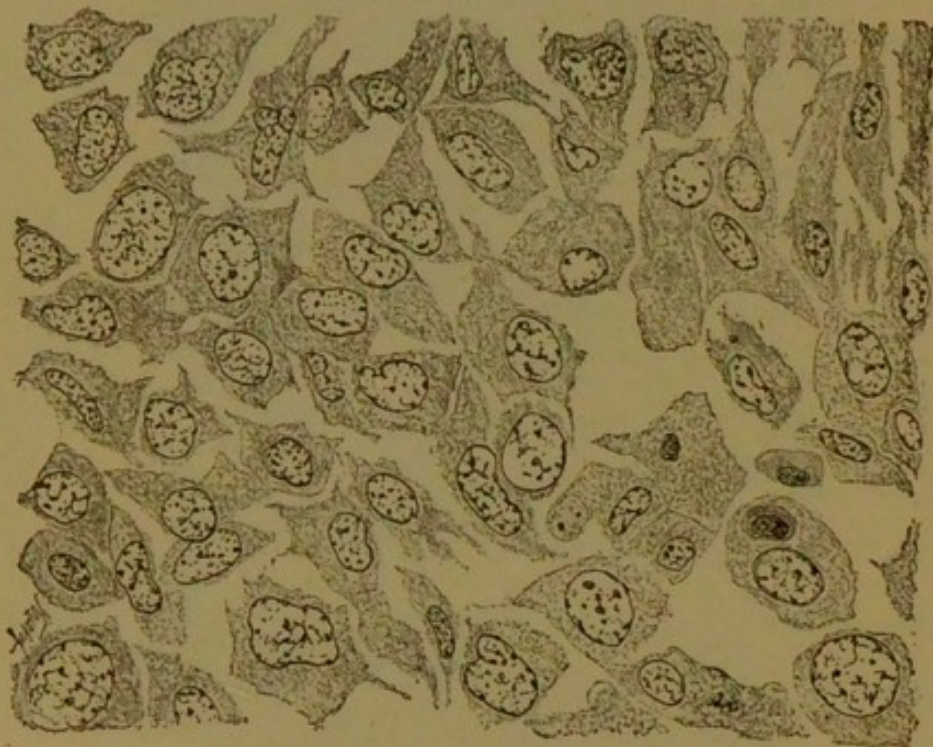
These tumors take their name from their resemblance to flesh. The

denser tumors, in which there are fewer cells, are relatively benign; the softer and cellular very malignant. The latter infiltrate and hence recur, and make metastases by way of the blood channels. As a rule, the metastases are later than with most carcinomas.

The manifold forms of sarcomata are dependent chiefly on the number of the cells and the structure of the fibrous portion and their relation to one another. We distinguish:

1. **Round-celled sarcoma**, made up of small or large cells, approximately round, but as a rule very irregular, between which there is a small amount of intercellular substance. (Fig. 72.) The stroma is

FIG. 73.

Large-celled sarcoma. $\times 350$.

often reticular. The small-celled are very rapid and malignant in growth, especially attacking muscle, bone, brain, and mucous membranes.

Lymphosarcomata, starting in the lymph nodes, belong to the small round-celled variety; they result from proliferation of lymphoid tissue, and differ from malignant hyperplasias in not remaining confined to the nodes, but destroying the other tissues (p. 150).

In a similar way sarcoma containing round cells may develop from marrow (myeloma). It perforates the bone and attacks neighboring tissues. The structure of marrow may partially persist, as marrow cells, fat cells, giant cells, and reticular stroma.

2. **Spindle-celled sarcoma** (Fig. 74) consists of small or large spindle- or star-shaped cells, often arranged side by side in bundles. They may lie close together and make up the whole tumor, or between them may be cell processes which make a fine fibrous tissue. Teased preparations show the cells better than sections. The cells may be large and irregular, at times round, with a single large vesicular nucleus, so that they strongly resemble the epithelioid cells of carcinoma. (Fig. 73.) In such a case the diagnosis depends not only on the cell,

FIG. 74.

Spindle-celled sarcoma with giant cells. $\times 350$.

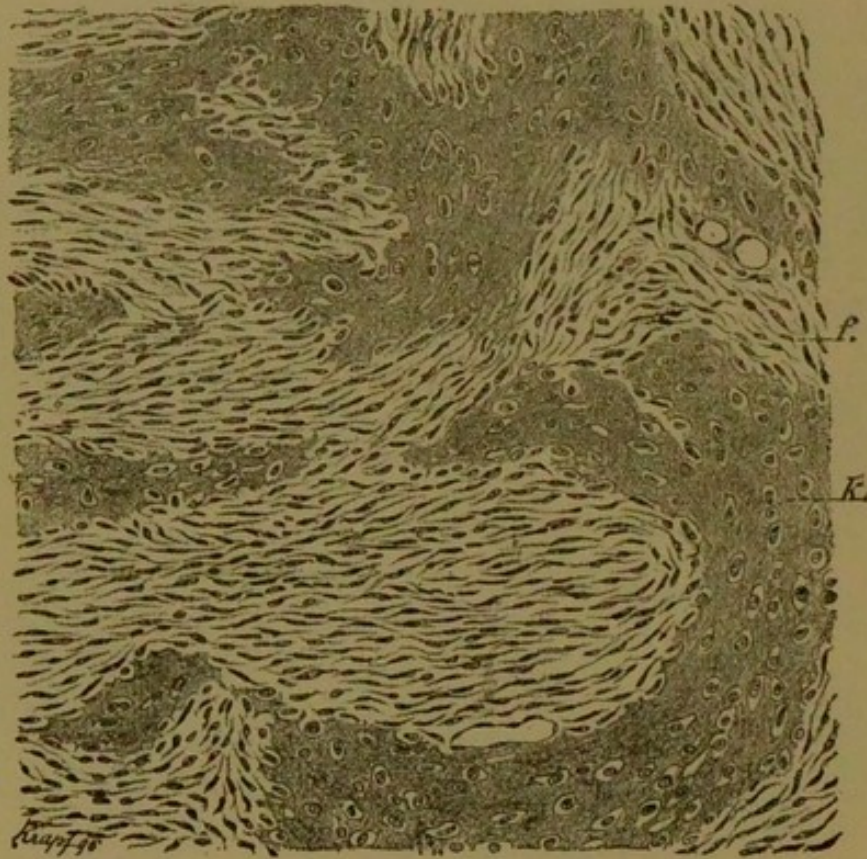
but also on the entire arrangement of the tumor and the relation between cells and stroma. Spindle-celled tumors are the commonest sarcomas, and start in any connective tissue.

3. **Giant-celled sarcomas** never contain giant cells alone, but display these in numbers among other forms, usually spindles. The giant cells have many small nuclei or a single large and polymorphous nucleus (p. 88), and the cell body is irregular and has coarse or fine processes. These tumors develop especially from bone, periosteum, and medullary canal.

4. A sarcoma with well-developed stroma is called a **fibrosarcoma**. In structure and prognosis it stands midway between fibroma and sarcoma. It is usually dense, not clearly defined, and occurs in skin, muscle, dura mater, periosteum, and elsewhere. It differs from fibroma in its numerous cells; and these have, like all sarcoma cells, a more distinct protoplasm, while connective-tissue cells present little but linear or spindle shapes.

When sarcoma starts in mucous tissue it may contain mucin, or

FIG. 75.



Chondrosarcoma. *f.* Fibrous parts resembling fibrosarcoma. *k.* Cartilaginous portions. $\times 250$.

bone when forming from bony parts; and metaplastic changes also occur, as osseous tissue in a tumor from simple connective tissue (p. 83). The following may be mentioned as belonging to this variety:

1. *Myxosarcomas* contain stellate cells with connecting processes in a mucous ground substance. When mucoid tissue is arranged in strands and meshes through the tumor it is called a *cylindroma*. Myxosarcoma occurs in skin, subcutaneous, nervous, and marrow tissue, and the fibrous parts of nerves.

2. Cartilage may appear in large or small masses in sarcoma, usually of the spindle-celled variety, and the cartilage cells lie in spaces more or less completely encapsulated. The tumor is called a *chondrosarcoma*. It arises from cartilage, periosteum, bone, and as a heterotopous growth, as in the parotid. The cartilage may calcify and become osseous.

3. When bony plates or trabeculae are found the tumor is an *osteosarcoma*, and its cells lie in spaces with dentated edges corresponding to bone corpuscles. Outside of a bony portion there may be either osteoclasts, round and polynuclear, which absorb the bone and make Howship's lacunae, or osteoblasts which make new bone. (See Chapter

FIG. 76.



Cylindroma. Hyaline strands, representing vessels and tissue about them, permeate the tumor. $\times 30$.

XIII., A.) When a sarcoma contains homogeneous osteoid tissue without deposits of lime in it, the term *osteoid sarcoma* is used.

Osteosarcomas are hence not sarcomas starting in bone, but such as contain new osseous tissue; they usually begin in the periosteum. All these various forms make combinations with other tumors or among themselves.

Sarcomas, in addition, may present peculiarities of cells and structure which differ from those named, and make differential diagnosis from other tumors difficult.

This is true of *alveolar sarcoma*, which, as a rule, has a scanty reticular stroma arranged in coarse meshes packed with cells, or in other places with a few fibres reaching between the cells. If this arrangement is noticed in many parts of the tumor it strongly resembles

carcinoma, and frequent morphological transitions to the latter occur (*sarcoma carcinomatodes*). These tumors may arise when endothelial cells enter largely into the formation of the tumor.

Another peculiarity arises from hyaline changes in the vessels of the tumor or the tissue about them, forming a cylindroma. The cut surface shows clear streaks in the lines of vessels, in places swollen, or radiating like the sticks of a fan, and the light parts may often be mucous. These tumors occur principally in the orbit, jaw, parotid, and dura. Those whose vessels are specially prominent, with the cells arranged upon them, are called *angiosarcomata*.

Other sarcomas have a telangiectatic character or are cavernous, so that they have a surface spotted with red, while hemorrhages and pigmentation are common in them. By softening in the tumor, cysts may be formed, sometimes of relatively large extent. The true *cysto-sarcomata*, however, arise from preformed lumina which dilate and are surrounded by sarcomatous tissue. Granulations in wounds are often accompanied by atypical proliferation of epithelial and glandular tissue; so the sarcomatous growth may lead to atypical gland multiplication, and occluded ducts may dilate to large cysts. When such a growth begins in the mass of a sarcoma and reaches a quasi-independent development of glands the tumor is called an *adenosarcoma*—a mixed epithelial and connective-tissue form.

Pigmented or *melanosarcoma* occurs especially in places where pigment is normal, as the choroid and the skin, in the latter often starting from congenital warts. Melanosarcoma often has an alveolar structure, and, as a rule, is very malignant (p. 77).

When certain cell groups or fibrous strands calcify the tumor is known as a *psammoma*, and is usually benign.

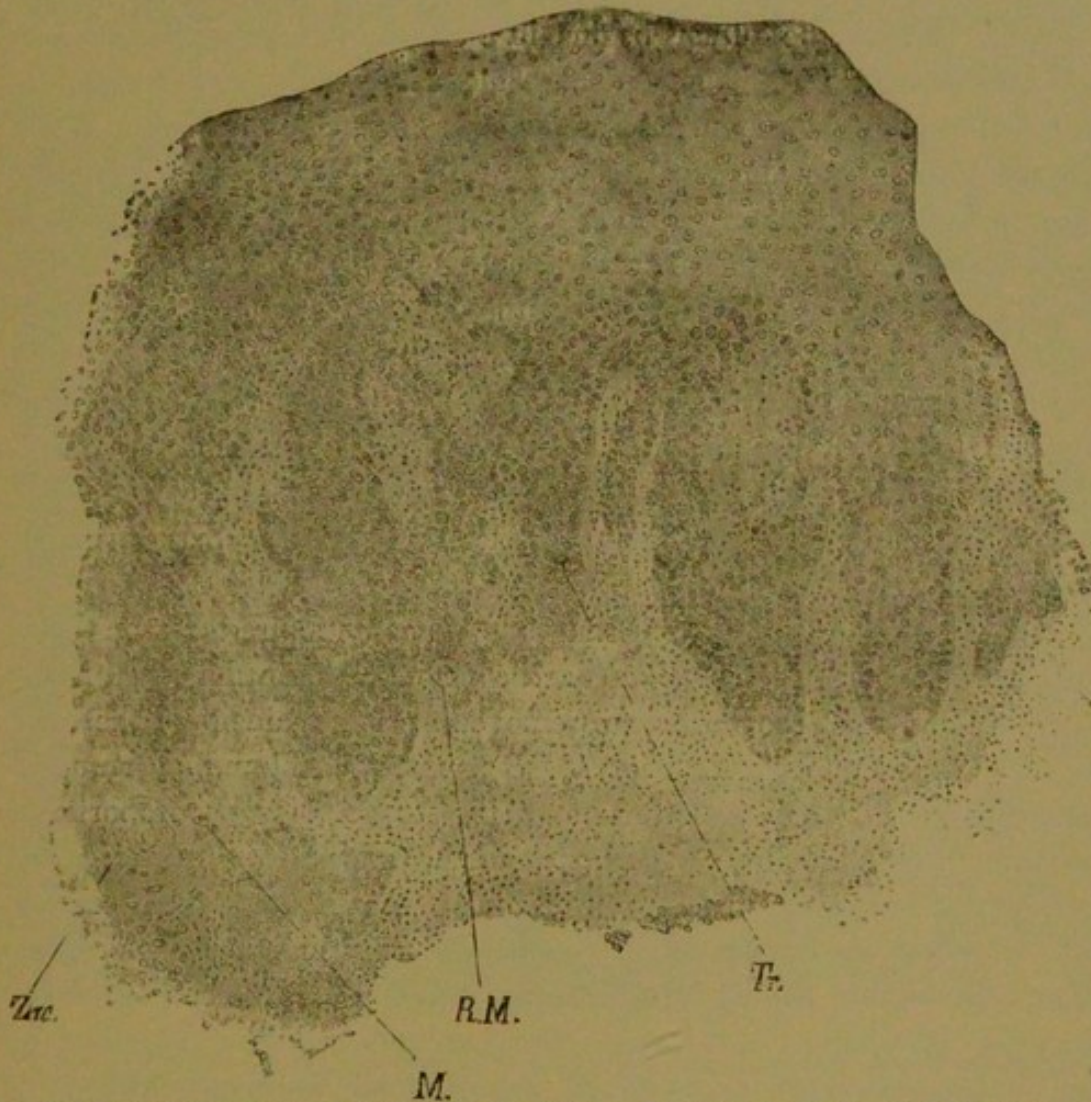
2. Carcinoma and Endothelioma.

Epithelia are cells in continuous layers which clothe surfaces and line spaces in the body. Between the cells there is never much intercellular substance, only a slightly developed agglutinating material. The numerous cells included under this definition are not equivalents of each other, for some, like the epithelia of blood and lymph vessels, are derived from connective tissue, and this relationship is expressed in many tumors starting from them. Hence the signification of *carcinoma* as a heterologous tumor from epithelium is not at present clearly delimited on all sides.

We shall discuss first the typical epithelial tumors, which arise

by proliferation of the epidermal, mucous, or glandular epithelia. From this standpoint we can define *carcinoma* as a malignant growth of epithelium which transgresses the physiological boundaries of this tissue and attacks organs destructively. In this we find the chief distinction from benign epithelial tumors, especially of adenomatous type.

FIG. 77.



Carcinomatous processes from squamous epithelium. *Zac.* Cancroid pearls. *R.M.* Mitosis in giant cells. *Tr.* Triaster. *M.* Mitotic figures. (After AMANN.)

In external form carcinomata are either nodular, fungous, polypoid, or diffusely infiltrating; but with them all the exact border of the growth is uncertain, for they send processes into neighboring tissues which may be visible macroscopically. The cut surface of these tumors is usually soft, grayish-red or white, and medullary. A "cancer juice" may often be scraped from the secretion. In many the alveolar structure can be made out in the gross, and pressure may

cause epithelial masses to protrude; in others with well-developed stroma the surface is white and dry, dense, and scar-like, but not well defined along the margins.

The histology of carcinoma is best approached from its development. Where the tumor starts in superficial epithelium, masses of these cells penetrate the underlying connective tissue in plugs and wedges. (Figs. 78, 79.) The tissue spaces are first entered and then distended. Where the tumor begins in a gland there is proliferation of the cells lining the walls and of the glands as a whole, and the epithelial cells penetrate the membrana propria and enter the spaces of the connective-tissue stroma as before. (Fig. 83.) Since the spaces form a system of communicating canals, the columns of cells which enter them have the form of a connected network. In microscopical sections either single streams of epithelial cells are cut, when they look like nests or cones (Figs. 79, 81), or their relations may be made out in the meshes described. (Fig. 78, A.) These cell bundles may also be hollow. The fibrous tissue remaining forms the stroma of the tumor, and represents the original connective tissue of the part; but with the advance of the tumor the stroma may increase, usually as fibres more or less infiltrated with lymphocytes.

Hence there are in all carcinomas two elements for recognition—the *fibrous stroma* and the *epithelial parenchyma*, in the form of cell nests and bundles. If the latter are removed there remains only the connective-tissue framework (Fig. 78, B), its fibrous bundles arranged as about alveoli. On the other hand, the stroma may be proportionately in excess, and leave but few islands of cells in it.

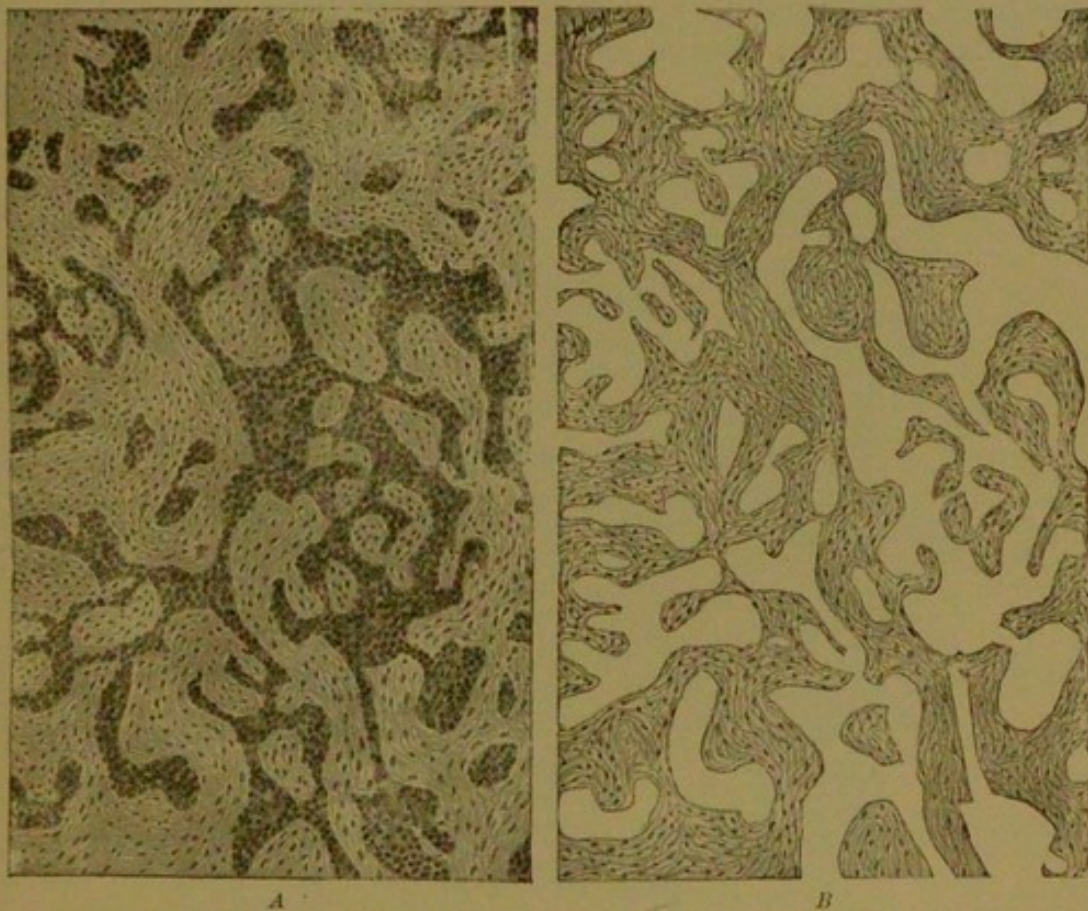
This characteristic structure of fibrous stroma and epithelial cells is an important distinction in carcinoma, and with higher magnification another is added in the arrangement of the cells. The cells lie close together and upon each other, and no intercellular substance is apparent, and even the edges of the cells are indistinct, so that a protoplasmic mass with scattered nuclei is found. (Fig. 78.)

In many cases the cells may be recognized simply by their form as epithelial, being cylindrical or typical flat cells. In many cases the cell form permits no certainty as to their epithelial origin, for they are polymorphous and irregular and modified by mutual pressure during their growth. Since similar cells occur in many sarcomata (p. 161, 2), it is clear that the diagnosis cannot be settled from the cells alone; but the arrangement of the cells is suggestive of carcinoma as well as their inclusion in fibrous stroma as bundles. Cancer tissue

fixed while alive presents many mitotic figures, corresponding to its rapid growth. Many of the cells are of extraordinary size; others show degeneration of nucleus or protoplasm. Among the cancer cells or included in them there may be polynuclear leucocytes, and other inclusions occur, as degenerated epithelial or white blood cells.

From its site of origin the cancer penetrates the nearest tissues, as the cutis and subcutaneous tissue, the muscularis mucosæ and sub-

FIG. 78.



A. Carcinoma of the skin, showing dark cell nests and strands and fibrous stroma. B. The same section after the cells have been brushed out and only the stroma remains, about alveoli which held the cells. $\times 30$.

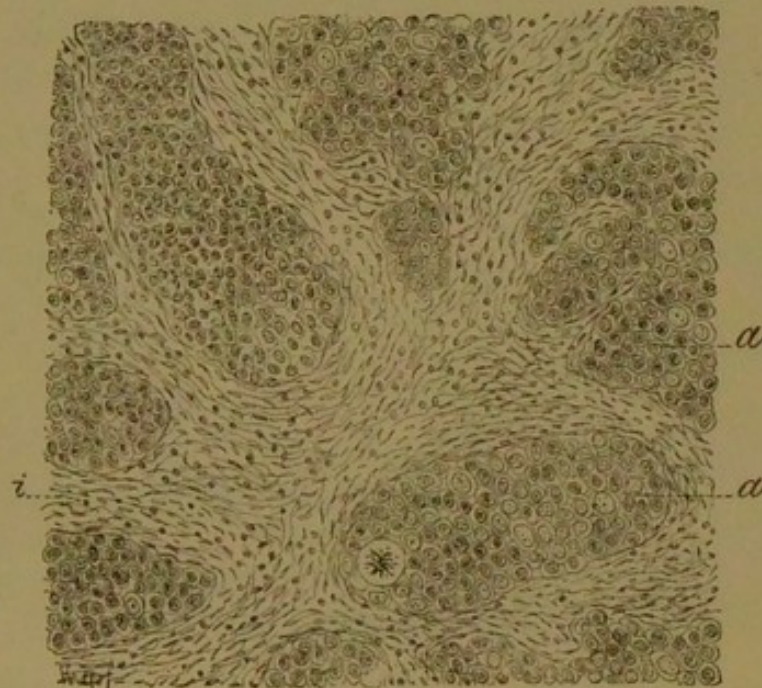
mucosa, etc., according to its location. This unlimited penetration of the growth into other tissues and proliferation in the new place are the most important characteristics of carcinoma. The advance is most rapid where the tissue is not dense, but neither tough fibrous nor dense bony parts can altogether resist the attack, though connective tissue may remain as the stroma of the tumor. In doubtful cases this entrance of epithelial columns where normally no epithelial cells occur is decisive for the diagnosis.

As the carcinoma penetrates lymph spaces and breaks into blood channels the opportunity is given for metastases. In the immediate neighborhood of the primary tumor, but separated by varying intervals, there occur small young foci of tumor formation from which, after operation, new carcinoma may spring. Metastasis through the lymph passages is early in the nearest nodes, and by the blood current it may occur in distant parts. The metastatic tumors are in all respects like the primary. At times there is a general and multiple appearance of tumors without apparently any primary focus.

Forms of Carcinomata.

In spite of atypical structure, many cancers preserve some resemblance to the tissue of origin, so that for a time it is easy to see whence

FIG. 79.



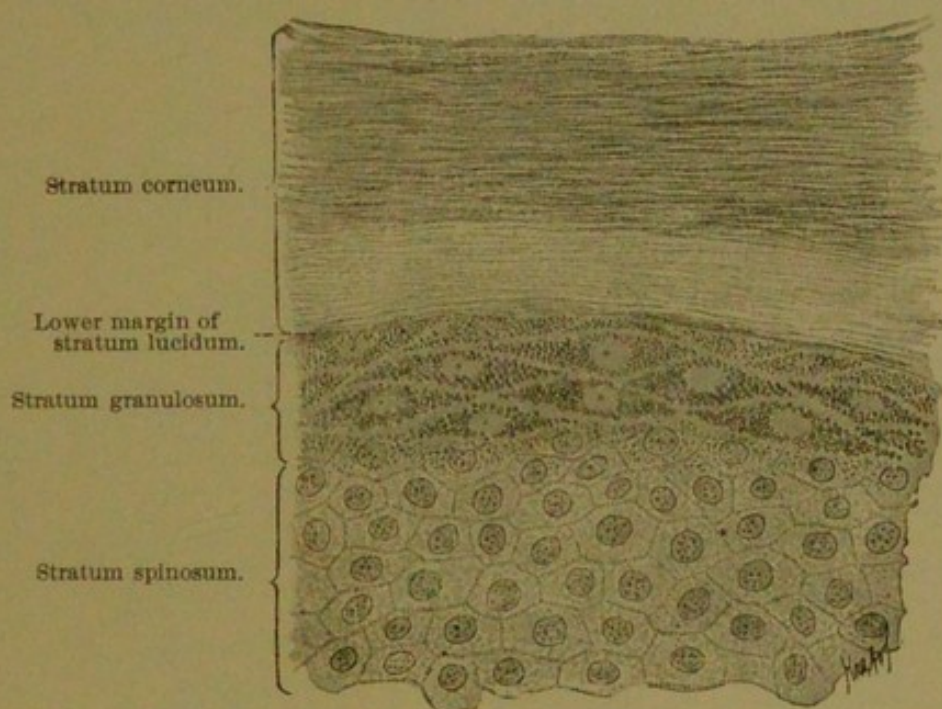
Carcinoma simplex from the breast. *a*. Nests of epithelial cells, in one a mitotic figure.
i. Stroma. $\times 250$.

they came, and as many kinds of tumors may be made as there are kinds of epithelia; but since many tumors have undifferentiated cells, this division cannot always be made. Three great groups may be recognized—those with irregular polymorphous cells, including carcinoma simplex; those whose cells are flat epithelia, squamous-celled carcinoma; and, lastly, the cylindrical-celled, which, at least in part, permit the recognition of their original cylindrical epithelia.

1. **Carcinoma simplex** (Fig. 79) arises most often in the great glands, as the breast, liver, thyroid, kidney, salivary gland, ovary,

testis, and prostate; but it may begin in other parts and proceed from one of the following forms. The glands, as also their epithelial cells, increase in size and number. Active proliferation of the cells fills the lumina and breaks through the basal membranes, and the cells entering the connective-tissue spaces form strands and bundles which frequently communicate. Here and there the cells lose their epithelial appearance, and by pressure assume the form which the containing space necessitates. Hence they may be round, angular, long, or with processes. Similar cells are common in sarcoma (p. 160). These tumors differ from adenoma by the solid columns of cells and their entrance

FIG. 80.



Section through human epidermis; the deeper layers of the stratum Malpighii are not shown.
 × 750. (After BÖHM-DAVIDOFF.)

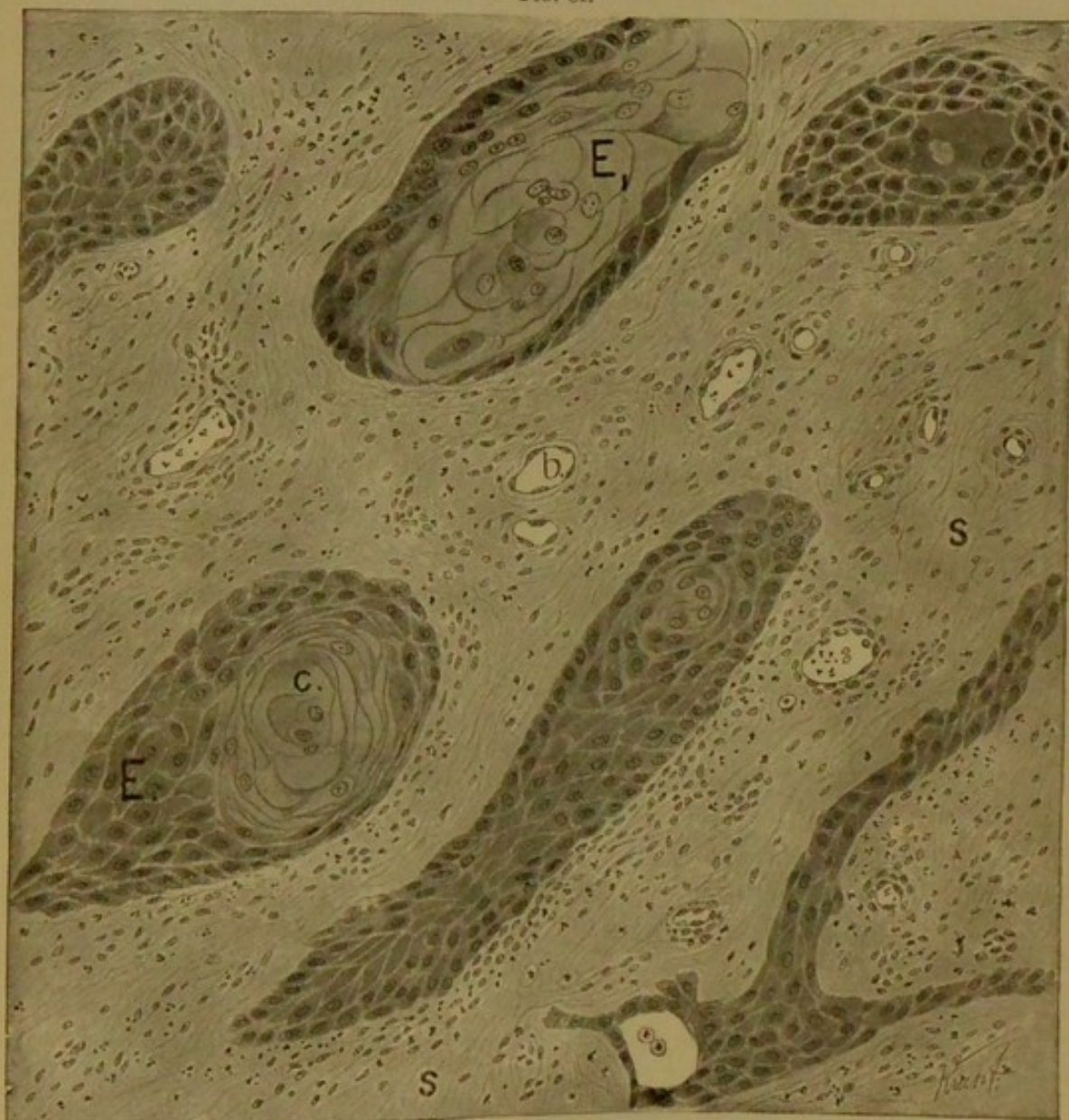
into connective tissue. While these gland carcinomas usually form large nodules, infiltrating tumors are also fairly common.

The two following kinds are characterized by a definite form in their epithelia:

2. **Squamous-celled Carcinoma.** This tumor, also called *can-croid*, starts in sebaceous glands, hair follicles, epidermic cells, and flat cells of mucous surfaces. In the cell nests there are often round cells with prickles and ridges, as found in the rete Malpighii, and longer cells from the basal layer, flat, horny, and non-nucleated scales, and other forms with irregular outlines, processes, and notches, as in transitional mucous epithelium. Pressure increases the irregular character of the

cells. On cross-section many collections of concentrically arranged flat cells are found in nests. (Figs. 81, 82.) The flat and often horny cells appear like fibres on cross-section, and their nuclei are spindle-shaped. The whole group of cells may become corneous and lose all nuclei. These groups are called *canceroid pearls*. Often the order

FIG. 81.



Squamous-celled carcinoma of the skin. *EE*. Epithelial strands with round cells outwardly, flat cells inwardly. *c*. Cells in pearls, elsewhere prickly cells. *S*. Stroma. *b*. Vessel. $\times 250$.

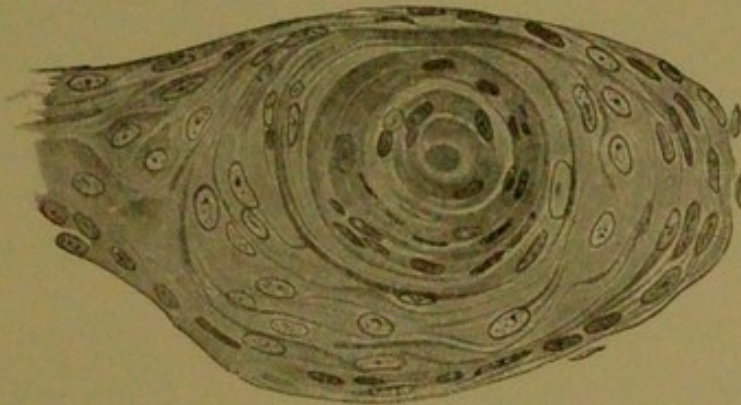
of the cells in such tumors is the direct opposite of the normal, presenting, from without in, cylindrical, round, flat, and then horny, instead of from within out toward the surface.

The presence of these pearls alone is not enough to determine the

diagnosis of carcinoma, for they may occur with benign tumors (p. 93); and ridged and prickle cells are not unusual in benign tumors. (Fig. 81.) In the margins of the cell nests lie long palisade cells like those of the normal basal cutaneous layer, but these may early be lost. In time the other characteristic distinctions are lost, and the tumor resembles carcinoma simplex. In some cases even distant metastases preserve the squamous nature.

Cancroid tumors are found in varying forms, as flat and superficial, or as deeper growths quickly invading the layers below, or as cauliflower masses when there is at the same time an enlargement of the papillæ (p. 152). Benign papillomata are distinguished from the malignant by the deeper penetration of the epithelial strands in the latter.

FIG. 82.

Cancroid pearl. Concentric, onion-like masses of corneous cells. $\times 350$.

On the cut surfaces the squamous-celled carcinomas show the alveolar structure, and slight pressure causes comedo-like plugs of softened epithelial cells to protrude.

The commonest site of squamous cancers is at junctions of skin and mucous surfaces, as the lip, nose, eye, external genitals; also the tongue, esophagus, larynx, bladder, vagina, and portio vaginalis. In general their course is slower and metastasis later than with other forms.

3. **Cylindrical-celled carcinoma** arises especially from glands of mucous membranes, but also from the breast, liver, ovary, etc. The glands begin to take on various forms, with irregular distentions and branchings outwardly and papillary projections internally; and their epithelial cells, proliferating in several layers, at last fill the lumen, becoming more irregular in outline. The characteristic fact is the rupture of the cells through the membrana propria, so that epithelial cells lie in the connective tissue under the mucous layer. The epithe-

lial bundles work their way into the muscularis mucosæ and the deeper layers. Some of the cells may remain cylindrical, but most of them become altered. They lie as solid bundles of such cylindrical or irregular cells (Fig. 83), or they become hollow, and the gland structure is apparently preserved. (Figs. 83, 84.) In the latter case the

FIG. 83.



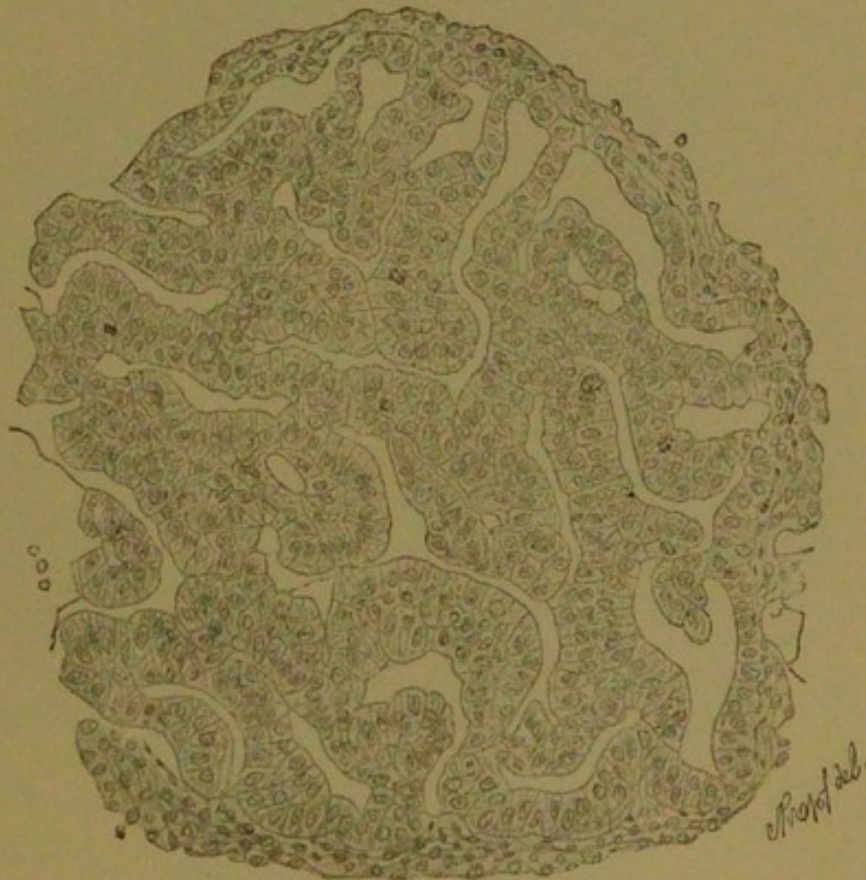
Cylindrical-celled carcinoma of the stomach. *a*. Epithelial bundles with lumen and cells in layers. *b b₁*. Small bundles entering connective tissue. *c*. Larger solid masses with irregular cells. *s*. Stroma. $\times 350$

tumor is called an adenocarcinoma or malignant adenoma. There are forms of this kind which so resemble mucous tissue and glands that malignancy depends wholly on the penetration of the deeper layers. The stroma is formed by the fibrous tissue of the parts involved, which undergoes more or less hyperplasia. The tumor with cylindrical

epithelium resembles carcinoma simplex in having a stroma and masses of epithelial cells in a meshwork, but in many cases these cells are cylindrical, and the lumen in the cell bundles resembles a gland. Sections present nests and connecting strands and hollow lumina.

Variations in the proportion of stroma make another series of cancer forms, with or without degenerative and metaplastic changes in one or the other. With largely developed stroma the tumor is called *scirrhus*, and is dense, hard, fibrous, and presents only a few cell nests.

FIG. 84.



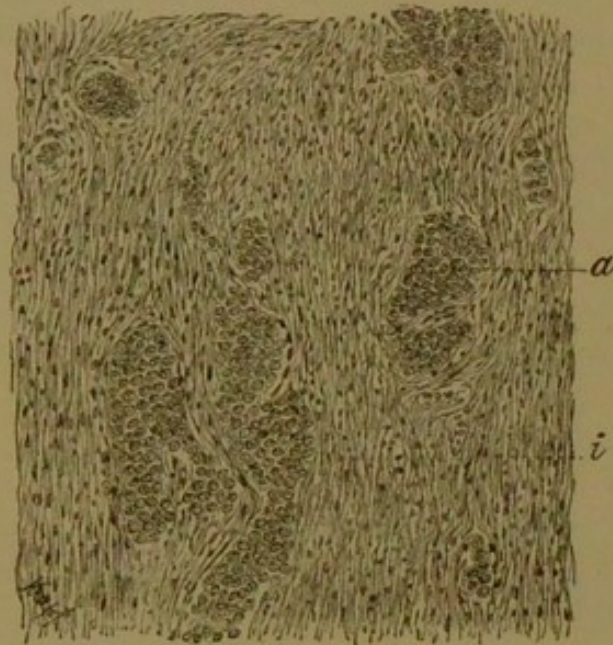
Adenocarcinoma. Superficial proliferation of gland epithelia; the stroma almost disappeared.
(After AMANN.)

(Fig. 85.) This occurs as circumscribed nodules, especially in the breast and alimentary canal. In the gross it resembles fibroma, and gives no juice on scraping. Its growth is slow, but it makes early metastases, which may be more cellular than the primary tumor.

Partial atrophy or degeneration of epithelia may occur with scirrhus forms, or with but few cells the tumor appears like a fibrous scar, as often in the stomach wall. It is possible for complete fibrous transformation to effect a cure of part of the tumor, but along the edges there are always more cellular portions, and the metastases demon-

strate a persistent malignancy. It is not uncommon for cicatricial contraction of the central portion to occur, making the so-called cancer navel.

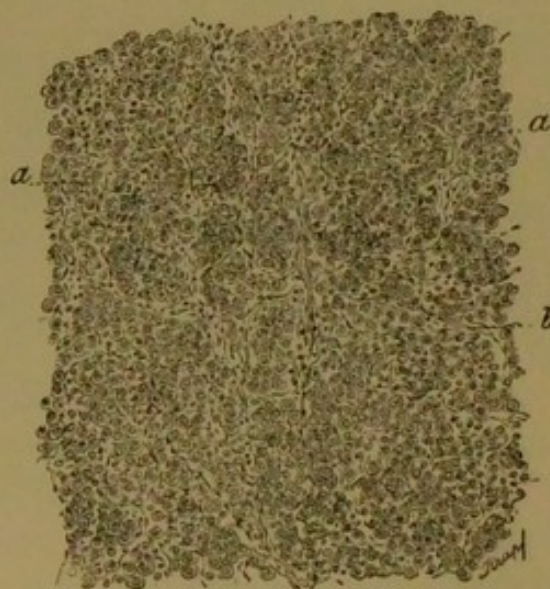
FIG. 85.



Scirrhus cancer of the stomach. *a.* Cell nests. *i.* Stroma. $\times 250$.

The opposite of the scirrhus is the *medullary* cancer, which contains more cells than stroma. (Fig. 86.) In many of these tumors

FIG. 86.

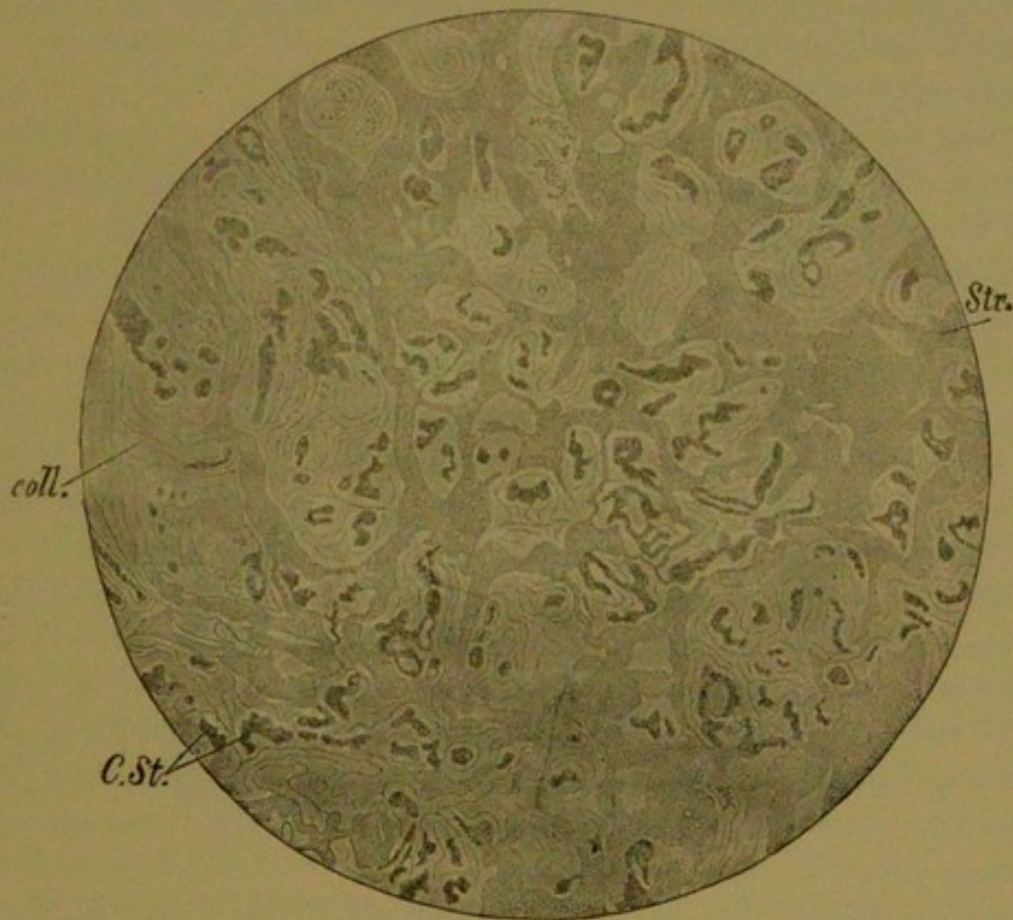


Medullary carcinoma of the stomach. *a.* Cell nests. *b.* Stroma. $\times 250$.

the stroma is represented only by remnants of fibrous tissue and blood-vessels. The tumor is soft and spongy, gray or reddish, and early breaks down and ulcerates. Scraping of the section gives much turbid

fluid containing cells, many of them fatty. This form is one of the most malignant because of its rapid growth, great destruction of the vicinity, early metastases, and ulceration. It is common in the breast and alimentary canal; less so in the kidney and other organs. This type and scirrhus correspond in form and arrangement of their cells to adenocarcinoma or carcinoma simplex, according as the epithelia are in compact or gland-like masses.

FIG. 87.



Colloid carcinoma of the cervix. *coll.* Gelatinous material. *C. St.* Epithelial cells. *Str.* Stroma. (After AMANN.)

Many cylindrical-celled carcinomas of the alimentary canal and some glandular carcinomas of the breast undergo marked mucoid or colloid degeneration of their epithelia, which fill and distend the alveoli. This form—*colloid* or *gelatinous carcinoma*—may be recognized in the gross by its translucent masses lying here and there in the tissue. The degenerated areas extend toward the surface, and involve large portions of the tumor.

Mucous changes in the stroma give rise to the form called *myxocarcinoma*, in which the epithelial cells lie in a myxomatous ground

substance. The gross appearance is soft and gelatinous. This form is less malignant than some others.

Regressive changes are common in carcinomata, as necrosis in the central portions and crateriform ulcerations externally. Softening and cyst formation, fatty degeneration of epithelia, calcification in spots, hemorrhages, etc., are also observed. Cancerous ulcers may have purulent and putrid secretions.

In general, carcinoma is a disease of advanced years, occurring seldom before the age of thirty-three years, except that the ovaries, kidneys, and prostate may be affected in early life. Heredity is clearly marked in certain families.

From the large percentage of cancer in the female breast and genitals the disease is more common in women than in men. The skin and the stomach are next in frequency.

Combinations with chondroma are observed in the testis and the parotid.

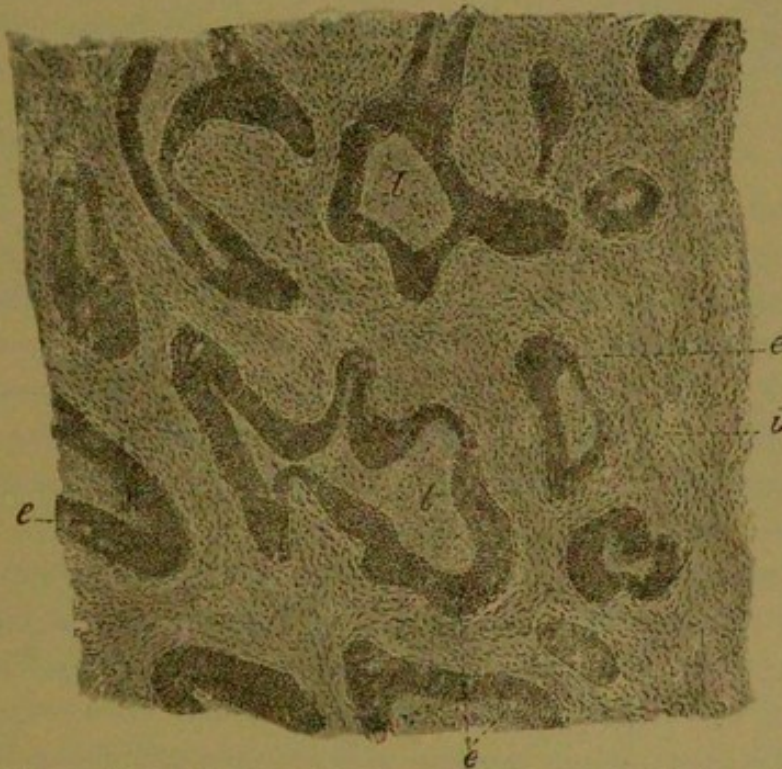
The etiology has already been discussed except as far as parasites play a part. None of the suggested parasites has withstood criticism; all other objections are theoretical. We know no parasite which causes unlimited proliferation of one kind of tissue, exceeding in energy all inflammatory processes. Inoculation, not implantation, has so far caused only a growth of epithelioid cells, as may be observed in any inflammation. So-called parasites have been only innocent fungi which will grow in any ulcerating surface or may be carried into open ducts and passively transported in metastases. The majority of the protozoa found are degenerative products of cells. Proliferation due to bacteria is noted in all cells affected by the injurious influence. A distinct epithelium into which a carcinomatous epithelium grows does not proliferate, but is destroyed. Bacteria are carried to various parts and set up a cell reaction where they lodge, as of fibrous tissue with tubercle bacilli. Tumors are spread as bits of living tissue, and where these stop they increase, the cells of the invaded tissue being destroyed. Transplantation of carcinoma from one animal to another does not prove a parasitic origin for the tumor, but resembles Reverdin's transplantation of bits of skin. And the rarity of successful transplantation speaks against an infectious nature of cancer. The transplanted piece may grow; if it were infectious the epithelial tissues of the animal would be excited to proliferate.

Beside investing and glandular epithelia, similarly shaped cells are found in lymph spaces, in the walls of lymph and blood capillaries, in

tendon sheaths, serous cavities, subdural and subarachnoid spaces, joints, and elsewhere. All these layers of single flat cells belong anatomically and genetically with connective tissue, and hence are distinguished from the true epithelia by the name *endothelia*.

Tumors due to the proliferation of endothelia present the general arrangement of cell groups in a stroma of connective tissue, but for the most part they spread along the lymph spaces, so that on cross-section there is an apparent alveolar structure. These tumors show tendencies toward sarcoma in the presence of more or less intercellular

FIG. 88.



Endothelioma of the periosteum of the jaw. *e*. Proliferating lymphatic endothelium.
l. Granular masses in the lumina. *i*. Stroma.

substance between the single cells, or in the processes by which they are connected with the fibrous tissue and each other, or, lastly, in the appearance, outside of the enclosed masses of cells, of large epithelioid cells which have processes running into connective-tissue fibres. All these peculiarities do not occur with carcinomata, and hence these tumors are classed as *endothelial sarcomata*.

Other endothelial growths retain the alveolar type so completely that from their structure they cannot be distinguished from carcinoma. The cells in proliferating lose their original character, and flat and cylindrical ones both assume the irregular polymorphous shape both in

carcinoma and in endothelioma, so that for many tumors we have only the arrangement on which to diagnose carcinoma, and this may deceive us with endothelioma. Hence in certain cases the determination of the point of origin of the tumor is absolutely necessary, and this implies study of serial sections, which may not always be possible. Since these alveolar endotheliomata act like carcinomata, being malignant and forming metastases, a distinction is not practically necessary, especially as at present the principal distinction between epithelium and endothelium is almost universally given up. Such tumors as are proved to have started in endothelia may be reckoned as *endothelial carcinomas*.

Endothelioma may occur in many parts of the body. Relatively often it is found in the membranes of the brain, and if the cells take on a high, cylindrical form and line cavities the resemblance to adenoma is strong. These may arise from the endothelia of the subarachnoid or lymph tissues. When the tumor starts from bone, the periosteum or the marrow cavity may be the point of origin. The flat bones of the skull and those of the orbit and face are sometimes the seat of the tumor, and in the latter case the neoplasm resembles rodent ulcer, destroying soft and bony parts. Other tumors begin in the adventitia of vessels, forming the so-called *peritheliomata*, or *angiosarcomata*; these are found in the brain membranes, the liver, testis, etc.

In the lymph nodes and the skin—especially in warts and pigmentations—similar tumors may arise; and at times a mass of endothelial tissue is found in the middle of a tumor otherwise clearly fibromatous or sarcomatous, so that a fibro-endothelioma may form which corresponds to scirrhous carcinoma, and this may make metastases.

Many endothelial tumors have hyaline masses along the vessels or in cell nests, or the change has affected the stroma. In the first case cylindroma results (p. 163). This is commonest in the orbit. In other cases the stroma is myxomatous. In the serous membranes, as the pleura, diffuse and flat neoplasms occur as callous thickenings of the membrane, with numerous nodules scattered over it. Microscopically the tumors have a carcinomatous structure. The cells are derived in part from the investing cells and in part from the endothelia of lymph spaces. Exudative inflammatory lesions may accompany the neoplastic. These tumors have been termed endothelial cancer by Wagner and lymphangitis carcinomatodes by Schottelius.

For syncytioma consult Chapter XIV.

Appendix. Differential Diagnosis of Carcinoma.

The important distinctions between sarcoma and carcinoma may be presented as follows :

<i>Sarcoma.</i>	<i>Carcinoma.</i>
1. General structure, may be visible with low powers. The cells lie diffusely arranged.	Two clearly distinguished elements, a fibrous stroma, and in it epithelial cells in bundles; with hollow masses, adenocarcinoma.
2. Between the cells either no intercellular substance, or it is fibrous and lies between single cells.	Stroma with high powers seen to be fibrous connective tissue, rich or poor in cells, may be mucoid or hyaline. In the cell masses the disposition is epithelial without intercellular substance.
3. Form of cells. Small or large round, spindle, star, often with processes which reach between other cells. If large, the cells may resemble those of 3a in carcinoma, and diagnosis depends on arrangement of cells, not on form. Giant cells common.	a. Cells irregular, polymorphous, or b, cylindrical, or c, squamous; cylindrical basal layer, round forms as from rete, thin, flat elements, the latter in pearls.

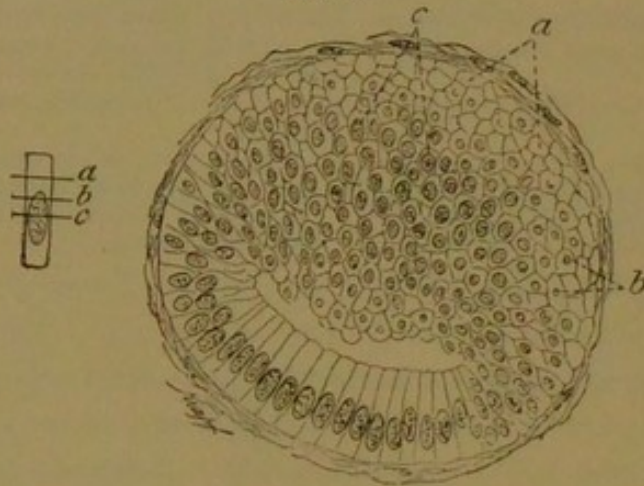
Practically more important is the recognition of a beginning carcinoma from a benign atypical epithelial growth and from an adenoma. This may be difficult. With papilloma the isolated cell nests do not lie beneath the epidermis, and the lengthening of the epithelial strands occurs because of increased thickness of the outer layer of the skin. Pearls may be present in either cancer or papilloma. Such proliferation of epithelia may occur on the edges of ulcers and in lupus hypertrophicus and granulating wounds. The papillæ grow, deep fissures may form between them, and the epithelia coming from the sides may penetrate into these. Here the epithelial wedges are few and large, and the under surface of the skin is free from them, while the scattered cell nests in connective tissue found with carcinoma do not occur.

Beginning cylindrical-celled carcinoma of the mucous surfaces may resemble adenoma. The decision is based on the penetration of deeper structures. Tissue must be examined on which a portion of submucosa remains, and the sections must run perpendicular to the surface; with cell nests below the mucosa carcinoma is evident. With small pieces the following points should be noted: If the piece is filled with cell groups and connected bundles it is probably carcinoma. Superficial sections through the rounded part of a gland fundus or duct must be distinguished from nests. In such a picture the nuclei grow smaller as they run out of the section, leaving a group of cell bodies which are free from nuclei. (Fig. 89.) With glandular arrangement in the piece studied note whether there are simply atypical glands or bundles of hollow epithelial cells in connective tissue. If the tubular

groups communicate freely, and there is no *membrana propria*, the growth is carcinoma.

The carcinomatous nodules of the great glands differ from adenoma by their lack of sharp margins, and microscopical examination of the margin shows carcinomatous processes in the one case and none in the other.

FIG. 89.



Slant section through a regular gland. Contrasted with atypical proliferated cells the nuclei grow steadily smaller toward *c* and *b*, and are lost at *a*. The opposite gland wall is given as cut perpendicularly. (After AMANN.)

Appendix 2. Cysts.

Beside the cystadenoma discussed above there are cysts with fluid or thickened contents, with fibrous capsules, which arise in various ways without neoplastic proliferation. They do not belong to the true tumors, which they resemble only in outward appearance. They may be simple or multilocular.

Certain of these cysts proceed from softening of tissue, as after anemic necrosis in the central nervous organs. Mucinous softening, localized degeneration, and destruction of delicate tissues by hemorrhage and trauma may result in cysts. Softening occurs in all varieties of tumors. In all these cases the inflammatory reaction forms a fibrous capsule, and the contents are replaced by clear fluid. A similar capsule forms about aseptic matters which cannot be absorbed, foreign bodies, and parasites.

Other cysts are found in preformed cavities of the body, as in serous spaces shut off by adhesions and filled by serous transudation from the wall. The most important of the cysts under this head are caused by retention of fluid when gland ducts are occluded. Among these are follicular and mucous cysts and those of large glandular canals. They

are lined by the epithelium peculiar to the part. The occlusion may be due to concretions, contracting scars, chronic inflammation, and tumors, and the latter may affect glands already included within the tumor.

Among the follicular cysts of the skin are comedones, milia, and the sebaceous tumors called atheroma. The latter contain detritus and cholesterin, often mixed with lime salts, and may be of hazelnut-size or sometimes larger. They may arise from bits of integument snared off during fetal life.

Mucous cysts occur in mucous membranes by occlusion and dilatation of its glands, and are especially common in chronic catarrh. Sometimes the widened glands project as polyps. These are common in the cervix uteri as the ovula of Naboth. They contain thin or colloid matter.

An example of a cyst from a gland duct is found in the oral tumor called ranula, while the canals of the breast, biliary passages, parotid, pancreas, ducts of Bartholin, and many other parts may be similarly dilated; many of these are clearly due to concretions. In the ovaries large cysts of the Graafian follicles form when, instead of bursting, fluid accumulates in them. (See Chapter XIV.)

From canals which at one period are open, but do not persist to later life, cystic formations may arise, as in the parovarium, testis (hydatids of Morgagni), and branchiogenic cysts of the neck. Ectasis of lymph vessels happens in other cases, as in many cystic lymph-angiomata, and tendon sheaths and mucous bursæ may also dilate. All these cysts are lined by endothelium.

Teratoid tumors will be treated in Chapter IV.

CHAPTER IV.

CONGENITAL ANOMALIES AND DEFORMITIES.

Introduction: Heredity. Certain pathological conditions for which no external cause is apparent are said to be inherited—that is, they are found in many generations and many members of both ancestry and posterity in certain families. Inheritance of qualities, upon which depends constancy of physiological varieties, may thus be exhibited pathologically. Heredity may be direct, as when a disease passes from parent to child, or it skips a generation or two, but reappears. With direct inheritance there may be variations, for the disease may pass from mother to sons or from father to daughters, and not to both sexes. In contrast to inherited disease, a family abnormality may be observed when from healthy parents many descendants are similarly affected. Collateral inheritance occurs when abnormalities are noted in side lines, as in uncle and nephew. When a peculiarity appears after a long period, with unaffected generations in between, it is spoken of as *atavism*, especially when the character was present in phylogenetic forerunners.

Examples of inherited abnormalities are found in the following cases: Hemophilia, which is inherited by males through females; color-blindness, hemeralopia, myopia, cataract, and other eye conditions; some forms of progressive muscular atrophy and pseudohypertrophy occurring in childhood; gallstones, especially common in females; polyuria and polydipsia; dwarf stature, polydactylism, hare-lip, dextrocardia, etc.; atavism, as supernumerary breasts and nipples and ribs; certain tumors, nevi, pigmented areas, neurofibromas; very important mental diseases and the neuropathic disposition, hysteria, psychoses, idiocy, and organic nerve diseases; infectious diseases, direct or in predisposition, and also immunity to infections; and constitutional anomalies, as gout, diabetes, and obesity.

The appearance, in the offspring of healthy parents, of diseases which the former may pass on to their children, points to a heredity in acquired characteristics which is vigorously denied by many authorities. All observations agree that accidental trauma is not inherited, as proved by experiments on animals and the century-long practice

of circumcision. But opposed to these external conditions there are internal disorders, as of the mind, which appear in previously normal individuals and are inherited from them. The objection is made, however, that in these cases the disease is not acquired, but only developed on a congenital basal condition, and that this fundamental disposition may remain latent a generation or two; but the possibility of acquired characters is not thereby disproved, and the appearance in certain persons of a disposition to diseases acquired in the generation before speaks for such heredity. If such possibilities are excluded it remains to assume that in the union of spermatozoön with ovum—for these alone can carry hereditary characters—certain pathological variations occur.¹ The new individual resembles the parents, but possesses new and peculiar traits, and similarly pathological characters may appear and be inherited by the next generation.

It is thinkable, furthermore, that the external influences which modify the body cells may modify the sexual cells in the sense, for instance, of a heightened disposition or increased immunity with regard to a special disease, and thus an inheritable peculiarity may occur in one parent. The morula which follows union of the two sexual elements may also be similarly influenced.

DEFORMITIES.

Departure from the normal may appear in the complete organism, and also in the fetal body which has just begun its development, at any point from the time of its development from the ovum to the time of perfection of its form, when it possesses the characters of the species and of an individual. It is clear that anatomical variations during the period of development must have consequences far more pronounced than those occurring later, for the former disturb the entire foundation of an organ which is yet to be, and hence all resulting forms derived therefrom. Hence defect, increase and decrease in the energy of growth—all influence the parts coming from the early foundation more seriously in proportion to the nearness of the influence to the starting point of the organ. Thus arise congenital abnormalities more or less marked, which if severe are called *monstrosities* or *malformations*, but if less evident simply *congenital anomalies*. The slight degree of such a variation may be at birth only a disposition, rendered

¹ Ziegler. Lehrb. d. allg. path. Anat., Jena, 1901.

active in later life by various accidental influences. It is clear that in the development of abnormalities there is nothing voluntary. The qualities which may be regarded as inherited in the sexual cells which lead to the normal development of the fetus follow a definite path to the normal type; the abnormal examples may be conditioned by abnormal foundations which follow an altered path toward completion, or the internal influences are complicated by external, which lead the course of development into pathological paths. The origin of the anomaly may be found in the progressive or regressive processes already studied. As soon as the primitive organs have reached a certain stage of growth they may be affected by lesions which are comparable to those of later life, as dropsy, circulatory and inflammatory disorders; and these produce malformations or copy diseases of the completed organisms, as in fetal endocarditis, rhachitis, scleroderma, and infections passed from parent to child. There are, then, actual diseases of the fetus, like those of advanced life. The tendency increases with growth, and becomes more marked as the fetus approaches extra-uterine life. The majority of malformations arise in the earlier periods of fetal life, the severe malformations all being referred to the first three months of fetal life, in which diseases are uncommon. The causes may be mechanical, as pressure, jarring, and limitation of the enclosing space as by fusion of the fetal envelopes. In the same way, or by circulatory disorders, dropsy of the amnion and placental and uterine disease may cause malformations. Of the internal causes the most important is heredity, which especially implies slight variations, as extra fingers, toes, and nipples; but it is felt also in severe cases, as in *spina bifida*. Quite commonly the defect appears in several members of a generation, though the parents and their ancestors may have been normal; in other cases the inheritance passes over a generation to reappear in a later one, as when abnormalities of the male genitalia are passed through unaffected females (*latent heredity*).

Contrasted with ordinary heredity there is the special case of *atavism*—a throwing back to another species form, in the meaning of the evolution theory. This is so uncommon in human pathology that there is hardly an authenticated case of it known.

Many malformations appear entirely as spontaneous variations; they may be called primary germinal anomalies. This is seen normally where an individual has the race and peculiar qualities of his parents and also characters of his own, which, however, express themselves within the limits of the species to which he belongs. Certain anomalies

depend upon the persistence of parts which normally do not last after the end of fetal life, as patent *foramen ovale* and *ductus Botalli*, branchial clefts, the thyroglottic and omphalomesenteric ducts, the urachus.

The different factors leading to anomalies cannot always be sharply separated from each other, for we have only the end products to examine, not the initial change.

Imperfect knowledge of the genesis of malformations prevents a proper classification of them, but they may best be divided according to external appearances, although the monsters by defect are better understood. The following groups are recognized:

1. **Monsters by defect**—a part or parts lacking or imperfectly developed.

2. **Monsters by excess**—the size, number, or time varying from the normal.

3. **Monsters by alien constitution**—abnormal relations of internal organs.

4. **Hermaphrodites**—with mixed sex.

All these forms, which may occur in a single individual, are considered as autosite malformations, and contrasted with double monsters formed by the fusion of one or more individuals.

I. MALFORMATIONS BY DEFECT.

These include all anomalies caused by restraint of growth, whether by mechanical, inherited, or spontaneous influences. *Aplasia* is the complete absence of an organ which either did not begin to form (*agenesia*) or was lost in an early stage. Aplasia may affect important vital organs, as the heart and brain, without entirely preventing the development of them if the blood supply is sufficient. In otherwise normal persons a part may be aplastic, as when one of a pair of organs is imperfect and the other usually hypertrophied (kidney, testis; see p. 99). When a part is partially developed, but not proportionately to the rest of the body, it is spoken of as *hypoplasia*; it may be caused by very slow growth as compared with the general development, or persistence of an early stage, or by atrophy occurring during fetal life.

A primitive organ may be split or snared off, and the detached portion may be placed and developed in an abnormal site. Hence arise duplication, outgrowths, and accessory organs. As a rule, it is one

of paired organs which is so affected, or organs which at first are double and then fuse and fail to effect complete union, as with double uterus. Organs made in this way may not fully develop. Harelip and cleft palate occur through imperfect union of parts about the mouth. Actual fission of primary organs and excessive growth account for other cases of deformity.

Small portions of the primitive spleen, kidney, and other organs are found, and from these cysts may form. When budding occurs in the embryo, as with the formation of the limbs and their parts, they may be strangled off by amniotic folds. Dislocation of the primitive source of an organ may cause it to develop in strange places, or it may make a teratoma, or remain quiet until late in life, and then form a neoplasm. (See Chapter III., E.)

The contrary process—namely, *fusion*—may affect parts which have a physiological relation or which should remain separate. Thus fingers and toes may unite (syndactylism), or the lower limbs may form but one (symmelia). With very superficial union the word *adhesion* may be employed. Fusion of dissimilar parts is exemplified by fusion of the amnion with parts of the embryo.

The causes of all these anomalies are varied. Spontaneous variation and heredity both act. Aplasia and hypoplasia may be due to lessened energy of growth, or imperfect vascular supply, or disturbances of tissue balance (p. 80). The clearest cases are those in which there has been an obstacle to development from the uterus or the fetal envelopes. General or partial adhesion of the amnion to the embryo, with deficient amniotic fluid and imperfect development, are observed, and partial amniotic adhesions are specially frequent at the ends of the somatic axis. A later increase in the amniotic fluid may so stretch these amniotic bands that they can snare and amputate fetal parts, or themselves be broken off and hang attached to some part of the fetus (see below, B, *e*). At the head, end fusion of the embryo and amnion may prevent complete formation of the cranium or face; at the caudal end, rudimentary or fused limbs may result; on the anterior aspect, imperfect closure of the abdomen and hernia of organs, or *ectopia cordis*. General narrowness of the cavity produces malformation of limbs, adhesions, and false positions. Similar effects follow uterine tumors and hemorrhages into the fetal membranes, which cause pressure and prevent perfect development.

PLATE XII.

FIG. 90.

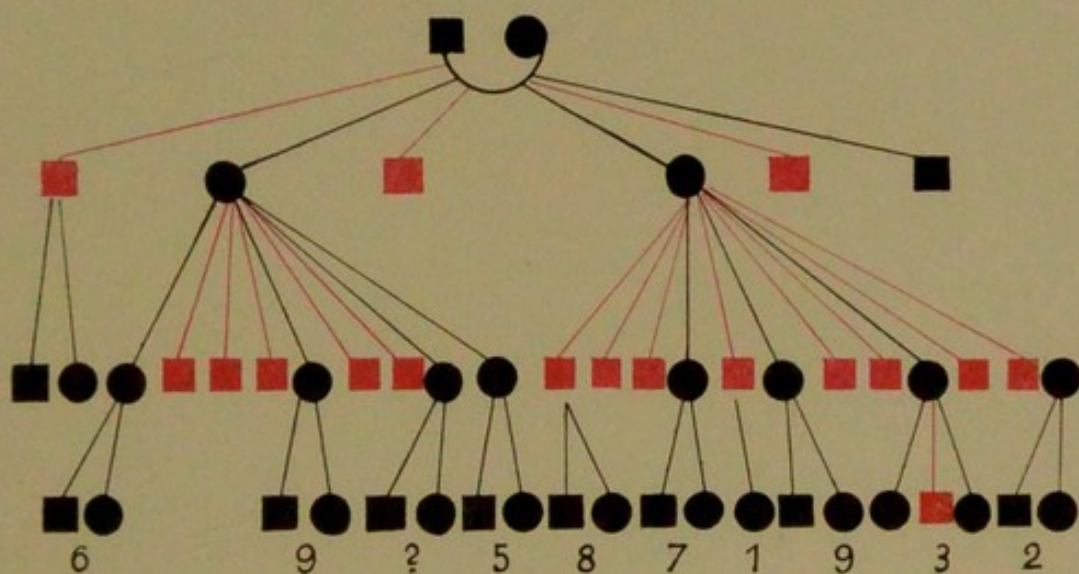


Diagram of Inherited Hemophilia in the Family Mample.

Red figures are bleeders; square, males; round, females.
(From LORSEN, in Kleb's Allgem. Pathol.)



THE VARIOUS FORMS OF DEFECTIVE ANOMALIES.

A. Involving the Entire Body.

Acardia. Very marked deformity, with heart, head, and extremities rudimentary or lacking. In the worst degree the whole body is but a shapeless mass covered with skin. Occurs in twin pregnancies with a normal fetus, having placenta and chorion in common; nourished by branches from artery and vein of other fetus (umbilical). According as one or the other part is more developed the following kinds are found:

1. *Acardiacus amorphus*, formless mass, without head or extremities.
2. *Acardiacus acephalus*, head absent, buttocks and legs more or less complete. (Fig. 91.)
3. *Acardiacus acormus*, round mass with rudimentary head; umbilical cord inserted at the neck.
4. *Acardiacus anceps*, head and extremities developed, the rest rudimentary.

FIG. 91.



Acardiacus acephalus.

FIG. 92.



Anencephalus.

B. Involving a Single Important Region.

(a) **Affecting the Head.** 1. *Cranioschisis* with *anencephalia*. Entire cranial vault lacking, so that basis cranii is exposed; rudiment of brain apparent here (area cerebro-vasculosa); skin absent where cranium is defective (adermia); if defect involves a part of the spinal canal also it makes *craniorrhachischisis*. (Fig. 92.) Caused by early fusion of amnion, before closure of medullary plates, by abnormal bending of fetus, imperfect development of cranial dome of amnion, hydrocephalus, etc.

2. *Acrania* with *Exencephalia*. A lower grade of previous form, rudimentary brain lying free.

3. *Hemicrania* with *Exencephalia*. A portion of the cranium absent, brain rudimentary or complete, more or less exposed.

4. *Encephalocele*. Defect of cranium in one place, which is often at the root of the nose (exencephalocele anterior), small fontanelle (exencephalocele posterior), or lateral fontanelle (exencephalocele lateralis). Through the opening a portion of the brain comes out (exencephalocele, hernia cerebri anterior, posterior or lateral, hydrencephalocele), and also its membranes, or the latter alone (meningocele, hydromeningocele). Cause mechanical, as trauma.

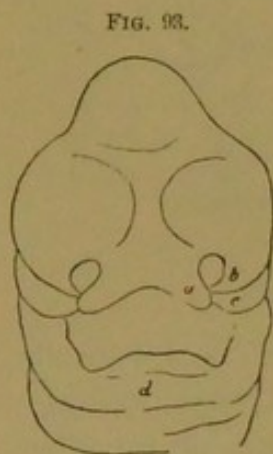
5. *Hydrencephalia*. Collection of fluid in the cranium, with secondary defect of the latter; in the highest degree, rudimentary brain as a large vesicle filled with fluid. (For Porencephalia, see Chapter XIII.)

6. *Microcephalia*. Head and brain abnormally small from general imperfect development. (See Cretinism, Chapters XII. and XIII.)

(b) **Affecting the Face.** 1. *Cyclopia*, *Cyclencephalia*, *Synophthalmia*. Occurs with restrained development of the anterior part of the brain, which remains single; eyes imperfectly separated; at the root of the nose an imperfect eye, and above it a rudimentary nasal process (ethmocephalia, Fig. 95).

2. *Fissures in the Face*. The oral opening is surrounded by the frontal process and the first branchial arch. From the former there develops a

lateral inner nasal process medial from the olfactory groove, and laterally from this an external nasal process (b). From the first arch the maxillary process and the mandible form (c, d). Between the nasal buds there is a furrow, called the nasal furrow, leading from the mouth to the olfactory groove; between the outer nasal bud and the maxillary process there is another furrow—the lachrymal—leading from the site of the eye to the nasal furrow (between b and c), forming with it the nasolachrymal (between a and c). By



Head of an embryo, fifth week. a. Inner nasal process. b. Outer. c. Maxillary bud. d. Mandible. (After GEGENBAUER.)

further differentiation and partial fusion of these parts the enclosure of the mouth by bone and soft parts is completed. From the middle unpaired part of the frontal process the septum and

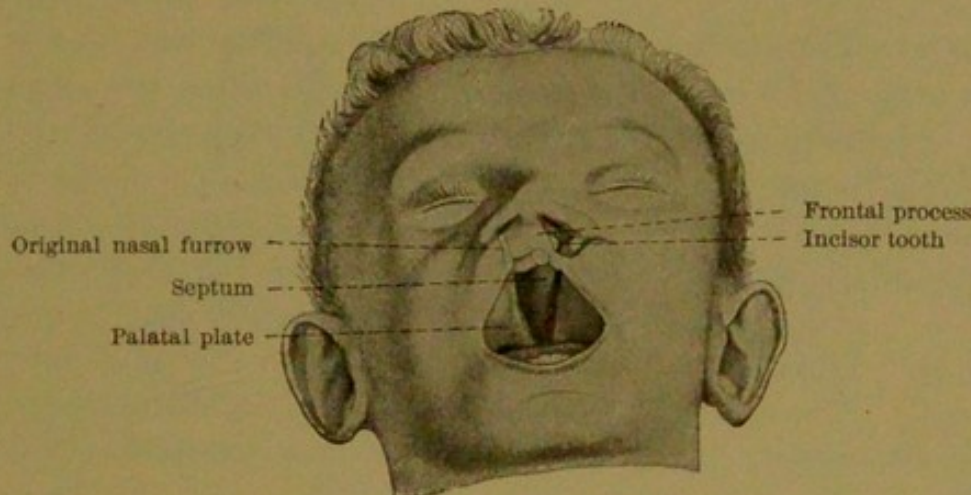
the premaxillaries are formed, and the primitive incisor teeth; soon the maxillary and premaxillary bones unite, and then the alveolar process, the upper lips, and the cheek develop. From the maxilla there spring toward the lower edge of the septum two internal horizontal plates—the hard palate—which unite with the septum in the

middle line. As the face develops the nasal cavities lie more deeply within the head. The outer nasal bud makes the ethmoid labyrinth and the cartilaginous roof of the nasal chamber, whose floor is closed in by the palatal process of the maxilla. Imperfect development of the parts enumerated may result in one of the following:

(a) *Os Leporinum, or Harelip.* Fusion of the maxillary process absent, split in the lip (cheiloschisis), or the jaw also (cheilognathoschisis), on one or both sides. Shallow furrow on the lip, or the nose also invaded. (Fig. 94.)

(b) *Cleft Palate, Palatoschisis.* Union of external parts normal; fissure of hard or soft palate, so that buccal and nasal cavities communicate. Caused by the horizontal plates of the maxilla failing to meet. The uvula may be forked.

FIG. 94.



Cleft palate. (After O. SCHULTZE.)

(c) *Cheilognathopalatoschisis.* Complete fissure of palate. Mouth and nose cavities communicate; septum narium projects free in the same and carries the imperfect premaxillary bone; hard palate represented by narrow ridges on the maxilla.

(d) *Vertical Buccal Fissure.* Non-union of frontal with maxillary bud.

(e) *Oblique Buccal Fissure.* Running from the mouth to the eye in various ways; secondary to fusion of the amnion and abnormal and partial union of maxillæ.

(f) *Macrostomia.* Transverse buccal fissure. Non-union at the corners of the mouth.

(g) *Agnathia and Micrognathia.* Lower jaw defective; mouth small (microstomia); ears united below (synotia). (Fig. 96.)

(h) *Median Facial Fissure*. Nose, jaws, perhaps also sternum, split in median line.

(i) *Schistoprosopia*. Large anterior median defects in the face, due to combined defect in union of several primitive buds.

(j) *Atresia Oris*. Imperforate mouth; and also duplication of the opening may occur.

(c) **Affecting the Back**. Common to all of these forms is imperfect closure of the posterior spinal arch, partial or complete.

1. *Rhachischisis Totalis*. Resembles cranial defect, and may complicate it, while adermia corresponds to extent of spinal fissure. The spinal canal is a shallow trough. The dura and pia may be open, in the worst cases the spinal canal also, and there appears on the anterior wall of the canal an area medullo-vasculosa, including glia and vessels

FIG. 95.



Ethmocephalia.

FIG. 96.



Agnathia, synotia.

microscopically, and in the gross appearing only as a thin film or mesh of delicate fibres.

2. *Rhachischisis Partialis (spina bifida)*. Canal open in the region of only a few vertebræ, with or without hernia of spinal cord, the protruded mass consisting of membranes (hydromeningocele) or of rudimentary cord also (myelocele, myelomeningocele). (See Chapter XII., A.)

(d) **Affecting Neck and Trunk**. *The Neck*. *Congenital fistula of the neck*, from open branchial cleft, usually on the lateral aspect, less often in the mid-line; as a derivative of the cervical sinus, a canal lined with mucous membrane, ending blind inwardly or leading into the larynx, trachea, or pharynx; or a protruding pouch from these places, with no outer opening. Congenital hydrocele colli may start in such ducts.

The Breast. *Thoracoschisis*, or *fissura sterni*, more or less complete, with or without adermia; ribs also defective at times.

Ectopia cordis, the heart, with or without the pericardium, protruding through the fissure.

The Abdomen. *Complete abdominal fissure*; anterior abdominal wall absent, or a thin, fibrous skin which continues into the amnion. The umbilicus and cord may not develop; the intestines lie in a sac made of peritoneum and amnion (*ectopia viscerum*).

Congenital umbilical hernia, a less degree of the former; a portion of the gut lies in the proximal part of the cord.

Vesicogenital fissure, dividing the lower anterior abdominal wall, bladder, and pubes.

Ectopic urinary bladder, complete bladder as a hernia through the fissure, or the anterior bladder wall also defective (*inversio*, or *extrophy* of the bladder).

Genital fissure, hypoplasia and duplication of the internal genitals; complete or partial fissure of the male urethra, so that it opens above (*epispadias*) or below (*hypospadias*); into the vagina in females.

Pseudohermaphroditism (masculine, when the testes alone are present; feminine, when the ovaries). The sex is single, and the glands may be hypoplastic, or vasa deferentia or tubes may be normal. External parts resemble the opposite sex, as *hypospadias* and fissure of the scrotum (*P. externus*); or internally there are parts of the opposite sex apparatus (*P. internus*), or both conditions may coexist (*P. completus*). (See Fig. 98.)

The Intestine. *Atresia ani simplex*, *atresia ani vaginalis*, *vesicalis*, *urethralis*. *Meckel's diverticulum*, a remnant of the omphalomesenteric duct. (See Chapter X.) In *cloaca formation* the urinary tract splits, and the lower end of the gut communicates with the bladder.

(e) **Affecting the Extremities.** 1. *Amelus*. No limbs; wart-like prominences in place of them. *Abrachius*, absent or imperfect arm; *apus*, imperfect leg.

2. *Phocomelus*. Defect of arms and legs; hands and feet directly attached to the shoulders or hips.

3. *Micromelia*, *Peromelia*. Abnormal smallness or further malformation of the extremities; fetal amputations; split hand or foot, with absent middle phalanges, making *adactylia* or *perodactylia*.

4. *Fusions*. *Sympus*, *symmyelia*, or *siren deformity*. Lower

FIG. 97.



Sympus apus.

extremities fused; feet united (*sympus apus*), partly separate (*sympus monopus*), or entirely separate (*sympus dipus*). *Syndactylia*, toes or fingers united with each other in slight degree, or complete webbing of the same.

5. *Monobrachius*, *Monopus*. One limb absent, either upper or lower.

(For the malformations of internal organs, see the various chapters of Part II.)

II. MALFORMATION BY EXCESSIVE DEVELOPMENT.

This group is characterized by over-production rather than under-production, and implies internal causes, as large primitive site or excess of growth-energy. There may be an increase in number, or size, or premature appearance of parts. Among the first are *polymastia*, or extra breasts; *polydactylia*, or extra fingers; supernumerary teeth, ribs, and accessory organs (*spleen*, *kidneys*). These depend upon division of the primitive organs, or reduplication of them, or overgrowth of normal rudiments, as feminine development in the male breast (*gynecomastia*).

Abnormal size may affect the entire body at birth, or only certain parts; as congenital elephantiasis in the skin, leontiasis in the face bones, hyperplastic single tissues, and giantism.

Abnormal development in time is observed in the genitals.

III. MALFORMATION BY VARIATIONS IN LOCATION; MONSTRA PER FABRICAM ALIENAM.

Situs inversus, or right-sided position of organs which normally lie on the left, and *vice versa*, is an example of this malformation. Involving all organs it may be termed *inversio viscerum completa*. It may affect all the abdominal organs or be limited to a single one of them. It is caused by mechanical influences which produce abnormal bending of the embryo.

IV. MALFORMATIONS BY MIXTURE OF THE SEXES; HERMAPHRODITISM.

The primitive sexual organs are indifferent, including for each sex a paired gland bud and two ducts on each side—the Wolffian and the

Müllerian. From these the male develops by differentiation of the gland as a testis and disappearance of the Müllerian duct; the female develops an ovary, and the Wolffian duct is lost. (Fig. 98.) Hermaphroditism occurs when on one or both sides the gland bud makes

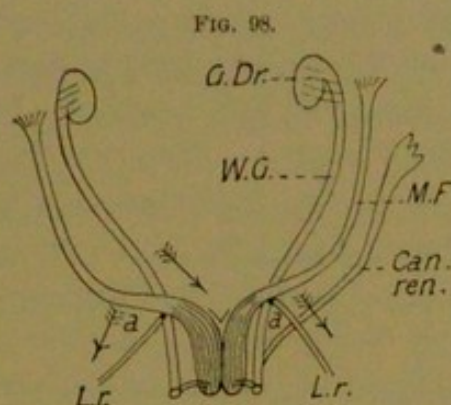


Diagram of primitive sex organs. *G. Dr.* Sexual gland. *W. G.* Wolffian duct. *M. F.* Müllerian duct. *Can. ren.* Ureter. *L. r.* Round ligament. (After VON WINCKEL.)

testis in part and ovary in part, or when one bud becomes an entire testis and the other an entire ovary. Hence there may be three forms of true hermaphroditism:

1. *Bilateral Hermaphroditism.* Double sex, gland on either side.
2. *Unilateral Hermaphroditism.* Double sex, gland on one side.
3. *Lateral Hermaphroditism.* Testis on one side, ovary on the other.

V. DOUBLE MONSTERS; MONSTRA DUPLICIA; MANIFOLD ABNORMALITIES.

Simple or autosite malformation is contrasted with double forms, in which the body, or parts of it, may be twofold or more. The etiology is obscure; but it is clear that the double monsters originate in a single egg and a single morula, and that at some time a duplication of the primitive trace or medullary groove may occur. The chief theories are:

Fusion Theory. Plurality of the primitive embryonal site, two or more forming independently and then fusing.

Fission Theory. Primitive site single, but divides into two or more. Each of the parts reproduces the lacking half (post-generation), but without complete separation of the two embryonal sites. If one of the parts divides again, threefold and other forms may result.

Bifurcation Theory. Divergent development of the single primitive site ends in duplication.

Radiation Theory. Within a primitive site two or more primitive traces form which unite at one point.

Double monsters consist of two partly separated individuals usually united at symmetrical points, and here the parts may be double or single. With fusion of this variety there is always some restraint of growth. Thus with fusion of two heads the face may be single or double (Figs. 99, 103, 104, 105); there are two ears or three, the latter made by fusion of the two which become apposed; there may be four eyes (tetrophthalmus, Fig. 108, *a*), or the two median bulbar sites fuse (triophthalmus, Fig. 99); or there may be two eyes (Fig. 108, *b*) and a single or double mouth. Similar grades of duplication occur in the trunk. The double thorax may present two or four upper limbs (Figs. 106, 108), or the two apposed arms may fuse, and the three-armed monster results. (Fig. 100.) In the same way, with fusion of the pelvis there may be two, three, or four lower extremities.

The doubling may involve the entire trunk, and the two individuals are connected only at some point of the trunk. The twinning then appears only at the head or at the pelvic end. The first kind is called *anacatadidyma*. (Figs. 105, 108.)

Catadidyma is the term used for monsters with doubling of the head end. It may not be limited to this, but may involve lower parts also, as two heads and more or less completely separate thorax, spine, or pelvis. The doubling lessens from above downward (*κατὰ*); as when the heads are separate, the thorax double, but not completely separate, and the buttocks fused. (Figs. 100, 101.) In the analogous **anadidyma** (*ἀνα*) the pelves may be separate and the fusion increase upward. (Figs. 103, 104.)

In proportion to the separation the twins are capable of complete development, as in the case of the genetically related, wholly separated twins which have the placenta in common and arise from a single ovum. The differentiated parts are strikingly similar, and the sex is the same in each. In many double monsters there are also anomalies by defect. One individual may be very much less developed, appearing as a dwarf (*heterodidymus*), or as an *acardiacus*, or as a rudimentary limb attached to any part of the developed half (Fig. 107), or a formless mass is attached as a parasite to the autosite. The mass may be surrounded by the autosite's tissues, making a fetal inclusion (fetus in

fetu, epignathus in the mouth, engastrius in the body cavities); or a tumor—a teratoma—may represent the parasitic portion.

The Single Forms of Double Monsters.

I. **Catadidyma** (*duplicitas anterior*). Doubling begins at the head and reaches more or less to the trunk. Union least at the pelvis.

1. *Diprosopus*. Head double, not separate; face more or less completely separate; cranial cavities single or double:

(a) *D. diophthalmus*. Two eyes, mouth double.

(b) *D. triophthalmus*. Third median eye in common. (Fig. 99.)

(c) *D. tetrophthalmus*. Two separate eyes between the noses.

(d) *D. triotus*. Cranium double, four eyes, and one median and two lateral ears.

2. *Dicephalus*. Two separate heads; doubling may involve body down to the pelvis.

FIG. 99.



Diprosopus.

FIG. 100.



Dicephalus tribrachius.

FIG. 101.



Dicephalus tribrachius tripus.

FIG. 102.



Ischiopagus.

(a) *D. dibrachius*. Thorax fused, two upper extremities.

(b) *D. tribrachius*. Median upper extremity fused. (Fig. 100.)

(c) *D. tetrabrachius*. Median upper extremities separate.

(d) *D. tripus*. The median lower extremity fused. (Fig. 101.)

3. *Ischiopagus*. Union only at the pelvis; the two individuals lie with heads directed oppositely, internal organs to a great extent doubled. (Fig. 102.) *Omphalopagus*; union at the navel.

4. *Pygopagus*. Union only at the sacral or ischial bones; the two usually turned with their sides opposed.

II. **Anadidyma** (*duplicitas posterior*). Doubling begins at the pelvis and lessens upwardly.

1. *Dipygus*. Lower body and extremities double; head single. *D. dibrachius*, two armed; *D. tribrachius*, three armed. (Fig. 103.)

2. *Syncephalus*. Double thorax, two heads fused. (Fig. 104.)

(a) *S. symmetros, janiceps*. Head completely double; two faces, one anterior, one posterior.

(b) *S. asymmetros*. One face developed.

3. *Craniopagus*. Doubling of entire trunk, fusion at head. (Fig. 105.) Epicome is a craniopagus in which only the head of one individual is formed.

FIG. 103.



Dipygus tetrabrachius.

FIG. 104.



Syncephalus.

FIG. 105.



Craniopagus.

FIG. 106.



Thoracopagus tetrabrachius.

III. **Anacatadidyma** (*duplicitas parallela*). Entire trunk double; union on breast or belly; area of connection may be small; the double upper or lower ends may be partly fused.

FIG. 107.



Epigastrius parasiticus.

FIG. 108.



Prosopothoracopagus.



1. *Thoracopagus*. Two individuals, united only on thorax, placed parallel.

(a) *T. tribrachius*. Median arms fused.

(b) *T. tetrabrachius*. Four armed. (Fig. 106.)

(c) *Xiphopagus*. Union only by ensiform process; the Siamese twins an example. With one individual rudimentary, thoracopagus

parasiticus, second portion attached to anterior wall of thorax or epigastrium. (Fig. 107.)

(d) *Heterodidymus*. Second individual doll-like in size and adherent to breast of viable autosite.

2. *Prosopothoracopagus*. (a) Heads fused, faces also; cranial cavities separate. (Fig. 108.)

(b) *Epignathus*. Parasitic form of the same; wholly rudimentary fetus in the buccal cavity of the autosite, or projecting from it; usually attached to the basis cranii. (Fig. 103.)

FIG. 109.



Dermoid cyst of the ovary. (After PFANNENSTIEL.)

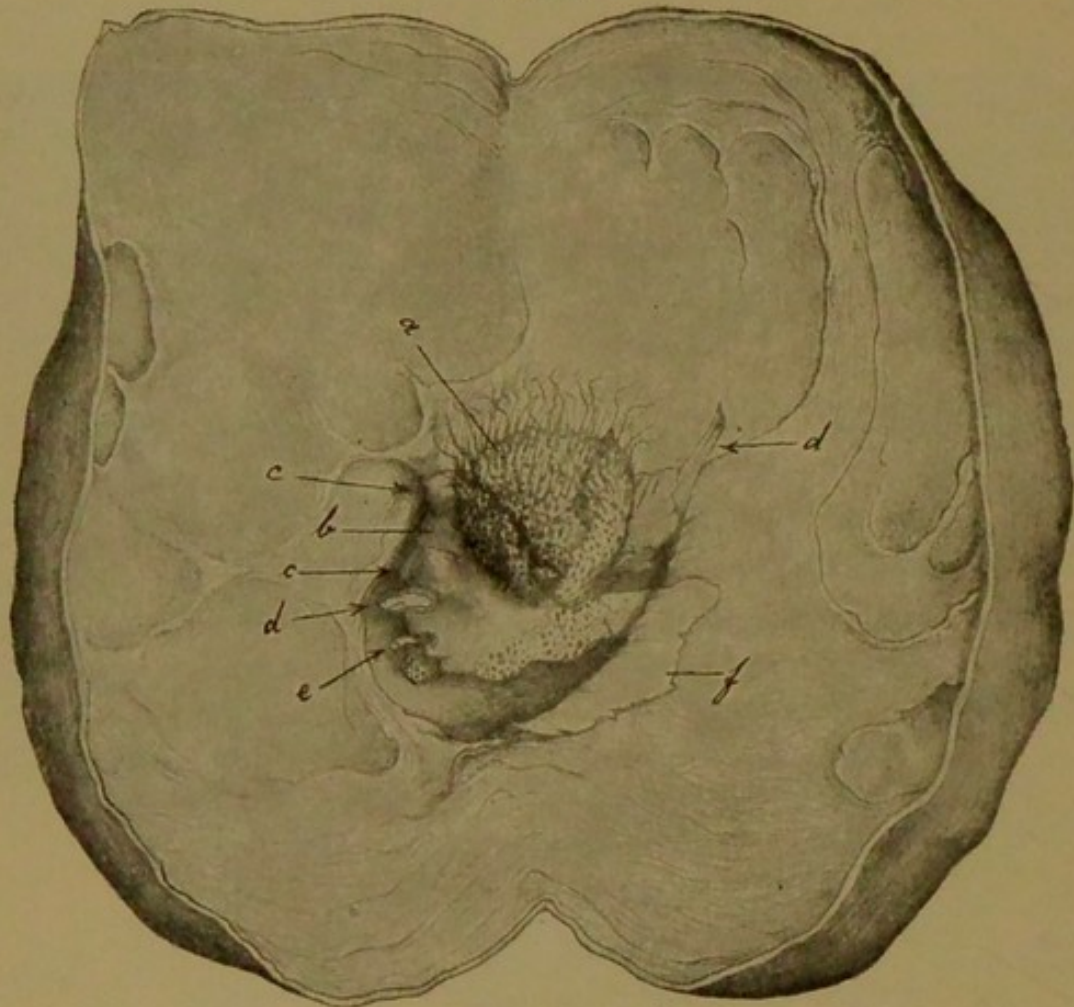
(c) *Rhachipagus*. Fusion of dorsal or lumbar vertebræ.

Monsters of three and more individuals are rare, but resemble the double forms.

Teratomata. The second fetus may be so rudimentary as not to be recognizable as an individual, and forms a more or less tumor-like appendage to the autosite. This may result from splitting or snaring

off of the primitive embryonal site or excessive growth of single tissues. Hence arise seemingly neoplastic formations, which may increase in later life, but differ from tumors by containing not only atypical tissues, but also rudimentary organs—teeth, bone, cartilage, muscle, glands, etc. Dislocation of fetal tissue may cause such growths to develop where their tissue is wholly foreign. Certain congenital tumors resemble these, as chondroma in the testis and parotid, and hypernephroma in the kidney.

FIG. 110.



Section of dermoid cyst of the ovary. (After PFANNENSTIEL.)

Among the teratomas belong many tumors which occur at the sacral or the cephalic end of the body, congenital or other, which contain rudimentary organs and may lead to cyst formation. These are known also as dermoid cysts and appear in special regions, as the ovaries, the subcutaneous tissue of the neck, the orbit, ear, and floor of the mouth; their walls correspond in formation to the skin. Teratomas include the following:

1. **Epidermoid Cysts.** Fibrous capsule, with corneous epithelium; contain soapy or dry and friable matter derived from epithelial cells. Among these is the cholesteatoma, nodular, lamellated, and peculiarly glistening, like mother-of-pearl, occurring in special parts of the brain and developed from the pia. The contents are irregularly arranged, or consist of concentric scales of corneous epithelia containing more or less cholesterin between them; the whole surrounded by a wall of vascular connective tissue, with several layers of epithelia resembling epidermis and transitions of these to the scales which fill the tumor.

2. **Dermoid Cysts.** Contain epidermis, and also hair and sebaceous glands. The contents are usually fatty, and after death thicken to an unctuous mass in which the hairs are found in bundles.

3. **Simple Teratoma.** Compound dermoid, with contents mentioned, where teeth and bones may be found in addition.

4. **Compound Teratoma.** Other organs and tissues are found, as salivary or sexual glands, mucous membrane, muscle, nerves, whole fingers or toes, parts of the eye or breast. These are due to fetal inclusion or development of scattered primitive organs. It is supposed that such tumors may arise from ova which begin to develop without impregnation, parthenogenetically, and hence imperfectly.

Both dermoid and teratoma may become transformed into sarcoma or carcinoma.

CHAPTER V.

PARASITES.

A. VEGETABLE PARASITES.

THE vegetable parasites of man belong to the cryptogams, including the fission fungi, *schizomycetes*, or *bacteria*; the *hyphomycetes*, or *mould fungi*; and the *saccharomycetes*, or *yeast fungi*.

1. Bacteria.

Among vegetable parasites the bacteria are the most important. They are simple, one-celled micro-organisms, measured in micromillimetres and fractions of the same (micron, or μ). Their morphology is restricted, and, classed according to form, but three divisions are made—the cocci, spherical or spheroid; the bacilli, with elongated bodies; and the spirilla, which are twisted in corkscrew form. In some bacteria, considered as undoubted bacilli until now, there is an apparent branching of the single cells, as is a common feature of the *hyphomycetes*; among these are tubercle and diphtheria bacilli.

A nucleus has not been certainly determined for all forms of bacteria, but they are enclosed in a membrane which may be demonstrated by proper methods. Externally this membrane is not sharply defined, but often fades into a gelatinous material which swells with water (Fig. 118); this is called the capsule. It stains with difficulty, but often reaches a notable size. Most of the encapsulated bacteria form this envelope only in the body of the host or on suitable media, and it is usually lost in cultivating the organism. In dividing, the bacteria may retain this capsule, and many young forms may be gathered within it. Such groups are called zooglea (*palmella*), and form the scum on mouldy liquids.

Many bacteria are motile when examined in fluids. This self-propulsion is not to be confounded with the molecular trembling and dancing of lifeless particles suspended in fluids. The kind of movement shown may be crawling, waving, serpentine, sometimes rapid, sometimes slow; and it is more often seen with spirilla, comma forms, and bacilli, less often with cocci. It is almost always produced by

cilia or flagella—hair-like processes, single or multiple, which are placed at one or both ends, or generally over the bacterium, making the monotrichous, lophotrichous, and peritrichous forms. In some actively motile forms, as the spirochete of Obermeier, no flagella have yet been found.

Bacteria propagate by fission or by spore formation. In the first case one individual constricts and divides into two. Cocci become slightly elongated before dividing, while bacilli after they remain short for a time. Endogenous sporulation occurs as localized thickening at some part of the bacterium, which is followed by the appearance there of a roundish, refractile body within the bacterium, often distending it, which takes stains but slightly. The spores are median, lying in the middle of the organism, or end spores. (Figs. 120, 121, 122.) When the end spore distends the bacillus it makes club and racquet shapes, called clostridia.

FIG. 111.

Spirilla. $\times 1000$.

The marked peculiarity of spores is their resistance to influences which destroy the enclosing bacterium, owing to the dense spore membrane which surrounds them, and hence they persist after the parent germ is lost. In favoring conditions these resting forms begin to develop anew.

Spore formation, almost confined to bacilli, is observed as the culture medium begins to be exhausted, but at times vigorous colonies also develop spores. A higher temperature is required than for the growth of the simple germ.

Another variety of spores is called arthrogenous, and develops, according to Hueppe, when a cell is surrounded and thus protected from injury by others which may be dying; but the greater resistance of arthrogenous spores has not been proved, and they are not considered as equivalent to the endogenous variety.

The propagating power of bacteria is enormous, and so in a short time countless individuals may be developed. With unhindered growth a single cell may at intervals of an hour divide to two, these to four, then to eight, and so on until in twenty-four hours there are sixteen million, and after three days forty-seven trillion.

Bacteria which are dying often present variations in forms, buds, constrictions, and dissolution of the regular type, which are grouped under the name involution forms.

In general, bacteria are easily and deeply stained by the aniline colors, and hold the stain more strongly than the tissue elements.

Certain bacteria are peculiar in staining only after long exposure, or with the aid of mordants, or by heating; but these retain the color longer than others, and may even be treated with strong mineral acids for a time without giving up the stain. This resistance to acid is an important distinction of many kinds of bacteria, and the diagnosis of the tubercle bacillus depends upon it (p. 225). Flagella and spores are stained with more difficulty than the cells, and require special methods.¹

Within the bacteria there appear certain granules in some staining methods, and these are supposed to be deposits of iron or sulphur or of unknown nature. In salt solution the plasma of the bacterium shrinks from the capsule, leaving clear spaces (plasmolysis). Pure water may swell the plasma and remove these. Other vacuoles occur in degeneration forms.

Review of the Chief Bacterial Forms.

I. Cocci. Bacteria of nearly spherical or short oval form, almost never motile. Propagation only by fission. According to grouping, divided into:

1. **Diplococcus.** After division of one, the two young forms remain adjacent to each other; the opposed sides may be flattened or pointed. (Fig. 116.)

2. **Streptococcus.** After division the young forms remain together in great numbers. Fission occurs in only one plane, and hence arise long or short necklace or chain groups, often in curves. (Fig. 113.)

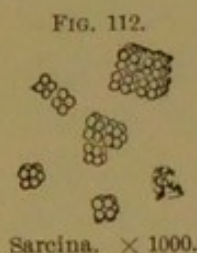


FIG. 112.

Sarcina. $\times 1000$.

3. **Tetrads, Merismopedia.** Division occurs in two planes at right angles to each other, and the young forms remain in fours. (Fig. 117.)

4. **Sarcina.** Fission in three dimensions, and the eight individuals remain in dice-like cubes. (Fig. 112.)

5. **Staphylococcus.** Micrococcus in the strict sense, in irregular groups and masses, or as grape-like cultures. (Fig. 115.)

II. Bacilli. (Figs. 119-126.) Long or short rods, propagate by fission or spores; the former by fission or crosswise, the younger forms separating or connected (streptobacilli). From the spore the bacillus develops by simple lengthening or by the rupture of the spore membrane and growth through the opening.

¹ Gram's method is of great diagnostic value. The bacteria are stained with aniline-gentian-violet, treated with Lugol's solution, decolorized in aniline-xylol (1:3), then carried through xylol and mounted in balsam. Certain kinds hold their color, others lose it by this method.

III. **Spirilla.** **Spirochetæ.** Both of these forms are spirally wound, like corkscrews. (Fig. 127.) In small portions they are called vibrio or comma forms, consisting of a single arc. (Fig. 128.) Endogenous spores or arthrospores.

The *biology* of the bacteria includes their conditions of growth and the expressions of their activities. For the former there must be a supply of nutriment, and it must contain organic carbon compounds, for the bacteria are without chlorophyll and cannot make their carbonic acid from carbon. Inorganic salts with nitrogen also are necessary, a certain percentage of water, and a particular temperature, between the limits of -5° C. and $+45^{\circ}$ C. Many of the true parasites must have a middle temperature, and show great variations as the heat changes in either direction. In respect to oxygen, two kinds of bacteria are known. The majority require a full supply of oxygen, and die when it is withdrawn; a smaller number will grow only when oxygen is excluded. The former are called obligate aerobics and the latter obligate anaerobics. Between these two stand the facultative aerobics, which usually grow in the presence of oxygen, but do not die in its absence. According to another view, the bacteria are divided into the obligate and the facultative parasites. The former live only on living tissue, as in the body; the others, known also as saprophytes, flourish in dead media. Between these groups there are others, known as facultative parasites, which can grow in the living organism or outside of it.

Deprived of what are considered necessary conditions for growth, various kinds of parasitic and saprophytic bacteria display a tenacity of life. They do not multiply, but remain capable of multiplication when new conditions are afforded. Thus tubercle bacilli may remain for months in a dried condition without perishing. Other and higher claims may be made for the spores, which may develop at the acme of vigor, and not, as supposed, when the medium is becoming exhausted. For this many kinds require excess of oxygen and higher temperatures; thus anthrax makes no spores below 18° C. and over 34° C., but freely at 30° C. When once formed the endogenous spores are very resistant against changes of temperature, lack of nutriment, unfavorable composition of the medium, and antiseptic chemicals.

Anthrax bacilli die after several days of drying, ten seconds of exposure to the action of 1 per cent. carbolic acid, short boiling, and by the normal acid gastric juice; the spores, however, withstand year-

long drying, thirty-seven days in 5 per cent. carbolic acid, short boiling, and the gastric juice.

Certain bacteria are of the utmost importance to man as friends, others as enemies. Some in growing on various media, such as the tissues with the parasitic kinds, destroy the medium and build it up into the bacterial cells, and also give out waste products. Among the latter are simple bodies, as carbon, hydrogen, sulphuretted hydrogen, ammonia, mercaptan, and also very complex principles.

An important power of many bacteria is the formation of ferments or enzymes. These are bodies which in the smallest quantities have the power to reduce complicated chemical matters into simpler compounds without themselves being used up in the process. The ferments act apart from the bacteria, as after filtration, and can be prepared as dry powders.

The ferments are of various kinds: as the diastatic, which turns starch into sugar; the inverting, making cane-sugar into grape-sugar; the pepsins, coagulating milk in alkaline media; the proteolytic, making glue fluid and dissolving albumin; and the ferment which softens gelatin.

Many bacteria cause fermentation—formerly defined as the solution of material, with the production of gases, but now including cases in which there is no gas formed. Examples are lactic fermentation, of milk-sugar into lactic acid; butyric, which converts starch and sugar into butyric acid; the acetous, mannite, ammoniacal, and alcoholic.

Putrefaction, which cannot be chemically defined, is held to be fermentation with the formation of stinking gases (albuminous fermentation). It occurs almost always with exclusion of oxygen, by anaerobic bacteria, and is essentially a reducing process. In the course of putrefaction there are ptomains formed—a kind of alkaloid—many of which have highly poisonous properties. Simple rotting is distinguished from putrefaction by occurring with free access of oxygen, and it is essentially an oxidation. The higher compounds formed by plants and animals are turned into simpler forms, and finally reach one in which they again serve as nutriment to higher plants. A specially important case of this is found in the change of organic nitrogen compounds and ammonias to nitric acid, which is the work of special soil bacteria of the nitrifying class.

Many bacteria have the power of forming pigments, as the *m. prodigiosus*, which makes a red color on bread; *b. cyanogenes*, which turns milk blue; *b. pyocyaneus*, which causes blue or green pus, etc. Some forms, like the pus organisms, make pigment in the artificial

media. Certain of these pigments are phosphorescent, and others make media fluorescent.

The most important powers of bacteria are those by which they become producers of diseases. Parasitic organisms multiply within the living body, and produce a virus which at first causes local disorders. Such causes of disease are distinguished from all others by the fact that they are self-propagating within the body; for while the direct action of mechanical, thermal, and chemical agencies ceases with their removal, the effects of such a virus persist as long as the conditions of production are favorable.

The invasion of pathogenic organisms is called *infection*, and the result is an *infectious disease*. Many of the bacteria require a certain time from the invasion to the outbreak of the disease (incubation). Many possess direct contagious power. The appearance of the disease may be sporadic, endemic, or epidemic. The general effects of the poison are observed as fever, nervous disorders, and other symptoms referable to various organs, showing that the entire organism is more or less affected. Many infectious diseases present a regular and definite type of fever (typhoid, recurrent fever). The cause of such diseases in the great majority of cases is bacterial; a few are due to other parasites, as moulds and protozoa. In many of these the actual bacterium is not known, but we assume that they are infectious from their course. In other diseases the micro-organism constantly appears, and can be raised in pure culture and again used to produce the original disease experimentally.

Among infectious diseases the contagious and the non-contagious are recognized. A *contagious* disease is one in which the infectious agent is passed out of the body of the affected patient, and by the air, food, or otherwise carried directly to others, causing a new infection; among such are many acute exanthemata, as variola. *Non-contagious* diseases are those in which the agent does not pass out of the affected person, as is the case with the parasite of malaria. The disease is then not directly transmitted from one to another, although malaria can be given by the injection of malarial blood into a healthy subject.

Distinctions have been made between endogenous contagion—when the agent did not persist outside of the body, as in syphilis, measles, and scarlet fever—and ectogenous, when the bacteria multiplied in the earth or persisted as spores, as in anthrax. If apparently confined to certain places and local conditions, the contagion was called a miasm; if developed in such places only in the presence of affected individuals,

it was termed a miasmatic contagious disease. Appearing over a great extent of territory and involving many people quickly, the disease is called epidemic; restricted to certain regions and but few patients at any one time, it forms an endemic disease. Volatile contagia are supposed to spread through the air; fixed contagions by long, direct contact.

The mode of entry into the body varies with different agents. Through the skin, mucous membranes, and injured organs, certain wound infections, gonorrhea, syphilis, and other diseases may pass. Many diseases enter through small wounds of the body surfaces; many through the uninjured skin by way of the sebaceous follicles and sweat glands, as with pus organisms. Other bacteria enter with the food and pierce the uninjured mucosa of the mouth and pharynx, or, reaching the stomach, perish in the gastric juice or pass through unchanged, especially when stomach disorders reduce the function of acid formation. The resistant spores usually reach the intestine unharmed.

Bacteria taken in with the air are deposited in the respiratory passages or the pulmonary alveoli. Tubercle and other bacilli may pass through into deeper structures, as lymph tissues, etc., where their pathogenic action may then develop.

A special case of infection is the passage of bacteria from parent to fetus, as may happen even in the earliest period of its existence or even affect the ovum. Syphilis, tuberculosis, typhoid, recurrent fever, anthrax, and erysipelas may thus pass to the fetus, and many of these micro-organisms have been recovered from its tissues. Such inheritance of disease may occur in one of two ways: either the virus enters the ovum with the spermatozoön, without preventing its further development, or, during pregnancy, the infection passes from the maternal blood through the placenta to the fetus. The former mode is called *conceptional* or *germinative* infection, and the latter *intra-uterine* or *placental*.

The effects of bacteria in the body vary according to the nature of the infecting organism and the peculiarities of the subject attacked.

The bacteria both live upon the elements of the body as a source of nutriment, and, more especially, injure it by their products. The latter chemical influence is widespread, and so excessive with certain bacteria that they need be found only at the port of entry, and set loose their products from here over the whole body. In such a case the action of the bacterium is essentially an intoxication, and hence these kinds are known as toxic bacteria. The infectious varieties, in a limited use of the term, are those which multiply and spread through

the body. Toxic action is not limited to the properly parasitic forms, but is observed also with those of putrefaction—the saprophytes.

The *putrefactive alkaloids*, or *ptomains*, are alkaline, contain nitrogen, are crystalline, and resemble amins, diamins, and triamins, or are compounds of an ammonium base. Among toxic alkaloids are peptotoxin in many peptones, neurin and muscarin in decaying meat, etc. *Non-poisonous ptomains* include neuridin, cadaverin, putrescin, and cholin, and occur in all dead bodies. In many cases there is an intoxication with ptomains formed within the alimentary canal. Cases of this kind are furnished in poisoning with meat, sausage, cheese, fish, shell-fish, etc. They may occur after eating spoiled food even when the latter has been cooked, for the heat does not always destroy the alkaloids. These diseases are partly due to infection, at the same time, with the bacteria in the decayed nutriment, and animals dead of septic processes are specially dangerous in this regard. Most poisonings from meat resemble acute enteritis or cholera, and are due to the *bacillus communis* of the colon and others like it, as *bacillus proteus*, which makes sepsin, and *bacillus botulinus*—a tetanus-like form which has been observed after poisoning from sausages. Shell-fish may passively carry the infection of typhoid and cholera, and bathing in tainted water may be the cause of Weil's disease—a form of contagious icterus.

By the action of saprophytes normally present in the intestine, as *bacillus coli*, infections may be caused when there is present a large amount of decaying matter whose products are absorbed from the intestine; this is an example of auto-intoxication. (See Chapter VI.) Some of the convulsions of children, and the general depression seen with dilated stomach, may be thus explained. Often infectious and putrefactive bacteria work together. They may cause gangrene of parts undergoing necrosis, with solution of the dead albumins and production of poisonous products. They are found in wounds which are exposed to the air and external infection, in bed-sores, wounds of mucous surfaces, bits of retained placenta or fetal membranes, with purulent processes everywhere, especially in phlegmonous inflammation which causes necrosis of tissue, and, lastly, they occur as a mixed infection with diphtheria. The general action of the putrefactive forms depends upon the toxins mentioned, which when absorbed, as from a gangrenous part, may produce severe symptoms or death from sapremia, or putrid infection. This is equivalent to intoxication or poisoning of the body by the products of saprophytic bacteria. Its

clinical course may be acute or chronic, and the lesions about the point of entry are often strikingly restricted.

In the production of the true infectious diseases the action of bacterial products is also of great importance. By chemicals which coagulate albumin, precipitations of amorphous poison may be obtained from many actively growing cultures of bacteria, and these are called *toxalbumins*. Many of these are of frightful power; pure tetanus toxin is three hundred times as deadly as strychnine. At present the view is gaining ground that the toxin is not strictly an albuminous body, but clings to the proteid as it precipitates, and many are proved not to be albuminous; hence they are called simply *toxins*, or specific bacterial poisons. These are found in cultures of many bacterial forms, and after removal or death of the producing micro-organism may be used to reproduce the symptoms which follow infection with the bacterium studied. Such toxins are known for tetanus, diphtheria, typhoid, cholera, and other infectious diseases. The general constitutional symptoms are especially the work of such toxic material, and the producing germ may be found only at the point of infection, as in tetanus, although this disease is a peculiarly generalized affection of the nervous system. Even after the tetanus bacilli have disappeared for a time from the original site, animals may be infected by the blood of the subject. The general symptoms of diphtheria depend similarly upon its toxin, and by injection experiments paralyses may be caused. Hence bacteria of these diseases are called toxic.

From the bacteria themselves poisonous matters may be prepared. By trituration and hydraulic pressure *bacterial plasmin* is obtained; by boiling with potassium hydrate a *bacterial protein* is recovered, which stands high temperatures and causes leucocytosis, fever, and inflammation, even suppurative. These products consist of material which was in the cells and made an essential part of the bacterial composition. The action of these proteins, to which the older tuberculin belongs, is not specific. The local effects which follow invasion are specially due to such proteins, and usually they are of an inflammatory character. All grades occur, from simple serous or serofibrinous transudates to severe suppuration and diphtherial necrosis, and also cell proliferation. The inflammatory infiltrate is explained largely by the chemotactic influence of many bacteria, by which they cause emigration of leucocytes. General leucocytosis may be due to the entrance of the bacterial proteins into the blood current.

Many bacterial products have a specific action, for typhoid bacilli

will cause only typhoid fever and tubercle bacilli only tuberculosis, and the pyogenic cocci produce serofibrinous or purulent or diphtheritic inflammation, but never circumscribed granulomata. At times tubercle bacilli cause diffuse, fibrinous, or purulent processes beside the tuberculosis, and similar production of diffuse exudation together with specific tissue proliferation is observed with some other forms. It is probable that many accessory factors are engaged in such processes, as the strength and duration of the infection, contemporary effects of metabolic products and bacterial proteins, and also the composition of the organs and the species of the invaded animal.

From the port of entry the bacteria or their products may be scattered through the body in a metastatic way, as already discussed with inflammation and tuberculosis (p. 131).

A few words may be here added on pyemia and septicemia. Pus-producing bacteria, as pneumococci, streptococci, and staphylococci, when disseminated through the body cause multiple abscesses in many organs, and death, usually after a general disease. Diffuse metastatic inflammation occurs, as purulent endocarditis, meningitis, pleuritis, pericarditis, arthritis, and osteomyelitis. This condition is called *pyemia*, and with it there are observed parenchymatous degeneration of many organs, cloudy swelling, and fatty changes in heart muscle, hepatic and renal epithelia, and often hemorrhagic nephritis. An acute inflammatory hyperplasia of the spleen is common. (See Chapter VIII.) Infectious thrombosis and embolism and infarction are also observed, frequently as the result of the purulent endocarditis. When the number of pyogenic organisms in the blood is very small they may all reach but one organ, or a few organs, and cause a slowly formed abscess or purulent inflammation of a single organ. In such cases there may be specially favoring circumstances, as when experimentally, after fracture of a bone, pyogenic cocci injected into the blood will cause osteomyelitis of the broken bone. Similar bacterial metastases occur with typhoid and gonorrheal organisms and many others.

Among bacteria many do not enter the tissues, but increase within the blood, and may be discovered there in quantity, though the distant effects in other tissues are absent unless the bacteria are pyogenic. Such diseases, in which the bacteria enter at some point and then are found only in the blood, are called *septicemia*. Among these are anthrax in mice, mouse septicemia, and others; and streptococci may have the same results. In the elements of the organs there are toxic

effects, cloudy and fatty degeneration. Since with purulent processes the two varieties of results cannot be separated, the name *septicopyemia* has been employed for them. Frequently such cases are complicated by the action of putrefactive intoxication from gangrenous areas.

Mixed infection occurs when two or more bacteria combine their effects, either as accidental coincidence or when one prepares the way for the other. Thus with tuberculosis the cavities in the lungs are largely the effect of pyogenic and other forms, and with intercurrent measles and influenza a tuberculosis already present may suddenly spread more rapidly. With purulent peribronchitis and tuberculosis the course of the disease is apt to be very severe; and with general disease, such as typhoid fever, the *bacillus coli* may cause infection and abscess formation in many portions of the body. Other examples of mixed infection are gonorrhea with metastatic abscesses, and typhoid fever with pneumonia. Many bacteria grow better in mixed cultures than alone, and thus two species together may cause a disease which with either alone would not develop. In other cases one variety of bacteria will overwhelm another by more rapid multiplication. Thus animals infected with anthrax may be rescued by a later infection with pyogenic cocci (streptococci).

The Conditions of Infection—Immunity, Antitoxin, Phagocytosis.

The first condition of successful infection is that a suitable point of entry be provided. For some bacteria this is a mucous surface (gonococcus); for others entrance into the alimentary canal is unimportant, because the gastric juice kills them. Infection through the lungs implies that the bacteria are suspended in the inspired air. From open fluids and moist surfaces bacteria do not enter the air unless drying occurs or the fluid foams or spatters. Micro-organisms attached to dry and firm matter seldom enter the air unless strong mechanical influences distribute the latter or it falls to powder. Hence tuberculous sputum rich in bacilli is not dangerous while it remains moist. A second condition is that the bacteria should be virulent. The virulence of very pathogenic forms may be lessened or even removed by artificial means. The various culture methods which are used compel the bacteria to assume a saprophytic existence, and sooner or later they lose their pathogenic activity, more or less, although still able to multiply. Positive decrease in virulence may be produced by treatment with certain chemicals (disinfection), cultivation at too high a temperature, and all measures which lead to the dying out of the

culture. Artificial attenuation can be so managed that animals very sensitive for particular bacteria suffer but a slight and temporary reaction from the weakened bacteria. A change in virulence, either an increase or a decrease, may be obtained with many forms by carrying the bacteria through certain animals; according to the more or less favorable conditions the resulting bacteria are stronger or weaker.

It is safe to assume a gradual loss of virulence under natural conditions, for the pathogenic forms after leaving the body retain their full powers for but a short time, and because of unfavorable nutritive conditions, drying, and variations of temperature their pathogenic activity decreases. This attenuation requires different periods for different bacteria, and the spores are particularly tenacious. But this natural decrease may explain why with one subject a severe or perhaps fatal general disease occurs, and with another a local and slight affection.

A third condition of infection is a sufficient quantity of the infecting organisms. Thus in tuberculosis, infection through the intestine is observed only when there are numerous bacilli in the food; with less there is no infection or only a local and rapidly healing lesion. With certain kinds of bacteria it must be assumed that a very few are enough. In cases where the organism cannot be found at the site of entry, as with diseases whose agent is unknown, and also with many septic forms, the infection is called cryptogenic.

Beside the conditions affecting the bacteria there are those of the receiving organism. Certain species of animals are specially liable to certain infections which may not occur spontaneously with other kinds. Many contagions are transmissible to but one or a few species. Anthrax germs may be carried under the skin or into the blood of cold-blooded animals without causing anthrax, while many warm-blooded kinds develop it with the fewest number of bacilli. Cattle are not immune for glanders, but are insusceptible to the bacillus of malignant edema. Thus it is evident that bacteria, like the animal parasites, prefer certain hosts, and not all kinds are receptive to all infections. Such immunity for special virus is called congenital immunity.

According to Buchner, fresh sterile blood serum destroys most bacteria, because it contains substances which are bactericidal. These he calls *alexins*, and they retain their power for a long time. They are albumins, and very sensitive to heat, sunlight, and other influences. They are supposed to form from leucocytes, and hence phagocytosis is

partly a correct theory. Inflammatory leucocytosis may thus be reparative. Alexins destroy also the red and white cells of other species. They are specific for some kinds, but there is no constant relation between the natural immunity of an animal and the bactericidal power of its serum. Baumgarten and Walz do not admit the existence of such alexins. *Natural immunity* means that an animal is not a favorable medium for the bacteria invading it. They rest their argument on the fact that the addition of slight amounts of nourishment to serum, otherwise bactericidal, removes this power and even permits free multiplication.

Natural immunity may be absolute or relative. In the latter case the use of special methods or large amounts of infective material may cause a disease. Thus with the dog—absolutely immune against typhoid, so that the largest doses do not cause an attack of the disease—tubercle bacilli in small amounts may not produce tuberculosis, while very large ones will. Here is a relative immunity with tuberculosis, and this is known as *species disposition*.

Infection does not necessarily occur in a predisposed animal with simple entrance of bacteria; certain protective influences exist. Experimentally introduced bacteria may simply disappear, and even the more pathogenic may cause only a local lesion. Pyogenic forms suspended in indifferent fluids may be put under the skin or into the blood and produce no effects; but when the infective agent remains for a time at the point of entry and multiplies there or in a lymph node, or if the fluid in which the cocci are introduced is but slightly soluble, or in itself irritating; or if an entire culture, with its contained bacterial products, be used; or, lastly, if there are wounds of the infected point, then the result may be a general infection. Bacteria which enter the blood may reach at first special capillary areas, as in the spleen, liver, and bones, and from there, if not destroyed, make metastatic suppurations. For a series of infections there are local conditions in the organs, as structure and blood supply, which are important in determining infection. Finally there is a *species immunity* as there is a species disposition, and also an individual disposition, as already discussed with tuberculosis.

Contrasted with natural, there is an *acquired immunity* which may result from surviving an attack of the disease, or may be produced by protective inoculation. The best known is the vaccination of Jenner against variola, produced by passing the virus of cowpox through the human organism. A slight and short attack of illness follows, and

the individual becomes immune against smallpox—that is, convalescence after a mild infection protects from a related but far stronger virus. In many cases protective inoculation is obtained by inserting attenuated virus in the organism to be immunized; a slight illness usually follows. The virus is attenuated in various ways. Simple standing will suffice for some cultures, others are cultivated on special media, others at a high temperature, others may be heated or dried or exposed to sunlight; or the virus may be passed through a relatively resistant organism, or mixed with chemicals. All influences unfavorable to bacteria without destroying them will decrease their virulence.

Inoculation with weak cultures is not the only immunizing method. Sterilized cultures in which the germs are dead or from which they have been removed, and hence in which only their products remain, may have similar effects. The use of cultures weakened by long standing was first made by Pasteur for chicken cholera, who also employed dry, attenuated material against rabies; while passage of the germ through another organism protects against swine erysipelas, and heating the infectious matter provides a fluid immunizing against glanders.

What happens to the infectious bacteria when they do not cause disease? How does immunity arise? In some cases the germs simply disappear. Bacteria injected into the blood may be captured by the endothelia of vessels, especially with a slow stream and in certain capillaries, as in the spleen, liver, and bone marrow. Where they lodge they multiply or die. In certain cases they are excreted by the kidney, skin, and intestine, while pyogenic forms may appear in the urine within a few minutes, and tubercle bacilli also pass out thus.

Various theories have been offered for artificial immunity. The idea of *exhaustion of certain materials* in the body, and hence cessation of bacterial growth—very much as fermentation stops when all the sugar has been converted—was advanced and held for a time; but it is not reasonable to suppose that a substance used up by the bacteria would not be reproduced by the body. The *retention hypothesis* assumed that the protective infection left bacterial products in the body which were inimical to later virulent bacteria. Metschnikoff's *phagocyte theory* sees in the power of leucocytes and other ameboid cells to englobe corpuscles and bacteria, a provision for the digestion of the latter by these cells—a view based upon the fact that with many infections, always in certain ones, ameboid cells are observed containing bacteria, and the latter are in a degenerated condition. A cure

would then depend upon the consumption of the germs by the phagocytes. Hence protective inoculation endows these phagocytes with the power of taking up fully virulent bacteria, even those which before could not be englobed. Against this theory there are several objections. In certain severe infections, as recurrent fever and typhoid, no phagocytosis has been observed, and yet the organism may recover; so the hypothesis is not of general application. The phagocytosis may also be delayed until after infection, instead of opposing it; and just where there are enormous numbers of leucocytes, as in the lymph nodes, the bacterial activity is not prevented. In suppurations healing spontaneously the pus cells may break down before the bacteria degenerate. In gonorrhea the germs do not die out, but the enclosing cells fall away, and still the disease heals. In many cases the bacteria actively invade the ameboid cells rather than being taken up by them passively. Moreover, the bactericidal action of a fluid rich in leucocytes remains after it has been frozen and thawed, which destroys the cells, but not the alexins. Where bacteria are picked up by the phagocytic cells it is probable that only the weakened or the dead ones are so "eaten;" but it is possible that the white cells produce an alexin which weakens the germs and then englobe them.

Great practical importance is given the fact that the blood serum of immunized animals may be used to protect other animals from certain diseases, as tetanus. With synchronous infection and inoculation, or even when the former precedes the latter, it has been found possible to prevent or heal the infection, as in diphtheria.

Behring's law—that the blood serum of animals which in any way have become immune against a specific disease possesses the power of conferring immunity to other species and individuals—has been demonstrated with several infectious diseases, and employed practically against diphtheria and tetanus in the human subject.

In both tetanus and diphtheria the germs are of the toxic variety, found only or especially at the point of infection, from which they send their extremely poisonous products over the whole body. Hence the basis of the general disease is an intoxication, and this may be caused by the incorporation of the bacteria or their products alone. The immunizing serum causes an immunity against both the infection and the intoxication, and is called *antitoxic*. Certain bodies form in the organism which are called antitoxins, which protect against the products of the invading bacteria, and have but slight action upon the bacteria themselves. Similar protection may be secured against certain

chemicals, as abrin, snake poison, and also against anthrax and rabies. The action is strictly specific—that is, the antitoxin opposes only the bacteria against which the animal was at first inoculated. The protective serum is obtained from animals by accustoming them to steadily increasing doses. Diphtheria serum is obtained from large animals, as the horse, which can furnish large quantities of serum. After each dose there follows a mild degree of illness, and then the antitoxins form in the body. From such gradually immunized animals the serum is at last drawn.

The exact nature of antitoxin has not been determined; it has no characteristic albumin reactions. The manner in which the bacterial poison is neutralized is also unknown. According to Behring and Roux, there is a direct neutralization of the poison—a destruction of toxin—and the antitoxin is the product of the body cells. According to Buchner, the antitoxins are bacterial products which have been deprived of poisonous qualities. Hence the immunity is not a destruction of the poison, but a rapid immunization of the cells not yet attacked by the poison.

The duration of acquired immunity varies according to whether it is active or passive. Immunity is called active when the body has withstood an attack of the disease and the antitoxin is self-formed. This variety is relatively persistent. Passive immunity is produced by the introduction of artificial antitoxin without the participation of the immunized organism. This variety is usually limited to a few weeks.

Immunity may be inherited directly through the maternal blood—not through the serum—and also through the milk during suckling; but the percentage of antitoxin in the latter is less than in the blood.

The immunity so far treated defends against bacterial poisons. There may also be an action upon the bacteria themselves; thus when patients have recovered from cholera or typhoid fever their serum shows a peculiar action upon the corresponding bacteria, to which the name agglutination has been given. If serum from a typhoid convalescent is mixed with typhoid bacilli in a hanging drop and observed through the microscope, the bacteria, previously actively motile, lose the power of movement, and adhere to each other in masses and often swell; this is called *agglutination*, or *Gruber's reaction*. Probably the capsules of the bacteria swell, and so they stick to each other. The substances which cause this effect are called *agglutinins* or *paralysins*, and cease to act if the serum is heated to 55° C.

Reversed, the action of bacteria with serum is used in serum diagnosis, especially in typhoid (*Widal's test*). The serum of a typhoid patient by the seventh or ninth day usually shows agglutinating properties with typhoid bacteria; but it has only a positive value, and must be used in certain dilutions.

The agglutination is specific in marked degree, but to a slight extent it is observed with bacteria nearly related to typhoid. The reaction is considered positive when it occurs with a dilution of 1 to 50, but it may often be obtained with 1 to 100 or even 1 to 1000 and higher dilution. A serum which in high dilution will react with typhoid may not react with colon bacilli below 1 to 40, and with other forms it is inactive or presents only the slightest agglutination.

In these cases the action is manifested against the bacteria, not against their toxins; but it does not kill them, for after a while the agglutinated forms may revive, when the addition of new serum may reproduce the reaction. Similar results are obtained in cholera as in typhoid.

The serum of an immunized animal acts similarly to the serum of human typhoid. A certain amount of it added to virulent typhoid or cholera germs, and the whole introduced into the peritoneal cavity of a second animal, causes the destruction and rapid disappearance of the bacteria (*Pfeiffer's reaction*). Here there is not only an immobilizing action, but an actual bactericidal effect, which is specific and is found only with the corresponding germ. The bactericidal substances are supposed to be formed in the spleen and the lymph nodes.

According to Pfeiffer, the agglutinating and the bactericidal actions are dissimilar. Others conclude that the bacteria, weakened by the agglutinin, are easily killed in the body cavity by the alexins. Perhaps the lack of oxygen in the latter situation may have something to do with the effect.

The Single Forms of Bacteria.

In spite of the limited morphology of bacteria, the various kinds known are very numerous, and often those which in appearance are quite similar show by their action that they belong to widely different species. Recognition of various forms is not usually accomplished by the microscope alone; the sum of all morphological and biological characters must be taken into account. This requires three kinds of study—microscopic examination of stained and living specimens; artificial cultivation, by which many life-conditions and processes have

become known; and animal experimentation, which demonstrates pathogenicity for those bacteria to which our animals are susceptible. We thus conclude whether a form of organism is saprophytic or parasitic, for what animals it is pathogenic, how nearly inoculation reproduces symptoms of human infection, and whether the bacteria or their products cause the disease.

Bacterial methods are so developed and technical, and determination of a species so frequently requires the entire technique, that only certain characters of bacteria can be discussed here—such as may be understood without technical experience.

From an invaded organism many kinds of bacteria may be taken and cultivated upon fluid or solid media; among the latter, potato, beef-peptone-gelatin and agar, and serum are most often used. With certain cautions a bacterial species may be cultivated without admixture of other kinds, in pure culture, and thus the various properties of the different kinds may be learned and afterward controlled by experiment. During growth on artificial media the germs present various points for study, as need of oxygen, destruction of the medium, and others. Many kinds soften the gelatin by excreting a peptonizing ferment; others do not. On potato many have a definite manner of growth, which enables one to recognize them at sight, among which is the typhoid bacillus. When bacteria have been divided throughout a fluid medium, which later may become firm and transparent (gelatin, agar), the single bacteria develop to colonies, and in many kinds these have characteristic properties.

I. Cocci. Streptococcus Pyogenes (*s. erysipelatis*, *s. puerperalis*). Grows in short chains or irregularly; single cocci often made of two half-spheres. One of the commonest pus producers; causes most attacks of erysipelas; phlegmons, and abscesses seldom (except with staphylococcus); lymphangitis, angina follicularis, bronchitis, pneumonia, pyemia, septicemia, puerperal fever; at times, also, osteomyelitis, peritonitis, pericarditis. Occurs in the blood in septic diseases. Found in many cases of nephritis, articular rheumatism, and exudate of anterior poliomyelitis. Important as a mixed infection with diphtheria of the throat, scarlet fever, and tuberculosis of the lungs; in the latter causes most of the suppurative processes in cavities and about the bronchi. In animals various inflammatory and suppurative processes are due to this coccus. In healthy people it is found in the secretions of the nose, mouth, vagina, and cervix uteri, but often in a non-virulent form; outside the body in water,

earth, and air. The coccus forms found in erysipelas and puerperal fever, formerly considered as a separate species, are varieties of this.

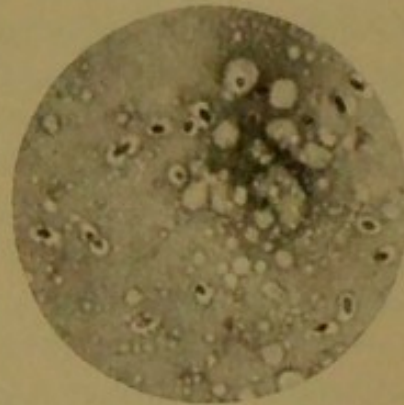
Streptococcus Lanceolatus (*pneumococcus* of Fränkel-Weichselbaum). Short chains, often of but two; single cocci, lancet-shaped, with pointed or blunt ends adjacent; in animal body capsuled, but this is lost in culture. A frequent cause of inflammation and suppuration. Found in many cases of croupous pneumonia, and at times in catarrhal pneumonia, in pericarditis, peritonitis, endocarditis, meningitis; less often in nephritis, inflammations of the female genitals, osteomyelitis, abscesses, septicemia, and erysipelas. It may be local in the tissues, and also pass into the blood and the milk. In many cases of purulent cerebro-spinal meningitis the lanceolatus is found, in others the streptococcus pyogenes, and in others a form nearly related to the first,

FIG. 113.



Streptococcus growing in long chains in bouillon culture. $\times 1000$. (PARK.)

FIG. 114.



Diplococcus of pneumonia from blood, with surrounding capsule. (PARK.)

enclosed within the cell body or the nucleus of cells. In animals inoculation is easy, and death, with intravenous injection, occurs as a septicemia; inhalation causes pneumonia. In health the coccus is found in the nasal mucus and in saliva.

Staphylococcus Pyogenes Aureus. Grows in irregular groups and produces a golden pigment. Common cause of suppuration, as abscess, furuncle, osteomyelitis, pneumonia, serous inflammation, septico-pyemia, meningitis, pneumonia, less often erysipelas; also found in endocarditis, empyema, acne, sycosis, and pemphigus. As a rule, this germ causes more localized inflammations, and the streptococcus more diffuse; it often accompanies other producers of inflammation and suppuration. Experimentally it causes abscess, pyemia, joint suppuration, and with injury to the heart valves, endocarditis, and to the bone osteomyelitis. Outside the body it is common in the dirt of finger-

nails, on the skin, in air and water. Occurs in the healthy mouth, vagina, and cervix.

There are many varieties of staphylococci, all pathogenic. Their external characteristic is the color of the pigment. The *s. pyogenes aureus* makes a golden-yellow, the *s. pyogenes citreus* a lemon-yellow, the *s. pyogenes flavus* a pale yellow, and the *s. pyogenes albus* a white pigment. Of them all the first is by far the commonest.

Gonococcus (*diplococcus gonorrhææ* of Neisser). This diplococcus is the cause of gonorrheal inflammations of mucous surfaces, and occurs in them in great numbers. The two cocci have a biscuit shape, and lie with their flat sides apposed. In contrast to other cocci occurring with them these lie within the pus cells. They are found as the cause of disease in the urethra, prostate, glands of Bartholin, and cervix;

FIG. 115.

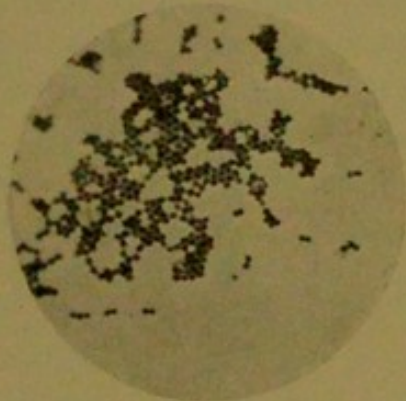
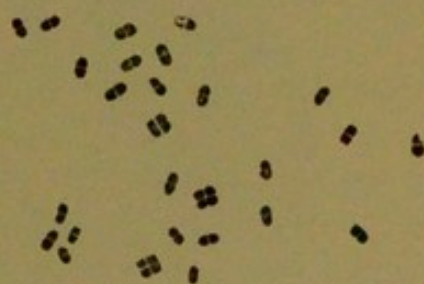
Staphylococcus. $\times 1100$. (PARK.)

FIG. 116.



Gonococci from a culture. (PARK.)

and from the epithelia they may penetrate into the connective substratum and cause purulent inflammation and cicatricial contractions. The gonococcus may cause endometritis, metritis, salpingitis, oophoritis, suppuration of joints, ophthalmia neonatorum from contagion during birth, and a similar conjunctivitis in adults. It is important for the diagnosis to see if the cocci are enclosed in the cells, and that they are decolorized by Gram's method. The secondary inflammations and suppurations in gonorrhea, as of testes, lymph nodes, joints, etc., are probably due not so much to the gonococcus as to other pyogenic organisms accompanying it. The gonococcus is hard to cultivate for even a short time, but thrives best on human blood serum.

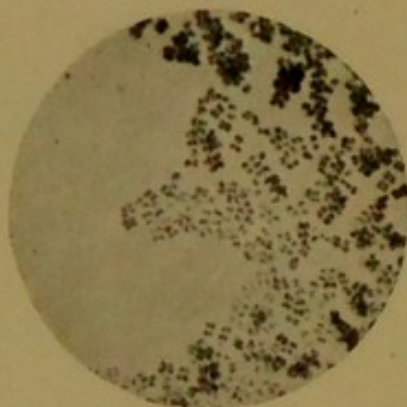
Of the *sarcina* forms there is found the *sarcina ventriculi* in the stomach, with chronic catarrh and dilatation of the organ, but probably there are several varieties here. The *sarcina pulmonum* is found in the bronchi of tuberculous patients; it is not pathogenic.

Micrococcus tetragenus occurs in the contents of tuberculous cavities and in the normal saliva of the healthy. It appears as groups of four quite spherical cocci. In man it may produce suppuration; in mice it causes a general infection.

II. **Bacilli.** **Bacillus Pneumoniæ** of Friedländer. A short rod, formerly considered a coccus, which in the animal body has a distinct gelatinous capsule, usually absent in cultures. This is the cause of many cases of pneumonia and bronchitis and of other inflammations. It is pathogenic for mice, killing them in a septicemia. Found in the healthy saliva and nasal secretion.

A similar bacterium causes a pulmonary disease of horses; and the rhinoscleroma bacillus, which is constant in the disease of the same name, is also like the pneumonia bacillus.

FIG. 117.



Micrococcus tetragenus. $\times 1000$.
(PARK.)

FIG. 118.



Friedländer's pneumonia
coccus. $\times 1000$.

The **influenza bacillus** is a very small short rod, often arranged in twos, one behind the other, decolorized with Gram's method. It is found in the sputa of the disease, especially in pus cells. It causes violent catarrh of the respiratory passages, and in alveoli of the lung pneumonia (lobular); pleurisy and pericarditis may also be due to it. The influenza bacillus is non-motile, is pathogenic for monkeys, may be accompanied by other pathogenic varieties, and so far has not been found outside of the body.

Bacillus tussis convulsivæ is oval, or a short rod, and is found in the sputa of typical cases of whooping-cough.

Typhoid Bacillus. This is a short, thick rod, sometimes growing in threads also, at times multiform. At the ends there are often refractile polar bodies; spores are not formed. Actively motile and surrounded by flagella. It does not stain by Gram's method. It occurs in the

intestinal contents, spleen, and lymph nodes in typhoid fever, and always in groups of several individuals; also in the blood and in the spots of the cutaneous roseola. Many of the complications of typhoid are due to it, as serous and purulent inflammation in the brain and cord and membranes, in the lung and kidney, and in erysipelatous and phlegmonous lesions in several organs. In other cases there is a mixed infection with typhoid bacilli and other forms, especially streptococci and staphylococci. In animals the ingestion of typhoid bacilli usually causes only an intoxication, though successful inoculations have lately been reported.

The diagnosis from the colon bacillus is very important (see the various text-books on bacteriology). (For Serum Diagnosis, see p. 215.)

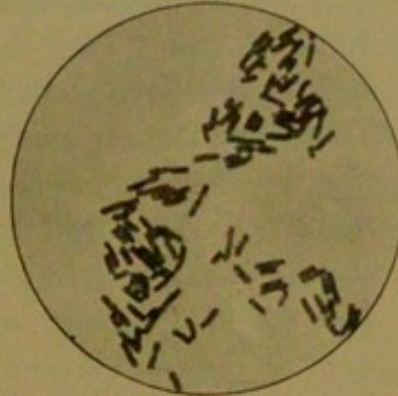
Outside the body typhoid bacilli occur in water and earth which have been contaminated by typhoid discharges.

Bacillus Coli. This germ is nearly related to the typhoid bacillus, and in morphology and cultural characteristics is very similar to it. The colon bacillus is a name for many forms, very numerous but not sharply distinguished from each other. It constantly inhabits the human colon, and from here may enter the liver and kidney. Usually it is a saprophyte, but in favoring conditions it produces typhoid and choleraic diseases, and beside intoxication may act directly as a pathogenic form. It may cause peritonitis, cystitis, and urethritis, abscess of the liver or kidney, and with incarceration or inflammation of the gut may perforate the intestinal coats and set up peritonitis. Less often it causes pneumonia, meningitis (infants), severe icterus, Winckel's disease, melena neonatorum, puerperal infection, cholecystitis, etc. Experimentally it may produce abscesses and septicemia. Outside the body it may be found in water, even from clean springs.

Bacillus icteroides is a short rod, resembling the typhoid bacillus, which has been considered as the cause of yellow fever.

Proteus, the *bacterium vulgare* of Hauser, derives its first name from the multiform appearance of the bacillus, as a thin rod, long thread, spirally wound thread, etc. It causes typical putrefaction, and is found in decaying meat, in water, the air, and the human intestine. It produces meat poisoning and similar intoxications, and is often asso-

FIG. 119.

Typhoid bacilli from nutrient gelatin. $\times 1100$. (PARK.)

ciated with bacillus coli and other forms in catarrh of the bladder, abscesses, gangrene of the lung, putrid carcinoma, etc. As the single pathogenic form it may be found with infectious icterus (Weil's disease), which has been attributed to bathing in polluted water.

Bacillus of Hemorrhagic Septicemia. This is a short, thick rod with rounded ends, not stained by Gram's method. In ordinary stains it presents a polar staining, which causes it to resemble two cocci lying together. It is not motile. Probably the causes of chicken cholera, rabbit septicemia, German swine plague, and cattle plague belong under this head. In the human subject a similar organism is found in the *morbus maculosus* of Werlhoff.

Pest Bacillus. This is a short rod, which, when derived from the body, but not in cultures, shows marked polar staining. It very quickly develops characteristic involution forms, as swelling and rounding to a more spherical form. It is found especially in the buboes of the disease, the primary skin pustule, the sputa of plague pneumonia, and usually in the blood and internal organs. The port of entry is the skin, followed by pustules and buboes, or the lung, followed by pneumonia; commonly it spreads throughout the body, causing plague sepsis. In animals infection may come through the alimentary canal, and probably this is true of man also. Immunization with plague serum has succeeded to a certain degree, and plague serum has an agglutinating power over the bacilli. Beside man the rat is very liable to the disease, and an epidemic among rats may precede that among men. It is possible that the bacillus becomes acclimated first in the bodies of rats.

Bacillus Ulceris Cancrosi. This form, not staining by Gram's method, is found in the tissues and secretions with *ulcus molle* as long chains of thin bacilli. It is the cause of this disease.

Bacillus Anthracis. This is a long, motile rod with endogenous spores, which in artificial cultures often grows to long chains. The spores, which are very resistant, are formed only in the presence of oxygen, at high temperatures, and not in the body.

Anthrax is a disease of cattle and sheep, seldom of horses and goats, widespread, and yet commoner in some localities, usually to be traced to infection through the food. The bacilli are facultative parasites which propagate and form spores outside the body. From the bodies of animals dead of the disease the bacilli are carried up to the surface of the ground, and can there be consumed with grass, etc. Other sources of infection are hair of infected animals, feces, blood, and

urine. In the human subject anthrax may infect small wounds when the individual handles infected animals, or wool of diseased sheep, and sorting rags made of the latter may also give the disease to man by inhalation of the spores. Through the intestines infection may occur by spores, for the bacilli are destroyed by the gastric juice. The bacilli are sometimes found in great numbers in the blood of the affected cadaver when there has been a general septicemia. Usually there are many local lesions, as carbuncle at the point of entry and carbuncle-like infiltration of organs.

Bacillus Tetani. This form occurs in garden earth, hay dust, on splinters of wood, in decaying fluids, and the feces of horses and cattle.

FIG. 120.

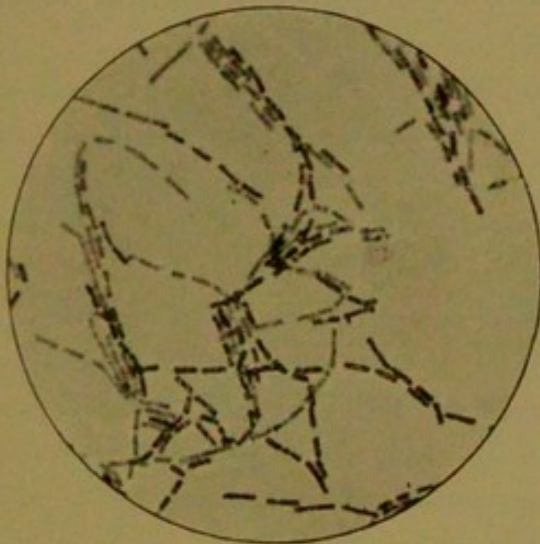
Anthrax bacilli. Agar culture. $\times 900$. (PARK.)

FIG. 121.

Tetanus bacilli, with spores in distended ends. $\times 1100$. (PARK.)

It is a fine and quite straight rod, bristle-like, which makes end spores, and with its swollen end resembles a drumstick or large-headed pin. It is motile and strictly anaerobic.

Tetanus is a transmissible wound infection. The bacilli are found only at the site of entry, and in other organs bacilli and lesions are not found. They produce toxins by which the general intoxication is caused. So-called rheumatic tetanus (without discoverable wound) is probably due to infection through the lungs. Immunization has so far succeeded for mice alone.

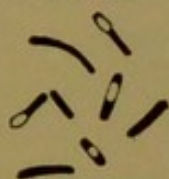
Bacillus botulinus closely resembles tetanus, and causes a certain number of meat poisonings in which the nervous symptoms are specially prominent (botulinism, sausage poisoning). Essentially it is an intoxication, the poison not being formed in the body, but solely in the meat.

All the symptoms are due to the toxin. The bacilli do not multiply in the body.

Bacillus of Symptomatic Anthrax. This is a disease of cattle, sheep, goats, and guinea-pigs, caused by a slender and fairly long bacillus, with somewhat rounded ends, motile, and anaerobic, and forming end spores in dead bodies. It produces strongly emphysematous crackling swelling of the skin and muscles, of a dark-red color.

Bacillus of Malignant Edema. In man the rather uncommon wound-infection of this name is due to a slender rod which is actively motile and makes spores in its mid-portion. It is strictly anaerobic. Experimentally it causes bloody edema at the point of infection, but does not multiply in living tissues or in the blood. Outside the body it is found in dirty water, earth, and decaying matter.

FIG. 122.



Bacilli of malignant edema. $\times 1000$.

Bacillus of Emphysematous Phlegmon. This causes gaseous phlegmon, foamy liver, gas in the blood and internal organs of cadavers; by various authors described as an anaerobic rod which is not fully understood. The colon bacillus is common with it.

Bacillus of Swine Erysipelas. This is an extremely small, motile rod, pathogenic for pig, rabbit, dove, and mouse, and in swine causes general infection and bluish-red spots on the skin, with severe inflammatory lesions of the organs. In test-tube cultures it forms a characteristic cloudy or foggy gray mass. The bacillus of mouse septicemia agrees almost entirely with this germ.

Diphtheria Bacillus (*corynebacterium* of Lehmann). Short, stout rods, about the length of the tubercle bacillus, but twice as thick, and with more varied morphology. Appears as slightly curved rods, or its ends may be swollen; wedge-shapes, long cylindrical shapes, branching forms and those with sharp ends may be found. In stained specimens appearance of septa has been noted in the bacillus, and also metachromatic granules. The cause of true pharyngeal diphtheria, found also in the larynx in the inflamed mucosa. Extremely toxic, and acts almost wholly by means of the poison it produces. Bacilli may be found in the blood, spleen, and other organs. Croupous rhinitis and conjunctivitis and some cases of otitis media may be due to this bacillus. Found in the healthy nose and mouth, especially in those waiting upon the sick.

In true pharyngeal diphtheria there is usually found streptococcus pyogenes in the mucosa along with the bacillus of the disease, and the

activity of the latter appears to be aggravated by the former, though the diphtheria germ may by itself cause diphtheria and general symptoms. Inoculation of animals produces in them local affections with false membrane, and also the general sepsis, whether bacilli alone or their toxins be introduced (p. 214).

Pseudodiphtheria bacilli resemble the true form, and occur in healthy subjects as well as with many diseases. The relation between the two is not wholly clear. Probably the pseudo forms are but weakened diphtheria bacilli.

Xerosis bacillus, which causes the disease of connective tissue of the same name, is also similar to the diphtheria organism.

FIG. 123.



FIG. 124.

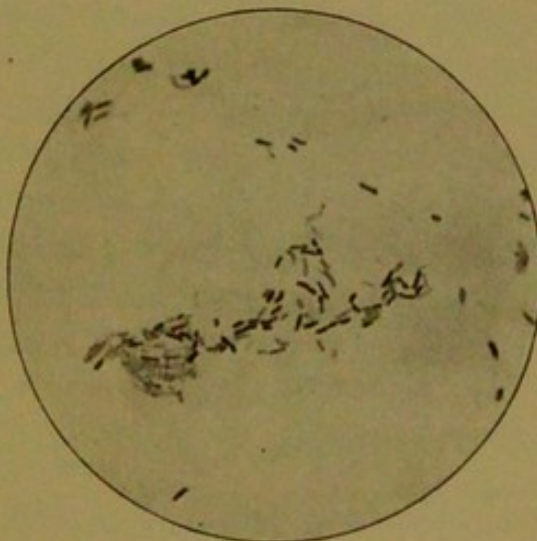


FIG. 123.—One of the very characteristic forms of diphtheria from blood-serum cultures, showing clubbed ends and irregular stain. Stain, methylene blue. $\times 1100$. (PARK.)

FIG. 124.—Glanders bacilli. Agar culture. $\times 1000$. (PARK.)

Glanders; Bacillus Mallei (*corynebacterium mallei* of Lehmann). This is a slender bacillus, thicker than that of tubercle, without motility or spores. When stained it appears to have septa, for the staining is interrupted. In general it stains less readily than others, not at all with Gram's method. Involution and branching forms are common in cultures. Infection usually passes to man from the horse. The skin and mucous surfaces are usually infected, but without wounds of the skin the bacillus may enter the hair follicles. In male guinea-pigs after intraperitoneal injection there is often a peculiar and characteristic swelling and suppuration of the scrotum and testes.

Bacilli of the Tuberculosis Group, Resisting Acids. Tubercle Bacillus (Koch), *mycobacterium tuberculosis* (Lehmann). This form is the cause of all tubercular infections. It is 3 to 5 μ long—a slender rod with

rounded ends, often slightly bent, sometimes in chains of five to six; branching forms occur in cultures; non-motile, spore formation not yet proved. In the stained specimen there may be regular colorless holes which do not represent spores. Lately it has been shown that true branching forms may occur, and clubbed or swollen shapes, as with the ray fungus, and in experimentally infected animals there may be gland-like clusters.

Tubercle bacilli are peculiar in their staining reactions, and by means of these their recognition is easy, except from lepra bacilli. They take up the stain slowly, but retain it, so that decolorizing fluids take the stain from all other forms first, leaving the tubercle bacilli stained when the process is stopped at the right time. The bacilli are

very resistant, enduring very high temperatures and month-long drying. In water, boiling for five minutes is necessary to kill them, and their virulence is but little decreased by putrefaction of the containing medium. They are facultative anaerobes — true parasites — and hard to cultivate outside the animal body (blood serum, glycerin agar). They form on the medium characteristic dry, white scales.



FIG. 125.
Diplococcus of pneumonia, with surrounding capsule.

Outside of the body the bacilli are found in dwelling-rooms, cars, street dust, and wherever tuberculous patients scatter their sputa; at times they appear singly in the air. In the healthy, as nurses, they may occur in the nasal mucus.

The bacillus is easily passed on to proper animals. Injection of a pure culture or implantation of tuberculous portions of dead bodies will be surely followed by tuberculosis.

Tuberculosis is a frequent disease of cattle; less common among sheep, goats, pigs, dogs, cats, rabbits, and guinea-pigs. In cows the bacilli often pass out with the milk, although the udder may not be diseased, and they may be recovered from butter in such cases. The flesh of tuberculous animals contains the bacilli with general miliary disease or with widespread tuberculosis of various organs, as in lymph nodes among muscles. Tuberculin, which is the protein from the bacilli, is employed to-day almost wholly for diagnostic purposes in veterinary practice. The "new" tuberculin is a plasmin.

There are many varieties of the tubercle bacillus, among which is the organism of bird (chicken) tuberculosis, which is specially active in birds, but pathogenic also for animals. By altering the culture conditions the bacilli may be adapted even for cold-blooded animals, for successful inoculations have been made on the frog and the lizard, and the disease has even been found in fishes.

Closely resembling tubercle bacilli are other forms, also resistant to acids, which cause nodular new formations in many animals (*pseudotuberculosis*), and may be found in milk, butter, on grass and dung, etc. Petri, Lubarsch, and Rabinowitsch have reported such cases, and Lehmann groups them under the name *mycobacterium phlei*. In contrast to tubercle bacilli, they all grow easily at room temperature. They are pathogenic for guinea-pigs, causing pseudotuberculosis as a fibrinous or fibrous peritonitis when inserted into the peritoneum (with butter at the same time). With a few bacilli the process may heal. Since these forms cause lesions like those of tuberculosis, they are of practical importance when present in milk and butter, for they lead to the mistaken belief that tubercle bacilli are found. When animals are injected with small numbers of bacilli and die, and the nodules contain many giant cells, the diagnosis is probably bacilli of tubercle; the true tubercle bacilli develop more slowly in cultures and in the body. In certain animals morphologically distinct bacteria may also cause pseudotuberculosis.

Lepra Bacillus (*mycobacterium lepræ* of Lehmann). This is shorter than the tubercle bacillus, takes stains sooner and without heating, and is also less resistant to acids; but we lack trustworthy distinctions between them. Lepra bacilli are found in the leprous nodules, within the so-called lepra cells, and also in ganglion cells, semen, and milk. It may be found in the nose, where perhaps the primary infection occurs. The serum of the patient agglutinates the bacilli.

Smegma Bacillus. This is a non-pathogenic rod found in the smegma about the glans penis and clitoris. Staining with carbolic fuchsin, and after-staining with concentrated alcoholic methylene blue, makes the smegma bacillus blue, while the tubercle bacillus remains red. A form like the smegma bacillus has been found in many syphilitic processes, and supposed to be the cause of them, but this is not yet proved.

Actinomyces Fungus. This stands close to the hyphomycetes, if not actually one of them. It causes infectious granulomata in horses and cattle, and at times in man (p. 139.) It occurs in the form of

“glands,” made up of a number of radially disposed threads, swollen on the ends, at times branching dichotomously, and hence compared to a rosette. Within these masses there are numerous granules, like sand, which are not spores, but come from degeneration of the rays. The club-shaped ends are due to thickening in an otherwise very delicate membrane, and they stain with orseille, while the threads stain with Gram’s method.

Infection comes by means of heads and other parts of grain, or splinters of wood, to which the fungus clings, and these have been found as foreign bodies in the foci attacked. The mouth, pharynx, alimentary canal, lungs, and skin are the ports of entry. At first there is always a local affection, but by the lymph or blood channels the fungus may spread by metastasis to various organs.

FIG. 126.

Actinomyces. $\times 250$.

III. Spirilla. *Spirillum Obermeieri*. This is the cause of recurrent fever, and occurs as long, spiral, actively motile threads. During the fever they are found in the blood; between the attacks they disappear from it. Just before the crisis they are present in the spleen, where they die and are taken up by wandering cells. They can not be cultivated, but blood which contains them will infect other men or monkeys.

FIG. 127.

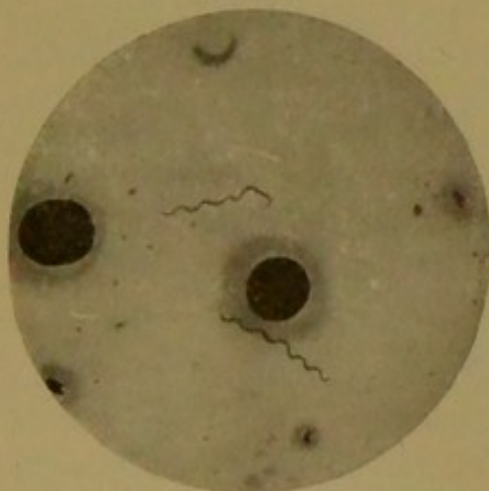
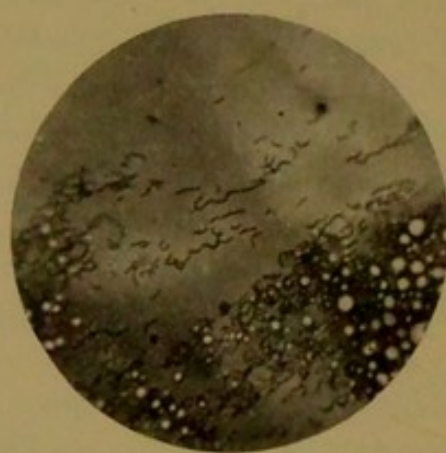
FIG. 127.—*Spirillum* of Obermeier in human blood. Carbolic fuchsin. $\times 1000$. (From SLATER and SPITTA'S Atlas.)

FIG. 128.

FIG. 128.—Contact spirilla preparation from plate culture of cholera. $\times 800$. (DUNHAM.)

Comma Bacillus (*vibrio*) of Cholera Asiatica (Koch). This is a short and thick rod, bent into comma form, with one, seldom two, flagella on the end; or without flagella, and then not motile. A series of commas may form a spiral figure. It is found in the intes-

tinal contents and tissues during Asiatic cholera. Its action is by toxins. It is seldom found in any number in the organs, but the rice-water discharges of the disease are almost pure cultures of the spirilla. During epidemics the spirillum may be recovered from the water of springs, rivers, etc., which have been polluted with cholera discharges, and also from the intestinal contents of the healthy.

There are many vibrios which resemble that of cholera. Cultures of the spirilla give the *cholera-red reaction* on the addition of sulphuric acid and heat, which depends upon the fact that the germ makes indol in the medium as it grows, and this in the presence of nitrites gives a red nitroso-indol reaction with sulphuric acid. This is not limited to cholera bacteria alone. (For the agglutination, see p. 216.)

Connected with the bacteria there are certain more highly organized forms, which present, like them, coccus, bacillus, and spirillum forms, and hence are called *pleomorphous*, in contrast to the other and *monomorphous* kinds. These make the botanical families of *cladothrix*, *leptothrix*, and *spirulina*. They are distinguished from the true bacteria, apart from their many forms, by their distinct terminal growth and more common branching. Many of the kinds that belong here are still unsettled. The *leptothrix buccalis*, which causes caries of the teeth, may be mentioned.

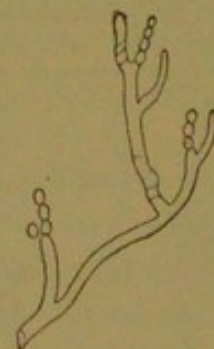
2. Hyphomycetes.

Thread or mould fungi (*hyphomycetes*) form a non-chlorophyllated mycelium (thallus) of frequently branching threads, of about 3 to 5 μ in diameter, and with many cross septa. Among these are included many which have no true spore carriers, but make spores, or conidia, by simple constriction from the ends of the hyphæ; those which have spore carriers, with the same method of sporulation; and also those which form true sporangia, within which the spores are formed. The botanical position of many of these is unsettled, but some belong to the higher fungi.

Among the simple forms without spore carriers are the following, which produce various skin lesions:

1. **Achorion Schonleini**, the cause of favus, present in numbers in the yellow crusts as rather broad threads, often with septa, tapering toward the ends. Spores moderately numerous, in chains.

FIG. 129.



Trichophyton tonsurans.
Diagrammatic. (After LEHMANN.)

2. **Trichophyton Tonsurans.** Like the former, and occurs in several shapes, not sharply defined from each other. The fungus of herpes tonsurans belongs here, and others occur with similar skin lesions.

3. **Microsporon Furfur.** Causes *pityriasis versicolor*. Many mycelial threads and spores, the latter in clusters.

Among the true mould fungi with spore carriers are:

1. **Mucor.** On the end of the spore-carrying hypha the sporangia form from a mother cell, in which, by continuous division, numerous spores develop, enclosed by the membrane of the cell. When the cell is destroyed the spores are set free. (Fig. 131.)

2. **Aspergillus.** At the end of the spore carrier there is a nodular swelling, and on the external surface sterigmata form, from which the spores separate (conidia). (Fig. 130.)

FIG. 130.

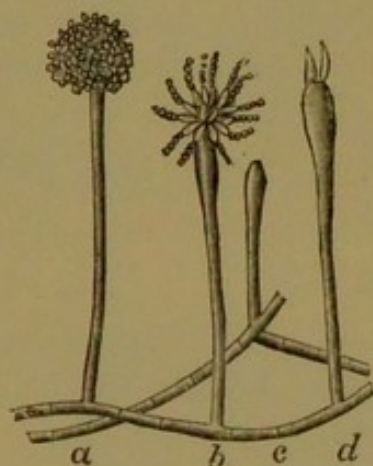


FIG. 131.

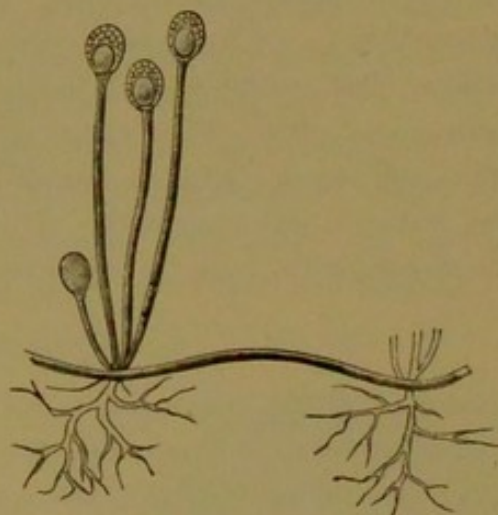


FIG. 130.—*Aspergillus*. At *b* a few of the spore-bearing sterigmata are shown; the usual picture is given at *a*. (After MEZ.)

FIG. 131.—*Mucor stolonifer*. (After MEZ.)

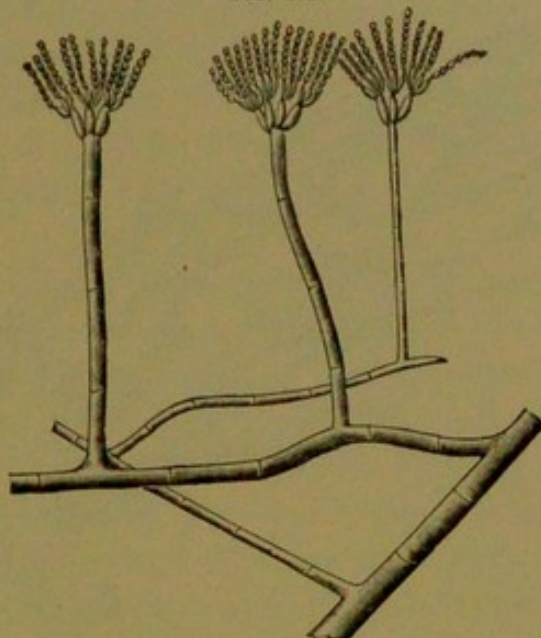
Both figures from Lehmann. Die Methoden d. prakt. Hygiene, Wiesbaden, 1901.

3. **Penicillium.** The spore carrier branches at the end, and on the single divisions (basidia) the spores (conidia) are arranged in series. (Fig. 132.) Among the simplest in organization is the oidium variety, in which the spore hyphae are not distinguished from the ordinary hyphae, and the conidia separate directly. (Fig. 134.)

In general, the fungi are not of great pathological importance, since most of them are saprophytes, but some of them have pathogenic power. Intravenous injection of some spores in rabbits will cause a general and fatal infection. In man certain aspergilli may cause local affections of the skin, ear, conjunctiva, and intestines, and in the

lungs there is known a *pneumomycosis aspergillina*. The invasion of these fungi is usually but an accompaniment of pneumonia in very debilitated subjects; but there can be no doubt that many mould

FIG. 132.



Penicillium. (LEHMANN, loc. cit.)

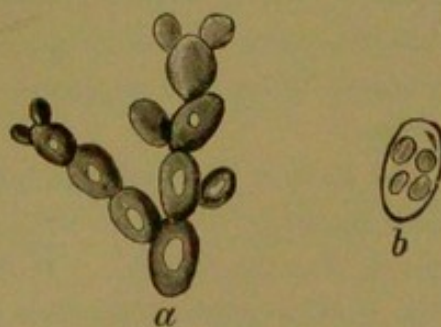
fungi not only attack parts which are necrotic, but may independently produce necrosis and suppuration, and, in certain conditions, a general fatal disease.

3. *Saccharomycetes* (Yeast Fungi).

These are one-celled fungi, which increase by budding. This occurs as slight projections on the side, which gradually attain the size of the original cells, and then may separate. The young cells may remain attached to the parent cell, and, by their later branching, form long chains or even a mycelium.

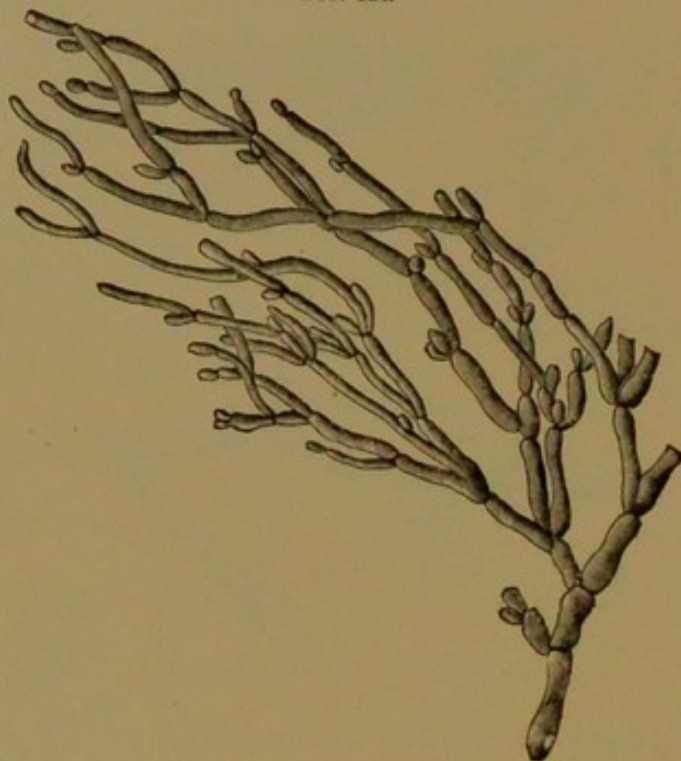
Yeast fungi occur in the stomach in digestive disorders. One pathogenic species is called *saccharomyces albicans*, the organism of thrush. It consists of subdivided threads, which present round or oval conidia at many places. It occurs in children and the debilitated, in the mucous surfaces of the mouth, pharynx, esophagus, stomach, small intestine, and

FIG. 133.

a. *Saccharomyces*. b. Cell with four spores. (LEHMANN, loc. cit.)

vagina, and in the nipples of suckling women. It may penetrate the epithelium, and form metastases to deeper organs (brain, kidney). By many authors it is put among the hyphomycetes.

FIG. 134.



Saccharomyces albicans. (After GRAWITZ, in Lehmann, loc. cit.)

B. ANIMAL PARASITES.

As among the vegetable parasites, the animal belong chiefly to the lower members of the class, although some rather highly organized forms, as insects, may be reckoned among them. Apart from the protozoa, which are one-celled and not so very distant from the vegetable kingdom, there are many worms which lead a parasitic existence. Invasion by animal parasites is called *infection*, as with the former species.

The animal in which the parasite occurs is known as its *host*. For every parasite the possible hosts are few; many are found only in man or a single animal. Certain forms are parasitic during their entire lives in the same individual; others have different hosts at different stages of their development. A great many parasites present what is termed *alternation of generations*; that is, regular and typical alternation of fully developed sexual generations and one or several non-sexual. These generations may be passed in one or more hosts. The

asexual forms develop from eggs or embryos only when taken up by certain definite animals; but in these they do not become sexually mature, but remain until they die or enter another host, and in the latter they become sexual. Thus the non-sexual forms of many tapeworms develop in the human or animal intestine to actual tapeworms, and the young echinococcus in the dog's intestine to the tenia echinococcus. This arrangement is called an alternation of hosts. The species in which the young form develops is called the *intermediate host*; that in which sexual maturity is reached is called simply the *host*.

Many other forms are parasitic only for one stage of their development, and live independently for the others; this is called periodic parasitism. This variety and the lifelong forms are grouped as *stationary parasites*, in contrast to others, as many insects, which frequent the host only for a time, and hence are called *temporary parasites*. Further, the *epizoa* are distinguished from the *entozoa*—the former living upon the host, and the latter within it. Many parasites move about within the host by the lymph or blood stream passively or in an active manner. Diseases caused by the entrance of parasites into the tissues are called invasion diseases.

Infection with parasites may occur in many different ways. Those that change their hosts often are taken into the digestive tract of the definite host with the organs of the intermediate host, the latter serving the former as food. The results are at times local, at times general disturbances. The animal parasites are chiefly mechanical in their action. In the organs attacked there may be a reaction which leads to the encapsulation of the parasite or atrophy and mechanical disorders of various kinds. In many organs there may be a special lesion, as icterus, when the echinococcus invades the liver, hydrocephalus with a cysticercus in the brain, hematuria with filaria in the blood, etc. General symptoms are either nervous, as with tapeworms, or febrile, as with trichinæ.

I. PROTOZOA.

From this class—one-celled organisms on the border between vegetable and animal forms—but few are parasitic in man; but the numbers increase as diseases formerly ascribed to bacteria prove to be due to protozoa (malaria), and hence their importance may yet have more consideration.

Protozoa are divided into four classes—*sarcodinea*, *flagellata*, *sporozoa*, and *infusoria*.

I. **Sarcodinea.** To these belong the rhizopoda—naked, contractile particles of protoplasm, at times with a silicious or calcareous envelope, with the power of extending protoplasmic pseudopods. Among these are the amebas—naked sarcodinea with lobulated pseudopods.

The *ameba coli vulgaris* (*ameba mitis*) occurs in the normal and the diseased intestine. Similar forms are found in tropical dysentery in the wall and contents of the intestine and the frequently complicating liver abscesses. *Ameba dysenteriae* (Fig. 135) is believed by some to be the cause of amebic dysentery.

FIG. 135.

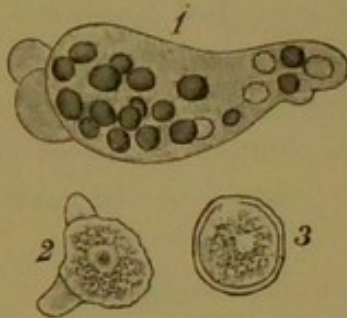


FIG. 135.—1. Ameba from dysenteric stool, with vacuoles and enclosed red cells. 2. Ameba from straw infusion. 3. The same encysted. $\times 600$.

FIG. 136.



FIG. 136.—*Trichomonas vaginalis*. $\times 100$. (After KÜSTER.)

II. **Flagellata** (*mastigophora*). Non-ameboid organisms, which move by means of one or more flagella. The body contains contractile vacuoles, and often shows a cuticle and an undulating membrane.

Trichomonas (*cercomonas*). Pear-shaped body, with four flagella on one end.

Trichomonas Vaginalis. From 12 to 30 μ long, 10 to 15 μ broad. In vaginal mucus.

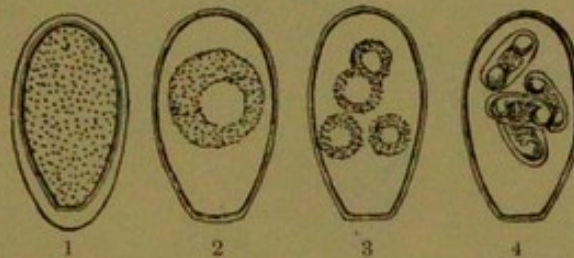
Trichomonas Intestinalis. Smaller than the former: 4 to 15 μ long, 3 to 4 μ broad. Occurs in the gut.

III. **Sporozoa** (*gregarinidae*). Protozoa without motion, living in the bodies of other animals. The body is long, with a cuticle. They become encysted in a capsule; then the individual breaks up into numerous particles, each containing a nucleus, of which each forms a

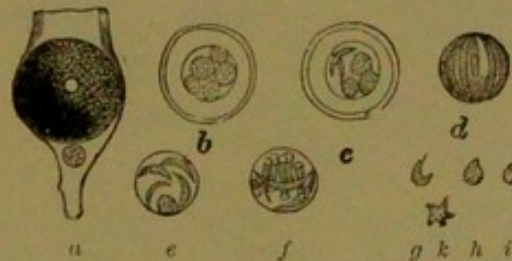
capsule. These are called *spores* or *pseudonavicella*, and from them the new sporozoa are formed.

Here belong the *coccidium oviforme*, which is common in the liver of the rabbit; also Miescher's sacs, found in the striated muscle of mammals, especially pigs. (Fig. 139.) These appear as whitish deposits in the muscle, lying with their long axes parallel with the fibres, and may be visible in the gross. They occur in the pig, sheep, horse, cattle, and house animals, and as a rule cause but little disturbance. They have a thin capsule, and contain small, sickle-shaped bodies, like those of the gregarinidæ.

FIG. 137.



Coccidium oviforme from the liver of the rabbit. 1. *Coccidium* in an epithelial cell from a bile passage. 2. Encapsuled *coccidium*, the protoplasm contracting to a ball. 3 and 4 arise from four *pseudonavicella*. In 4 the C-shaped spores are seen. (After LEUCKART.)



Coccidium from the gut of the mouse. a. Naked *coccidium* in an epithelial cell from the gut. b, c. The same encapsuled, the contents dividing into sickle-shaped bodies, which at g become free and begin ameboid movements, h-k. (After LEUCKART.)

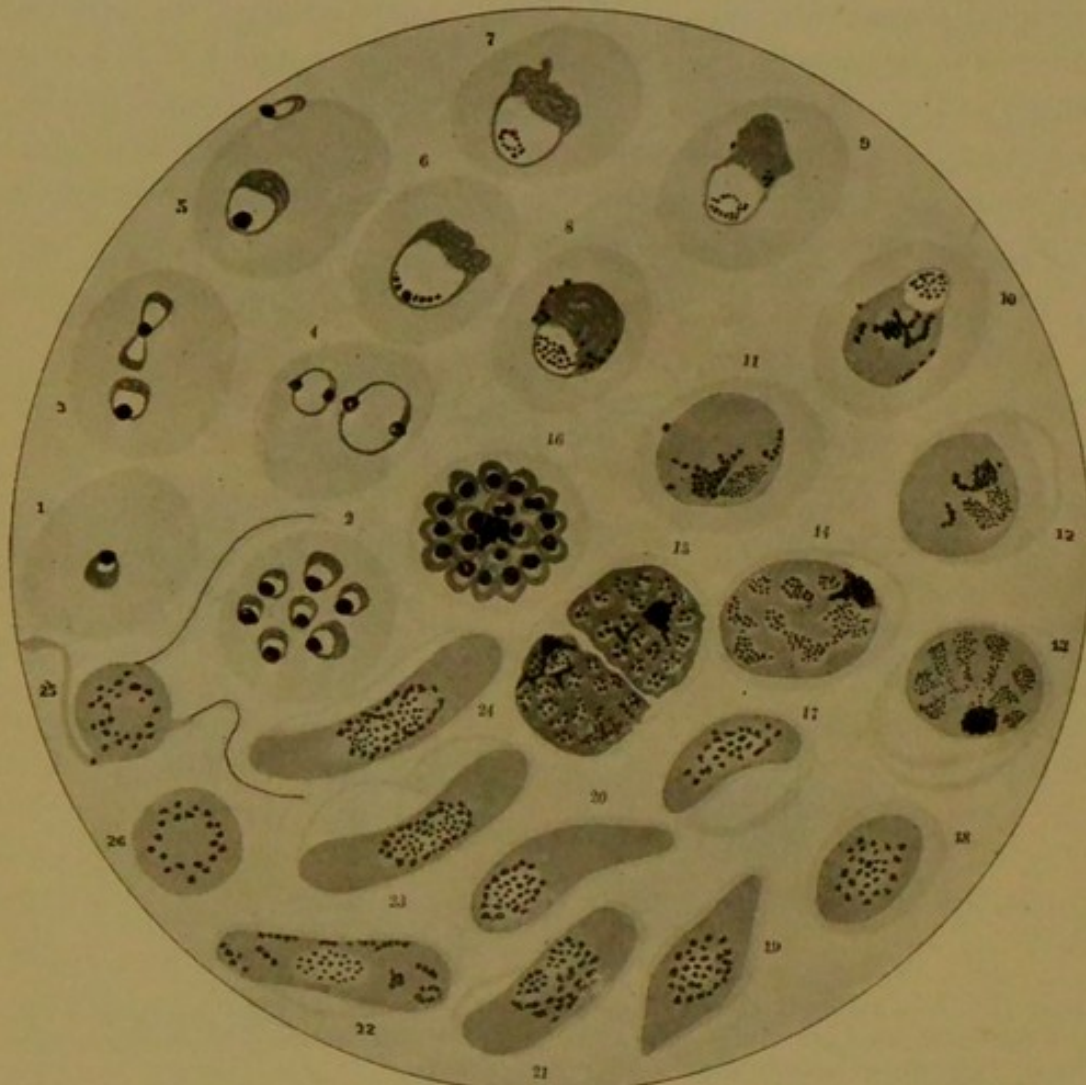
Coccidia are found also in *molluscum contagiosum*, which they probably cause; and also as accidental parasites in many tumors.

Among the sporozoa are the *hemosporidia*—ameboid, motile parasites living in the blood. The most important of these is the plasmodium of malaria, of which several species are known.

The infection in man follows the bite of a mosquito belonging to the anopheles variety. The parasites enter the blood and then pass into the red cells, where they show ameboid movements and grow into various forms. They destroy the substance of the red cell, and in its middle portion pigment collects. When the parasite has grown to occupy nearly the entire red cell it divides into a rosette-like group

of regular portions—the merozoites. These become free, and as entire plasmodia enter new red cells. The fever coincides with the entrance into new cells.

FIG. 138.



Cycles of estivo-autumnal parasite. 1. Very young form. 2. Infection of one cell with seven young parasites. (Drawn from a marrow-smear.) 3. Triple infection; two parasites joined by single chromatin mass. 4. Double infection; peculiar rings with two chromatin grains at opposite poles. 5. Double infection; small ring adherent to cell. 6, 7. Signet-ring forms; subdivision of chromatin. 8, 9. Later ring forms, with subdivided chromatin and few pigment grains. 10-12. Full-grown forms with finely subdivided chromatin and gradual concentration of pigment. 13, 14. Stages of presegmenting forms, with concentrated eccentric pigment. 15. Double infection with separate presegmenting bodies. 16. Estivo-autumnal rosette. 17, 18. Young crescent and ovoid. 19. "Pulsating" crescent. 20-22. Various forms of crescents. 23. Two bows about single crescent. 24. Fully developed crescent; two masses of chromatin; achromatic substance; double wreaths of pigment. 25. Diagrammatic flagellating body. 26. Extracellular sterile body.

According to the species, the developmental stage lasts a varying length of time—forty-eight hours with the tertian, seventy-two hours with the quartan. The pernicious autumnal form, or quotidian, is a tertian parasite in which a slighter attack of fever on the second day

gives the appearance of a quotidian. This is due to a peculiar form, which resembles that of tropical malaria.

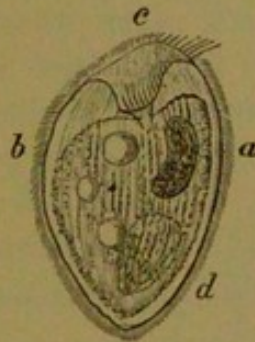
Certain of the merozoites form crescentic parasites in the human blood—the so-called crescents of Laveran—which enter the intestine of the mosquito. There they differentiate to a female macrogamete or a male microgamete, the latter possessing flagella. A flagellum is not an organ of locomotion in this case, but breaks off and functionates as a spermatozoon, entering the body of the macrogamete. This breaks up into numerous small, worm-like bodies, which penetrate the gut

FIG. 139.



Miescher's sac. $\times 50$. (After LEUCKART.)

FIG. 140.



Balantidium coli. a, Nucleus. b, Vacuoles. c, Peristom. d, Food particles. $\times 300$. (After LEHMANN, loc. cit.)

wall and enter the salivary glands of the mosquito, and from there again pass into human blood during the bite of the insect.

IV. *Infusoria*. These are parasites with permanent form, with a homogeneous, transparent cuticle and cilia or flagella. The mouth and the anus are present as depressions in the surface, and there are one primary and one or more secondary nuclei.

Here belongs the *balantidium coli*—an occasional inhabitant of the human colon, without known pathogenic action. (Fig. 140.)

II. VERMES (WORMS).

The worms have a laterally symmetrical, flattened, or rounded body, without skeleton or limbs. They consist of a soft parenchyma enclosed in a chitinous envelope, possess paired excretory tubes, and some also a gut. Many have clasping organs on the head. The parasitic forms belong to the flat worms, or platyhelminths, and to the round worms, or nemathelminths.

1. *Platyhelminths* (Flat Worms).

Body flat, long, often segmented; gut present in many, may end blindly, or be absent (cestodes); central nervous system is a double brain nodule, from which nerves proceed; excretory apparatus on two main branches, which end behind in common, into these numerous small canals open; blood and respiratory system usually absent. Most forms are hermaphrodite, with a complicated sexual apparatus.

A. Cestodes. These are flat and long, usually segmented, without mouth or intestine, the head furnished with two to four sucking disks. The head, or scolex, is slightly swollen compared with the parts just behind it, and often presents a rostellum and a double row of hooks. Behind the head is the neck, in which segmentation is not clearly shown, and then follow the segments, or proglottides, which increase in size toward the hind end. These break off, and may live for a time apart from the worm. Each segment has its own male and female organs, whose ducts open in common either on the side or the surface; the uterus is specially prominent. Only the old segments are sexually mature.

The anterior part, which reproduces the segments after they have broken off, is found as a scolex in the young worm, which inhabits and becomes sexually mature in another species, there being an alternation of hosts. The sexually complete worm produces eggs from which larvæ develop in the body of the intermediate host. These are asexual, and become tapeworms in the definitive host. The various stages are as follows:

Within the egg an embryo forms, provided with six hooks; and when the proglottides leave the intestine of the host and fall apart in water, or on plants or manure, the eggs become free, and they develop to another worm only when they enter the alimentary tract of the intermediate host with its food or drink. Here the egg membrane is digested off, and the free embryo, unless passed out of the body, bores into the intestinal wall, and reaching the blood is carried to various organs, where it becomes a larva. Among certain cestodes the embryos now make the cysticercus forms, losing their ring of hooklets, and developing as large vesicles filled with fluid. (Fig. 144.) From the wall of such a cyst a hollow projection reaches inward, and in its cavity develops a rostellum, with hooks and the sucking disks. A tapeworm's head is thus formed—a scolex—but

it is retracted and inverted within the cyst, like the reversed finger of a glove, and remains in this condition until received by an intermediate host. When the cyst has been dissected out a gentle pressure may make the head project, and the bladder part then appears as a relatively large appendix of the scolex, which in its natural form presents the rostellum, hooks, and suckers on its outer surface. Usually but one scolex forms from each cyst, but in some forms (cenurosis) many develop. In the echinococcus there are formed from the first cyst a number of daughter vesicles, and from these, again, granddaughter forms; and scolices may develop in all or most of these. Other varieties make no cysts, but small, solid bodies, which are called plerocercoid, in which the head is not distinguished from the solid tail, though originally inverted.

FIG. 141.



FIG. 142.

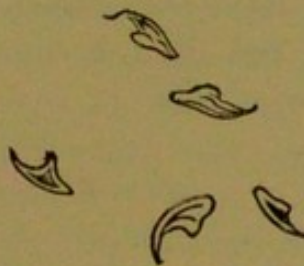


FIG. 143.



FIG. 141.—Head of *tenia solium*. (After HELLER. Ziemssen: Hdb. d. spec. Path., Band vii. 1876.)

FIG. 142.—Hooklets of *tenia solium*. (After HELLER, loc. cit.)

FIG. 143.—Segment of *tenia*. (After HELLER, loc. cit.)

The encapsuled, plerocercoid form of *bothriocephalus* may grow in length and resemble a small, mature tapeworm, but it never grows in an intermediate host to a mature sexual tapeworm. When these larval forms enter the alimentary canal of suitable animals the scolex protrudes, the bladder portion is digested off, the young scolex adheres to the intestinal wall by its suckers, and begins to form the proglottides.

Human tapeworms belong to the *teniadæ* and the *bothriocephalidæ*.

(a) **Teniæ.** Head roundish, with four suckers; sex-opening lateral; young form bladder-like.

Tenia Solium. From 2 to 3 metres long; head 1 mm. in diameter; has rostellum, with twenty-six hooks, in two circular rows. (Figs. 141, 142.)

Mature proglottides are 8 to 10 mm. by 6 to 7 mm.; in number there may be 800 to 900. The uterus has seven to ten branches, which divide peripherally. Segments are passed only with the feces of the host.

FIG. 144.



FIG. 144.—Diagrammatic section through a cysticercus bladder in which a tapeworm is sprouting. (After FLEISCHMANN. Lehrb. d. Zool., Wiesbaden, 1898.)

FIG. 145.



FIG. 145.—Egg of *tenia solium*. (After SEIFERT-MÜLLER.)

The eggs (Fig. 145) are oval, with peripheral radial markings, and contain, when ripe, a round embryo. They are about 0.03 mm. in diameter.

The *cysticercus cellulosæ* makes usually single vesicles, of the size of lentils or beans, in the muscle tissue; in these the young scolices form. (Fig. 144.)

Mature *tenia solium* is found only in the small intestine of man; the further development of the eggs occurs in another host, especially in the pig, which obtains them from human excrement. In its stomach the shell is dissolved, and the free embryo bores with its hooks into

FIG. 146.

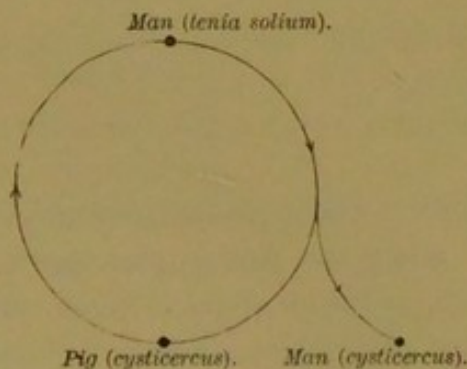


FIG. 146.—Plan of alternation of hosts with *tenia solium*. (After BOLLINGER.)

FIG. 147.



FIG. 147.—Flesh of pig with cysticerci. Natural size: heads of worms shine through. (After HELLER.)

the gut wall, and wanders or is carried by the blood to various organs, where it forms a cysticercus. The time required is two to three months. In the intermediate host it may exist, without further

development, for three to six months. If it finally dies the bladder shrivels or calcifies.

The cystic form may be found in great numbers in the flesh of the pig, especially at the root of the tongue, but at other places also.

Man is infected by the use of raw, smoked, or imperfectly cooked flesh of swine. The worm is freed in the stomach, and in the small intestine makes completely mature segments in ten to twelve weeks; it may persist for ten to fifteen years. The worm is most frequently found in those who often eat or handle raw pork, as butchers and cooks. In different countries the occurrence of cysticeroid forms varies; in Germany 1 pig in every 324 is thus diseased.

Beside the tenia, its larval *cysticercus* is found in man in various organs, as the brain, eye, muscles, heart, subcutaneous connective tissue, lung, liver, etc. In the brain they may lie free in the ventricles; elsewhere they are usually capsuled, and from the size of a hazelnut upward, solitary or in great numbers. Often they form clusters of grape-like arrangement (*cysticercus racemosus*). Since the eggs lose their covering only in the stomach, not in the intestine, it is necessary that they be swallowed, as with vegetable salads or from unclean hands; or in vomiting the eggs may reach the stomach from below, and there be set free (self-infection). In all cases the embryos pierce the intestine and reach the viscera, where they become cysticerci.

Tenia Saginata (mediocanellata). Head larger than that of *tenia solium*—1.5 to 2 mm., with four large suckers; rostellum rudimentary, no hooks. The whole worm is larger and stronger than *tenia solium*—7 to 8 m. long; segments, when ripe (Fig. 148), measure 18 mm. by 7 to 9 mm.; the number may be 1200 to 1600. The uterus has twenty to thirty dichotomously dividing branches, which are finer than in *tenia solium*. The segments crawl out of the anus spontaneously, apart from defecation, often in chains, and continue in active motion. The eggs are very similar to those of *tenia solium*.

The *cysticercus* form occurs in numbers in the pig, and also in the muscles and viscera of cattle, but smaller than the *cysticercus* of *tenia solium*.

The complete worm occurs only in man, and is more common than *tenia solium*; the eggs may appear in the feces. The development of the larva proceeds in the muscles and organs of the cattle which have eaten grass, etc., soiled with human excrement or drunk infected water.

Human infection results from the use of infected beef which is eaten raw or half cooked, and is common where this practice prevails. Further development is like that of *tenia solium*.

FIG. 148.



FIG. 149.



FIG. 150.

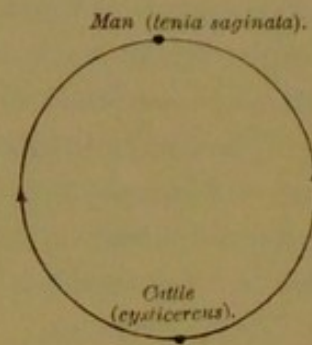


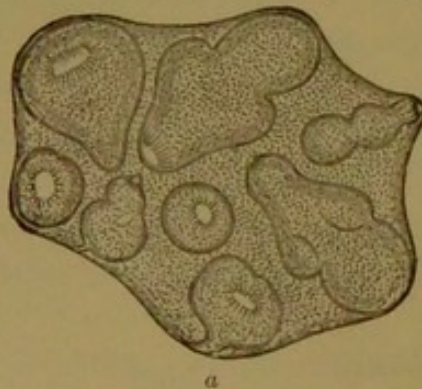
FIG. 148.—*Tenia saginata*, head strongly pigmented. (After HELLER, loc. cit.)

FIG. 149.—Segment from *tenia saginata*. (After SEIFERT-MÜLLER.)

FIG. 150.—Diagram of the hosts of *tenia saginata*. (After BOLLINGER.)

Tenia Echinococcus. Smaller, 3 to 6 mm. long. A parasite of the dog. Head with rostellum and double row of hooks, fourteen to twenty-five in number; made up of three or four segments, of which the last usually exceeds in length the rest of the worm.

FIG. 151.



a



b

a Brood capsule of echinococcus with tapeworm heads. b. Scolex retracted. (After HELLER.)

The young echinococcus makes cysts of various sizes, from a few millimetres in diameter to the size of a child's head. Its wall is a chitinous cuticula, $\frac{1}{2}$ to 1 mm. thick, on the inner surface of which there is a delicate layer of parenchymatous tissue. It is filled with clear fluid in which there is no albumin, but succinic acid may be found in it.

The bladder may remain sterile or proliferate. In the latter case scolices develop directly from the parenchyma layer, or a brood capsule forms (Fig. 151), in which the heads then grow. The single scolex is about 3 mm. long, with four suckers, a rostellum and two rows of hooks, and fine granules of lime salts are scattered through it. A brood capsule may contain as many as twenty-five scolices. From the cyst wall secondary bladders with a chitinous wall may form; these may become loose, and within them others develop, and from all these scolices may be produced. By rupture of the capsule they may become free. Contrasted with this endogenous proliferation there is an ectogenous, in which the daughter cysts protrude; and if they remain connected with the primary cyst, grape-like clusters of them may be found all through an organ. The latter form is called *echinococcus racemosus*, *multilocularis*, or *alveolaris*.

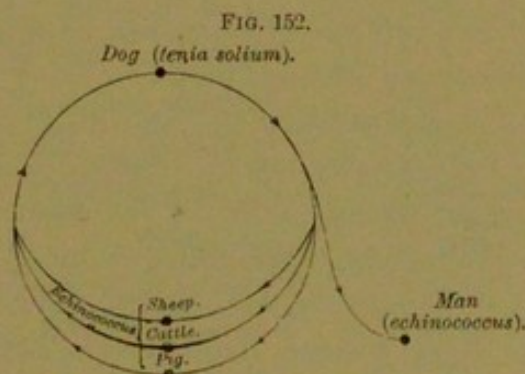


Diagram of the hosts of echinococcus. (After BOLLINGER.)

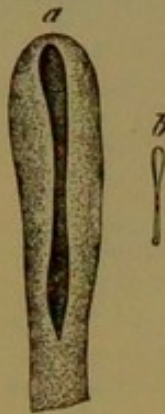
Tenia echinococcus is usually found in great numbers in the intestine of dogs, which are inoculated by swallowing infected meat. In various ways the eggs reach the alimentary tract of man or house pets. Direct contact with the dog's snout, which often touches his anus and brings away the eggs, or with the hair, on which eggs may hang, explains many human infections. The eggs develop and the embryo wanders into the organs and forms cysts—most commonly in the liver, lung, pleura, kidney, muscle, brain, spleen, bone, eye, and subcutaneous tissue. Its growth is slow. After nineteen weeks the cyst may be as large as a walnut, and after five months the brood capsules are formed. The effect in the tissue is usually that of mechanical pressure and atrophy. With larger size they make extensive tumors. The echinococcus may die and be absorbed, or the shrunken bladder is filled with lime salts and detritus. After puncture and other wounds the cysts may suppurate. Perforation into various cavities

may occur, with metastatic transport of portions. The most favorable perforation is through the skin; at other times it occurs through the vagina, bladder, bronchi, etc. Embolism may infect distant organs with small cysts.

The diagnosis depends upon finding the chitinous membrane or scolices or single hooks; the latter are 0.03 to 0.04 mm. long.

The distribution of echinococcus varies in different regions, and usually runs parallel with the number of dogs. It is commoner with women, on account of their more intimate fondness for dogs.

FIG. 153.



a. Head of *bothriocephalus latus* from the side, enlarged. b. Natural size from the flat. (After HELLER.)

(b) *Bothriocephalus* (*bothriocephalus latus*). Head flat, with two slit-like suckers, no hooks; sexual opening on the flat of the segment. The largest tapeworm in man—5 to 9 m. long; segments number 2400 to 3500. The mature proglottides measure 10 to 12 mm. broad by 3 to 5 mm. long. In separating several break off together. The uterus forms a rosette, like a winding tube, in the middle of the segment. The eggs are oval, surrounded with a membrane, which at one pole makes a cover. (Fig. 155.) In

water and air the eggs become dark brown and the uterus more clearly seen. The embryo is ciliated.

The young form is a plerocercoid, made up of a scolex and a solid tail-piece, not sharply distinguished from the head. It occurs in the

FIG. 154.



FIG. 155.



FIG. 156.

Man
(*bothriocephalus latus*).

Fish (asexual
bothriocephalus).

Unknown intermediate
host (plerocercoid).

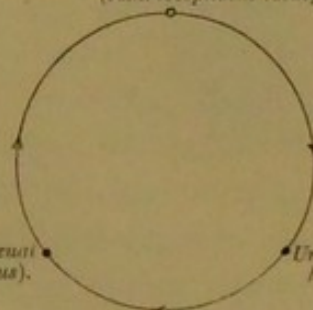


FIG. 154.—Segments of *bothriocephalus latus*. (After SEIFERT-MÜLLER.)

FIG. 155.—Egg of *bothriocephalus latus*.

FIG. 156.—Diagram of hosts of *bothriocephalus latus*. (After BOLLINGER.)

flesh and intestine of fishes, especially of the pike and catfish, and the mature worm is found in both man and dog.

The embryos develop after the eggs have reached water, becoming free from loosening of the cover, and the young moving by their cilia. The latter are lost after a time. Since the muscles and intestines of fish contain only complete plerocercoids, never undeveloped ones, and since these bore through the gut of the fish, it is probable that they develop first in some small water animal which fishes eat, and thus have two intermediate hosts. Human infection follows use of the fish as food.

In many countries *bothriocephalus latus* is endemic, as in Western Switzerland, Sweden, parts of Russia, Poland, and North Germany.

B. Trematodes (*sucking worms*). These are flat, leaf-shaped, non-segmented, with a mouth orifice and a double intestine which ends blindly. Suckers are found on the front end and the ventral surface.

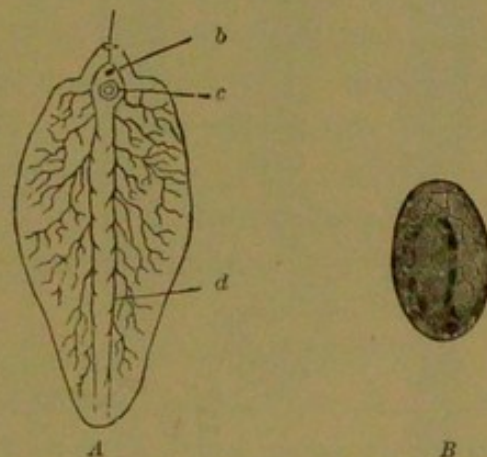
At the bottom of the former lies the mouth opening. Most of these worms are hermaphrodite. Development occurs with many alternations of generation and intermediate hosts. The eggs develop outside the body, most often in water, as ciliated larvæ. These enter snails, frogs, and mollusks, and form sporocysts or germ sacs, which multiply either by division or budding. The sporocyst develops rediæ asexually, which then become very motile cercariæ, provided with a tail, suckers, and a gut. These leave the host, swim in the water, and bore their

way into another water organism, in which they become encapsuled. With the flesh of this second host they enter the definitive host, and after the capsule has been digested off they become free and sexually mature.

Human trematodes belong to the *distomidæ*, which have two suckers—one at the anterior end and one on the ventral surface.

Distomum Hepaticum. From 28 to 32 mm. long. Suckers close to each other, and between is the genital pore. Anterior part of the body conical; hind portion leaf-shaped. Found in the intestine and bile-ducts of many domestic animals, as sheep; at times in man. Eggs oval, with a lid, 0.13 mm. long. Infection of sheep occurs

FIG. 157.



A. *Distomum hepaticum*. $1\frac{1}{2}$ times natural size. a. Anterior sucker. b. Genital pore. c. Ventral sucker. d. Limbs of the intestine. (After LEHMANN.) B. Egg of *distomum hepaticum*. (After SEIFERT-MÜLLER.)

probably by the use of water plants in which the cercaria is encapsuled.

Distomum Lanceolatum. From 8 to 10 mm. long. Lancet-shaped. Fairly frequent in man.

Distomum Hematobium. Sexes separate. Body long—male with strong sucker; along the posterior edge a shallow fold, which acts as a gynecophoric canal and encloses the female; the latter is long and thin. They live as paired parasites in the portal vein and the veins of the intestine and bladder. Found on the northern coast of Africa, especially in Egypt. Produce hematuria, chlorosis, hyperemia, bleeding and inflammation in intestine, ureters, and bladder.

2. Nemathelminths (Round Worms).

The round worms are long, cylindrical, with many segments in rings; and to these may be attached appendages, as hooks, papillæ, or bristles. They have a nervous system, and excretory organs in the form of two slender canals. They are without bloodvessels or respiratory organs. The sexes are commonly separate.

1. *Acanthocephali*. Head distinguished from the body, and used for clinging; no mouth or intestine; *echinorhynchus hominis* the only and rare example.

2. *Nematodes* (thread worms). Long, usually pointed at both ends; bristles or papilla-like appendages, especially at the mouth and genital opening; anus usually ventral and posterior. The larger forms annulated and marked with four longitudinal lines. Mouth surrounded with lips. Alimentary canal divided into mouth cavity, bulbous pharynx, esophagus, stomach, and chyle gut. Many round worms lay eggs; others are viviparous. They vary from microscopic size to several decimetres in length.

FIG. 158.

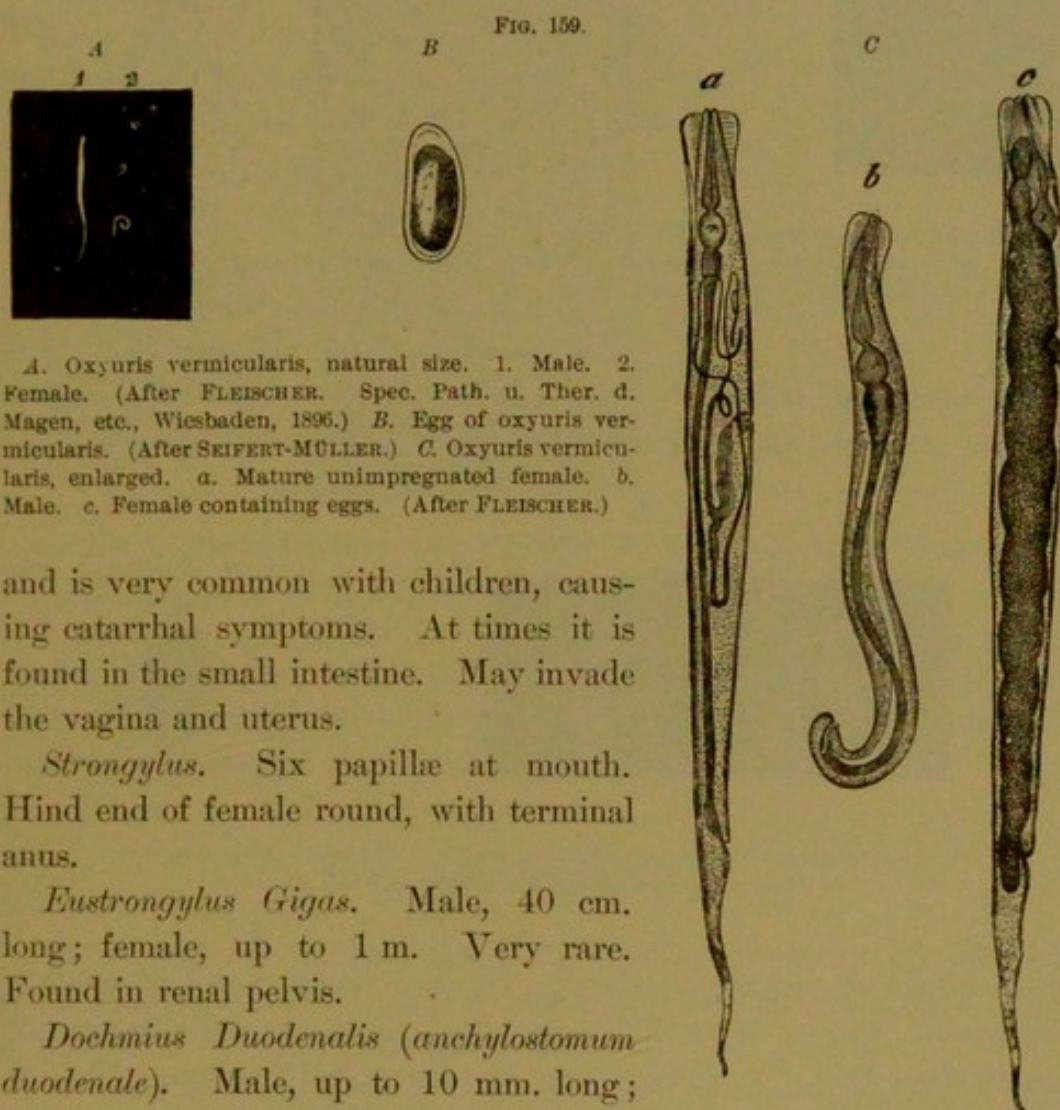


Egg of *ascaris lumbricoides*.
(After SEIFERT-MÜLLER.)

Ascaris Lumbricoides. Spool or round worm. Mouth has three papillæ as lips. Hind end of male curved ventrally, with two posterior spiculæ. Length, 250 mm.; female, 400 mm. Cuticle annulated. Bodies more pointed anteriorly than posteriorly. Female sexual pore at the boundary of the front third. Uterus double, much convoluted. Eggs 0.05 to 0.06 mm. long, with a thick shell and an outside layer of albumin. The worm occurs in the small intestine of man, and can pass to the colon,

stomach, gall-ducts, esophagus, or respiratory passages. The eggs leave the body with the feces, a few at a time or by hundreds.

Oxyuris Vermicularis Male 4 mm. long; female, 10 mm., and at hind end has an awl-shaped prolongation; male blunt at hind end. Three small lips at mouth. Eggs oval, 0.05 mm. long, 0.024 mm. broad, and contain embryos when laid. The worm lives in the colon,



A. *Oxyuris vermicularis*, natural size. 1. Male. 2. Female. (After FLEISCHER. Spec. Path. u. Ther. d. Magen, etc., Wiesbaden, 1896.) B. Egg of *oxyuris vermicularis*. (After SEIFERT-MÜLLER.) C. *Oxyuris vermicularis*, enlarged. a. Mature unimpregnated female. b. Male. c. Female containing eggs. (After FLEISCHER.)

and is very common with children, causing catarrhal symptoms. At times it is found in the small intestine. May invade the vagina and uterus.

Strongylus. Six papillæ at mouth. Hind end of female round, with terminal anus.

Eustrongylus Gigas. Male, 40 cm. long; female, up to 1 m. Very rare. Found in renal pelvis.

Dochmius Duodenalis (*anchylostomum duodenale*). Male, up to 10 mm. long; female, 12 to 18 mm. Mouth with strong horny teeth on the edges of the capsule—two ventral teeth, one dorsal. The worm attacks the intestinal wall, lives in the duodenum of man, and is frequent in Italy, Switzerland, Brazil, and causes Egyptian chlorosis. The intestine of the worm is always filled with blood. Infection occurs probably by drinking water, and without an intermediary host.

Tricocephalus Dispar (*whip worm*). Front end much elongated; hind end of male spirally wound. Male, 40 to 50 mm. long; female, about 50 mm. long. Anus terminal; spiculum in sac, but protru-

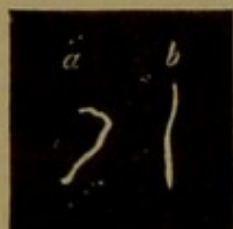
sible. Occurs in the human cecum, its thread-like front end buried in the mucosa. Pathological effect slight.

Trichina Spiralis. Male to 1.5 mm., female to 3 mm. long. Hind end but little thicker; in the male provided with two ventral pegs.

Sexual opening of the female laid far forward; viviparous. Number of young in the female may reach 1500. Just born they measure 0.01 mm., and do not leave the host, but develop further within it.

Human infection is due to eating trichinous pork. In the human intestine the encapsuled trichinae become free, copulate, and in three or four days produce motile embryos, intestinal trichinae, after five to seven days. These bore through the wall, and actively wander to the muscles or connective

FIG. 160.



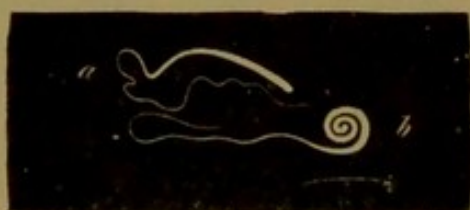
A



B

A. *Anchylostomum duodenale*, natural size. a. Male. b. Female. (After FLEISCHER.) B. Egg of *anchylostomum*. (After SEIFERT-MÜLLER.)

FIG. 161.



A



B

A. *Tricocephalus dispar*, natural size. a. Male. b. Female. (After HELLER.) B. Egg of *tricocephalus*. (After SEIFERT-MÜLLER.)

tissue, or are carried by the blood. In the muscles they perforate the sarcolemma, and in the primitive bundles, which are partly destroyed, they increase to 0.8 mm. long, and become spirally rolled. They lie in degenerated muscle substance for a time. The sarcolemma is distended, and under it a capsule forms about the worm, and this becomes calcareous in five to eight months. In each capsule there are one to three worms, which remain alive for years.

Infection similar to the human occurs in rats, mice, pigs, foxes, cats, and skunks. Rats eat the dead bodies of their race, and so keep up the infection among themselves. Pigs are infected by eating rats or offal from trichinous pigs.

Filaria. Long, with rounded head end and no lips.

Filaria Sanguinis. Young form, in great numbers in human blood, reaches the kidneys, causing hematuria and inflammation, and passes out with the urine. Length, 0.35 mm. Found in Australia,

FIG. 162.

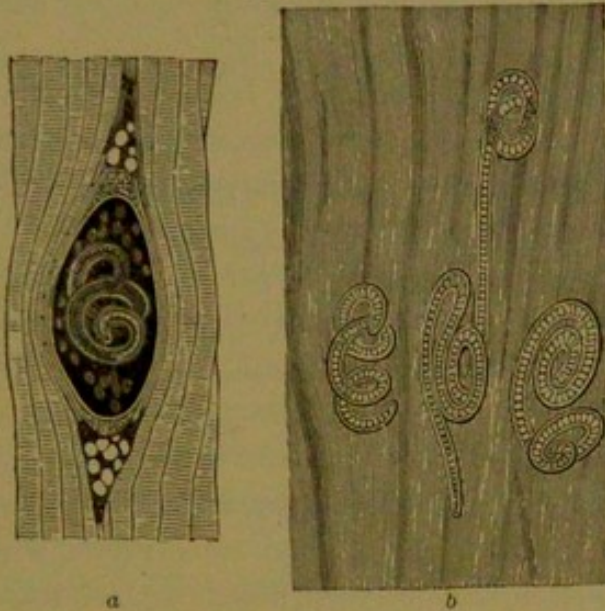


FIG. 163.

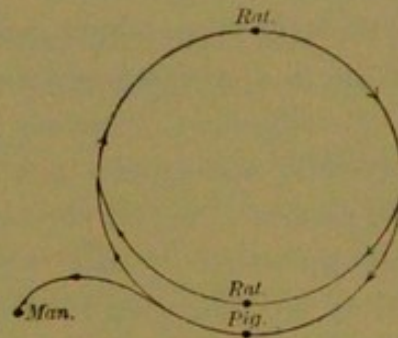


FIG. 162.—a. Encapsuled muscle trichina. (After LEHMANN.) b. Young muscle trichinae. (After HELLER.)

FIG. 163.—Diagram of the hosts of trichina. (After BOLLINGER.)

India, West Indies, and Brazil. The developed worm is the probable cause of tropical lymphangiectatic elephantiasis (p. 102), living in the thickened tissue and reaching a length of 8 cm.

III. ARTHROPODA.

Arthropods are divided into head, thorax, and abdomen, with segmented appendages and many cuticular appendages on the skin. They propagate sexually, for the most part.

1. *Arachnoidea* (spiders). Breathe by tracheae or air sacs. Head and thorax fused; two pairs of jaws and four pairs of legs; abdomen without appendages. Parasitic forms are acarinae and linguatulids. The former, called mites, have head, thorax, and abdomen in one; bodies with chitinous cuticle and usually many appendages, while the mouths are adapted to biting, piercing, or sucking.

Sarcoptes Scabiei (cause of the itch). Male, 0.2 to 0.3 mm.; female, 0.33 to 0.45 mm. long. Small bristles on the back—larger on the sides and rear—in groups. In the female the first two pairs of feet have pedicled clinging disks, the hind pair long bristles. On

the male the third pair have setæ, and the fourth a disk. The itch mites live in furrows which they make in the skin of man, and which they fill with eggs and feces, causing the well-known eruption. The female is at the end of the burrow, which is about 1 cm. long and produces about fifty eggs, from which the young emerge in a few days to dig their own channels.

Demodex Folliculorum. Long body, annulated behind. Sucking proboscis on the head, with stilet and three-segmented antennæ. Male 0.3, female 0.4 mm. long. Occurs in comedones, especially of the face, and causes acne and pustules.

Pentastomum Tenioides (belongs to the linguatulids). Body long, distinctly annulated; two evertible hooks anterior, between which is the mouth. Sexual pore in the male near the mouth, in the female near the anus. Male, 18 to 26 mm. long, 3 to 4 mm. broad; female 70 to 130 mm. long by 8 to 10 mm. broad. Occurs in the nasal and frontal cavities of many animals and man, causing catarrhal inflammation. The eggs may pass out with the mucus and reach others with the food; then the free embryos become encapsuled in the liver. Larvæ only 5 mm. long, and formerly regarded as a separate species (*pentastomum denticulatum*). Developed larvæ pierce their capsules, wander to the lungs and bronchi, and are in part coughed out.

2. *Insecta*. Segmented animals, breathing by tracheæ. Body divided into head, thorax, and abdomen. On the head one pair of antennæ, one pair of mandibles, two pairs of maxillæ; on the thorax three pairs of limbs and two pairs of dorsal wings. Among them are many epizoa, and numbers of these are but temporary parasites.

CHAPTER VI.

GENERAL BODILY DISORDERS FROM DISTURBED ORGANIC FUNCTIONS.

1. CARDIAC INSUFFICIENCY—CHANGES IN THE GENERAL DISTRIBUTION OF THE BLOOD.

IN discussing local circulatory disorders the general blood distribution was touched upon as influenced by weakened constitutional states and functional cardiac disorders, and compensatory hypertrophy of the heart has been seen to relieve such conditions for a long time. Such general circulatory disorders will be discussed singly and together in this section.

By the heart's activity the difference in pressure within the arteries and the veins is preserved, by which the circulation is assured, for the current is from the higher intravascular pressure toward the lower. The heart accomplishes this by driving a certain quantity of blood into the great vessels at every systole, the arterial pressure decreasing toward the capillaries. In the veins the pressure is low, and in the *venæ cavæ*—at least during inspiration—negative, so that the blood is sucked into them.

Lessened cardiac action *without variation in the amount of blood or of vascular resistance*. Deficient cardiac activity results from degeneration in its muscle, fibrous or fatty, and imperfect nutrition from partial or complete closure of the coronary arteries, in fever, and certain poisonings. The lessened power may depend partly upon imperfect stimulation of the cardiac ganglion cells, or increased stimulus of the inhibitory nerve (*vagus*), or paralysis of the accelerator nerves. The immediate result is a diminished amount of blood driven into the aorta with systole, and a similar effect occurs when the rate of contraction is slowed.

With normal or increased cardiac activity the beneficial effects of its systole may be lessened when, from serous or hemorrhagic fluid in the pericardium, diastole is incomplete, or when synechia of the pericardium leads to incomplete contraction and incomplete emptying of the ventricles. The same must occur with narrowing of the valvular

orifices or their incomplete closure. With stenosis less blood passes the ostium; with insufficiency part of it regurgitates. Various pulmonary conditions have a similar influence on the cardiac function, especially substantive emphysema (see Chapter IX.), in which there is atrophy of the septa between air vesicles and loss of many blood-vessels; hence the total area of blood space is lessened, and the right side of the heart has to work against an obstacle.

The immediate effect of diminished cardiac function is imperfect filling of the arteries, and hence lower pressure in them. The pulse wave will be lower also, apart from slow beat and aortic insufficiency. The imperfect emptying of the heart chambers hinders the flow of blood from the great veins into the right side of the heart. If the right ventricle is partly filled there is resulting stasis in the corresponding auricle. In some conditions the cardiac impulse is carried in the reverse direction through the veins, giving rise to a venous pulse; this is noticed with tricuspid regurgitation. But with imperfect emptying of the left side there may also be venous stasis. The width of the lung capillaries and the lower pressure of the blood in them transfers the stasis in the left auricle over to the right ventricle, then to the auricle, and finally to the *venæ cavæ*.

From such back pressure there is overfilling of the veins and increase of pressure in them, which may affect even the finest veins and the capillaries nearest them. In the latter there is slowing of the stream, for the lowered pressure in the artery and the increased pressure of the venous current approach each other. Hence there is general venous and capillary stasis, cyanosis of the body from accumulation of blood containing carbon dioxide, increased transudation, edema, hemorrhages and cyanotic induration, catarrh of mucous surfaces, and hypostatic congestion in dependent parts.

In the lungs, where the circulation is slowed and the pressure increased by left-sided heart lesions, there is an increase of stroma, brown induration, with hemorrhagic infarcts from marantic thrombi and embolism. Hypostatic congestion occurs in the posterior part of the lower lobes and elsewhere. Edema of the lungs is a frequent terminal symptom, partly caused by the negative pressure in the alveoli during inspiration. More blood collects in the lungs than can be passed into the left auricle, the heart chambers are not wholly emptied, and the edema is combined with hyperemia. In many cases early paralysis of the left ventricle, with retained vigor in the right, is the probable causation. Where edema of the lung occurs with stoppage

of the air passages—as edema of the glottis, stenosis of the trachea, etc.—it is produced by the forced inspiration, which causes negative pressure in the alveoli.

An extreme degree of cardiac weakness results in syncope or collapse. The circulation in the capillaries ceases and the surface turns pale and cool; the skin, being elastic, is applied more closely to the parts below it, and hence the sharpening of the features (*facies Hippocratica*). Since the cardiac capillaries are not filled, the nutrition of the muscle ceases, and asphyxia occurs, with cessation of breathing. Collapse may result from such depressing influences on the heart, or from lesions of the muscle or the coronary arteries, with marked anemia of the part, or as a reflex from various nerves (Goltz's experiment). The pulse is rapid and small.

Increased Vascular Resistance. When the work of the heart is but moderately increased there is at first an increase in its rate of activity. The cardiac muscle, like others, possesses a certain amount of reserve power. When the resistance increases, so does the violence of systole; and in time this extra effort results in hypertrophy of the cardiac section, which has the greater demand made upon it (p. 99).

Such compensation is usual with valvular defects. When the aortic is stenosed more effort is required to send the charge of blood into it. With regurgitation a portion returns, and the left ventricle becomes dilated; but so long as compensation lasts there is a tendency toward the normal lower pressure in the pulmonary vessels and higher pressure in the arteries. With mitral stenosis the left auricle must work harder to pass the blood into the left ventricle; with mitral insufficiency a portion returns from the ventricle.

General atheroma of the arteries much increases the work of the heart, for there is a loss of elasticity in the arterial coats, and hence its aid in maintaining the circulation is removed. The lumen of different vessels is diminished, and this adds to the friction to be overcome; hence atheroma alone may be a cause of marked hypertrophy of the left ventricle. In other cases the hypertrophy is not found, and, according to some authors, the two have a common cause. It is supposed that atheroma will produce cardiac hypertrophy only when certain regions are affected, as the vessels of the abdomen—possibly also the thoracic aorta.

Hypertrophy with renal disease has been explained as resulting from difficult circulation in the contracted kidney, or from plethora because of water retention, or from chemical stimulation of the heart because of

retained excreta, and, lastly, as due to a general arterio-fibrosis. The latter consists in a thickening of the intima, and is common with kidney diseases. None of these hypotheses has entirely explained the condition. Excretion of urine is important for maintaining intravascular pressure, and it can be accomplished in kidney disease only when this pressure is raised. Moreover, such increase of pressure is almost constant with such lesions, but by the time it compensates for the conditions in the kidney it is far too high for the general system. Just how this comes about is unknown. Serous plethora might explain the hypertrophy of the left ventricle, but that of the right has been ascribed to loss of power in the hypertrophied part, and hence venous engorgement in the lungs and increase of work for the right side. Late researches seem to prove a hypertrophy for both auricles also, and hence the mechanical hypothesis must be given up, especially as hypertrophy with atheroma occurs only when the abdominal arteries are affected.

Primary hypertrophy of the right ventricle occurs in all conditions in which the lungs offer a hindrance to the circulation through them, as in phthisis, emphysema, etc.; or when there is a loss of the factors which secure regular outflow of blood from the lungs, as in mitral lesions. With mitral stenosis the left ventricle may even be atrophic. Hypertrophy of both ventricles is found with combined valve defects, synechia of the pericardium, plethora, and great muscular activity of the body generally. (See Chapter VII., *a.*)

The hypertrophied heart has really less reserve power than the normal, and is sooner exhausted by severe exercise, and in time the point is always reached when the compensation is lost and cardiac insufficiency appears.

Where increased function is not partially used in overcoming obstacles, but all the extra power passes into the arterial system, there is a marked increase in pressure and rapidity of the stream, and there may be active congestion or even hemorrhages in certain parts.

A decrease of cardiac activity occurs with a lessened demand upon it, as in anemia and after severe bleeding. If permanent, the heart fits the condition by becoming atrophic, and the pulse is weaker and the circulation is slowed.

2. ASPHYXIA—SUFFOCATION.

The anatomical changes in death from these conditions are few and not characteristic. The blood is dark, usually fluid, or with large

coagula in the heart and great vessels. Post-mortem hypostasis is darker than usual and widespread, occurring both externally and in the organs, as the posterior halves of the lungs, the kidneys, etc. The right side of the heart and the large veins are usually filled with blood, while the left chambers are empty. An important accompanying change is found, as small hemorrhages under serous membranes, the skin, and conjunctiva.

Because the internal conditions are so negative there is the more importance to be given to signs of violence. In death by hanging there is a characteristic furrow from the cord, which usually runs obliquely from in front and below upward and backward, and is apt to be lost near the ear. As this is usually found it is slightly mummified, dry like leather, brownish, and as a shallow groove. Signs of choking and of foreign bodies in the air passages must be searched for, even in the fine bronchi, where food particles and mucus may be inspired. (See Aspiration Pneumonia, Chapter IX.)

After death by drowning there are the signs of asphyxia and also those of the effect of water—paleness and coolness of the surface, cutis anserina, shrivelled penis and scrotum, nipples and areolæ, and maceration of the skin on palms and soles. Fluid may be aspirated into the lung (terminally) or swallowed, and the lungs may be distended, with froth in the nose and pharynx.

3. DISEASE FROM TEMPERATURE VARIATIONS.

Abnormally high or low temperature may cause local or general effects on the organism. Burns and scalds result from the contact of flames, steam, hot fluids, or heat rays. Three degrees of burns are recognized:

Burns in the *first degree* consist in redness and edema, with later scaling. In the *second degree* vesicles form in the epidermis, filled with clear fluid at first, which later becomes turbid, and after drying these fall off as crusts. In the *third degree* the skin is necrosed and sloughs off. Near the part there is almost always burning of the other degrees. The slough separates by inflammatory demarcation, and healing by granulation follows. The scars are apt to contract and produce false positions of the head or limbs.

The general effects depend more on the extent of the burn than on its degree. It is said that death follows burns which involve a third of the surface, but it may occur with less. The actual cause of the

fatal ending is not clearly understood. Paralytic dilatation of the vessels, with lowering of pressure and insufficiency of the heart; overstimulus of nerves; loss of cutaneous function; destruction of blood cells, with solution of pigment in the serum, and coagulation or stasis in various organs have all been advanced to explain it. It is certain that blood changes occur. In the cadaver the external lesions correspond to the degree of burn and vary with the cause, whether hot fluid, flame, etc. The internal organs in recent cases are negative. After a few days there is fatty degeneration of parenchymatous organs, or perhaps only cloudy swelling, hypostatic and embolic processes in the lungs, and ulcers in the stomach and duodenum, probably due to stasis.

Heating of the entire body over the normal temperature can not be long withstood. Animals so treated die in a few hours or days, with symptoms of rapid heart action, dyspnea, and coma, and the organs show fatty degeneration. The ganglia cells may be affected also.

In man excessive heat causes insolation or heatstroke or thermic fever, especially when active bodily exertion accompanies high external temperatures, as with soldiers on the march, farm laborers, etc.; and tight clothing, even when the sky is cloudy, leads to such effects. The autopsy findings are negative. Sunstroke may present hyperemia and beginning exudation in the cerebral membranes.

Death by lightning may be devoid of gross lesions, or there are tree-like tracings burned on the skin, with occasional tears of organs.

Cold locally causes coagulation, or hyperemia and slight infiltration, frost-bites, chilblains, redness, and swelling; and after mechanical injuries of the frozen parts there may follow ulceration and scar formation. High degrees of cold cause necrosis of the part. (See Chapter XV.)

Cooling of the entire body is endured better than heating; but small children and old people, and the marasmic, suffer more than healthy adults. The lowest temperature from which recovery is possible appears to lie near 24° to 30° C. Death occurs from paralysis of all important centres.

Practical experience groups the ill-explained results of exposure to low temperatures—which in specially disposed subjects takes the form of rheumatic, catarrhal, or inflammatory symptoms—under the term “catching cold.” The effect is often apparent in parts of lessened resistance at a distance from the part exposed. Personal disposition is important, for one case will develop respiratory and

another intestinal catarrhal disorders, while another suffers from joint affections. In general there is a reflex nervous action, which causes circulatory disorders in the part affected. In many infectious diseases there is a clear relation between catching cold and the onset of the illness.

Appendix—Fever.

The normal bodily temperature of the human subject is considered to be 36.2° to 37.5° C. in the axilla, and 36.8° to 38° C. in the rectum; in children it is higher in both localities. Certain daily variations occur; thus it is lowest at midnight, and rises during the day with nutrition and exercise.

In the symptom-complex of fever the most marked phenomenon is the rise of bodily temperature; others are disorders of metabolism, digestion, circulation, etc.

The cause of fever is assumed to be certain pyretogenous substances, which in most cases are produced by bacteria or contained in them; but products of destructive lesions in tissues, as in aseptic wound-fever, may also cause it. This is seen with destruction of blood corpuscles after transfusion or watery injection, with formation of fibrin ferment; and physiological secretions, as milk and urine, cause fever when injected into the veins.

With infection it is possible to refer some of the fever to auto-intoxication with the products of destroyed cells acting with the toxins. Increased heat production may be supposed to result from greater chemical activity in the cells and their destruction. Pyretogenous matters circulating in the blood are supposed to make the supply of oxygen more available to proteids, and hence to increase their consumption (zymotic theory). The increased catabolism of albumins may be deduced from the changes in the urine, which contains more urates and urea, even to three times the normal. Creatinin and other nitrogenous matters are also in excess in the urine. The respiratory interchange of gases is increased. There appears by late researches to be not so much a rise in the general metabolism as a lessened absorption of nourishment, and this may explain the emaciation which accompanies fever.

The regulative function of the vasomotor system is of great importance in fevers, for dilatation of the vessels results in greater loss of heat, while constriction of them diminishes this loss. A disorder between heat production and heat loss—a heat accumulation, in other words—is one of the most important factors in fever.

The nerves influence bodily heat chemically by exciting the muscles (and glands?), for with paralysis of the muscles one of the important sources of body heat is lost. Purely vasomotor fevers occur also, usually temporarily, as with certain colics, catheterism, and in some central nervous lesions.

The course of the fever, as shown on the plotted curve, is divided into the *stadium incrementi*, often beginning with a chill; the *stadium fastigii*, or *acme*, the high level on which there may be slight variations in either direction; the *stadium decrementi*, or *defervescence*, which may enter suddenly as *crisis* or slowly develop as *lysis*. The crisis is apt to occur on special days of different diseases.

The form of the fever may be:

1. **Febris continua**, when the variations between the two extremes of temperature do not exceed the normal.
2. **Febris remittens** (subcontinua), when the variations are greater than normal.
3. **Febris intermittens**, when periods free from fever (apyrexia) occur between fever paroxysms.
4. **Febris recurrens**, when there is a febris continua, then a crisis, with apyrexia, then another fever period, and so on.

Lesions in the organs accompanying fever are as follows:

Circulatory. Rapid heart and pulse; cardiac weakness from direct influence of the heat on the muscles of the heart, and exhaustion because of extra work with diminished nutrition, and direct action of toxins. Cardiac insufficiency and lowered blood pressure may end in collapse and death.

Respiratory. Increase of gaseous interchange and dyspnea.

Digestive. Early reduction of the absorptive processes, loss of appetite, and diminished supply of digestive fluids; cloudy or fatty changes in secreting epithelia. The result of the digestive disorder is the febrile emaciation.

Urinary System. Changes in the composition of the urine, increase of urea and nitrogenous elements, slight albuminuria, degeneration of epithelia of convoluted tubules.

Cutaneous Surface. Contraction or dilatation of the vessels and increased or diminished perspiration; sweating may be profuse at the crisis.

Nervous System. Vasomotor and general symptoms, as headache, depression, hyperesthesia, coma, delirium, stupor.

4. INTOXICATIONS.

Poisons are those substances which injure the body chemically. The lesions, but especially the general effects, are known as poisoning or intoxication. Practically, poisons may be divided into: 1. Chemical—which occur in nature as such—or are artificial and often used for technical purposes; these are partly organic and partly inorganic, the former being obtained chiefly from plants, and more or less used in medicine. 2. Bacterial poisons, toxins, ptomains, proteids (p. 207). 3. Animal poisons—physiological products of various animal glands, as snake poison; or formed only in certain conditions, as in shell-fish. 4. Poisons formed within the diseased body. Among these belong the causes of so-called auto-intoxications.

The action of poisons may be local or general. The former is seen with corrosive substances and caustics, which cause necrosis of the parts attacked, or inflammatory reaction and suppuration; many have general effects also. Those which affect the entire organism are usually divided into the blood, heart, and nerve poisons, according to the organs where their action is most evident.

Poisons enter the body through the alimentary canal (see Chapter X.) or through the skin, the blood by injection, the lung by inhalation, the genital tract by douches with strong antiseptics, etc. (For Blood Poisons, see Chapter VII.)

Heart and nerve poisons may produce no apparent lesion, and death is explained as the result of functional disturbance. Of late certain changes in ganglion cells have been found with many of these poisons, but these are not specific. Of the heart poisons digitalis is a good example; of the nerve poisons, alcohol, ether, chloral hydrate, nicotine, strychnine, etc. But they all affect the heart's activity somewhat. Chloroform may leave its odor, and ether also, for a long time in the lungs after death; opium, morphine, and atropine have no characteristic lesions. Fungi cause especially a reaction along the alimentary canal.

With some general poisons there are local lesions, as with phosphorus and arsenic (see Chapter X.), after which fatty changes are common; while fibrous lesions follow alcoholism, and in chronic ergot poisoning there are lesions of the posterior columns of the cord, as in *tabes dorsalis*.

5. GENERAL DISEASES WITH DEFECT OF GLAND FUNCTIONS—AUTO-INTOXICATIONS.

Disorder or absence of certain gland functions may lead to accumulation of poisonous excreta in the body, and obstacles to the outflow of gland products may have the same effect, as does also decay of excreta. All the general diseases which follow such conditions are grouped as auto-intoxications.

Imperfect renal action and retention of urinary constituents may cause **uremia**, but which element of the urine produces this condition is unknown. Uremia may appear as coma or convulsions. It appears with nephritis, closure of the ureters by calculi and tumors, and experimentally may be produced by ligation of both renal arteries. Chronic catarrhal enteritis is common with uremia, caused by compensatory excretion of urea and its change to ammonium carbonate, and, by the action of bacteria present, the inflammation may be diphtheritic.

Retention icterus occurs with entrance of bile into the blood when the ducts are closed. This is called **cholemia**, and beside the general yellow color in the skin produces slow pulse, etc., because of the contained biliary salts. The most severe form is called **icterus gravis**, and may be fatal. Auto-intoxication may be due to decay in the contents of the intestine. With imperfect breathing and the accumulation of carbonic dioxide in the system another form develops.

Certain glandular organs are known as ductless—the hypophysis, thyroid, adrenal, etc. Their functions are not understood, but they are necessary for health and life. Removal of the thyroid causes tetany or a cachexia (*strumipriva*), in which the skin becomes swollen and inelastic, and finger pressure leaves a pitting, which persists for a time. This is called **myxedema**, and is apt to be marked in the face. The mental powers are diminished, the tongue is thick and slow in its movements, and the hand becomes like a paw. Similar effects follow atrophy and tumors of the thyroid.

In young animals when the thyroid is removed the development of the skeleton remains imperfect, and similar conditions in the human subject are endemic in certain countries. This is called **cretinism**. It is supposed that the thyroid contains a peculiar thyroiodin which is necessary for the organism, and which when supplied as a medicine may control the cachexia in such conditions. The diseased thyroid may also furnish poisonous products and directly injure the organism.

Metabolic products which pass from the thyroid body into the blood are called its internal secretion, and a similar function is supposed to belong to the liver, pancreas, adrenal, and other glands.

Hepatic cells form and excrete bile, but in addition they pass urea and sugar into the blood. Disorders of this internal secretion may be the explanation of jaundice, especially of the variety formerly called hematogenous, occurring without obstacle to the flow of bile, as in acute yellow atrophy of the liver.

The pancreas may be related to **diabetes** in a similar way. In this disease the blood may contain as high as 0.5 per cent. of grape-sugar, there is excretion of sugar by the urine, increased urea (two to three times the normal), and, in spite of sufficient food, a general emaciation and weakness, with a tendency to furuncles and tuberculosis. It is supposed that in diabetes there is lessened or absent power to oxidize sugar, and hence it accumulates in the blood. In some of these cases the pancreas is affected, and removal of the organ from dogs may cause diabetes; hence we conclude that there is a causal relation between the gland and the disease, and that the gland normally secretes a substance which is important in the metabolism of sugar.

Excretion of the sugar by the urine—glycosuria—may arise in other ways, and should be distinguished from true diabetes. Puncture of the floor of the fourth ventricle (Claude Bernard's experiment) and nervous disorders, especially with poisons, may cause excessive transformation of the hepatic glycogen; but the glycosuria is absent when the liver was free from glycogen before the experiment. Phloridzin diabetes may be due to renal conditions which permit increased excretion of sugar without higher percentage in the blood.

Addison's disease—bronzed skin, *cutis aenea*—is characterized by a peculiar discoloration of the skin and sometimes of mucous membranes also, by a free deposit of pigment in the deeper layers of the rete Malpighi and the papillæ (p. 77), and by the appearance of a cachexia, with digestive disorders, anemia, and nervous symptoms. In most cases the adrenal bodies are affected, but not in all, and the commonest change is a tuberculous process; atrophy, hemorrhage, gummata, and other tumors of the adrenal may be found in some cases. (See Chapter IX.) In animals removal of the adrenal causes death, and probably the internal secretion of the gland is necessary for general health.

It is very remarkable that diabetes and Addison's disease may not occur when the gland in question is the seat of a carcinoma. It is

possible that the cells of the neoplasm retain some secretory powers, corresponding to the epithelia from which they arise, and hence prevent the development of the general disease. (Hansemann.)

With persistence and hyperplasia of the thymus, usually atrophied about puberty, certain cases of sudden death without lesions otherwise sufficient to account for them have been explained as due to the **status lymphaticus**. The fatal termination has usually occurred in the first stage of chloroform narcosis for minor surgical procedures, with a spasm of the larynx. At autopsy there may be cardiac paralysis, an enormous thymus in children, and persistence of the gland in the adult. Normally the thymus grows until the second year, and remains undiminished until the tenth to the fourteenth year, and then atrophies to a small mass of fat and fibrous tissue. The skin is pale in these cases, all lymphoid tissues are swollen, the aorta is small, and the whole condition is termed the lymphatic-chlorotic constitution. It often accompanies rhachitis and scrofula. It is regarded as a congenital anomaly, or a dyscrasia, or an auto-intoxication with abnormal products of the organs involved, and secondary nerve symptoms, so that with slight stimuli convulsive action may be set up in various parts of the body and end in syncope.

General effects, resembling defect of functioning organs, may follow removal of the sexual glands (castration).

Basedow's disease and puerperal eclampsia may also be forms of auto-intoxication. The former is characterized by rapid heart action, swelling of the thyroid, and exophthalmus. The thyroid lesion may be simple hyperplasia. It is thought that there is an increase of the thyroid secretion, but it is questionable whether the thyroid hyperplasia is primary or secondary to the general neurosis.

Puerperal eclampsia, formerly ascribed solely to nephritis, is now regarded not merely as a result of renal inflammation, for the kidney changes seem rather to be secondary to other pathological processes.

For some of the cases a nephritis of pregnancy must be recognized, and hence the disease is rightly termed uremic. In other cases the auto-intoxication depends upon the circulation in the mother's blood of poisonous products from the placenta, whereby coagulation may be produced in different parts, with hyaline and blood-plate thrombi, occlusion of vessels, and hemorrhagic or anemic infarcts. In favor of this view the presence of placental giant cells in the mother's blood and organs is an argument. But placental embolism is probably not so much a cause of the convulsions as an accompaniment. In a similar

way embolism of liver cells may occur when parts of the organ are dying. There are also cases in which the eclampsia may be due to the presence of bacteria in the genital organs, which in the peculiarly disposed may produce convulsive attacks.

The most important lesions in death from puerperal convulsions are: In the kidney, slight or marked fatty degeneration, thrombi, necrotic areas, hemorrhages, and infarcts, or parenchymatous nephritis; in the placenta, necrosis, white infarcts, and inflammation; in the liver, stasis, thrombosed vessels, and white or red infarcts; in the severe cases with icterus there may be acute yellow atrophy; in the lung there are fat embolism, edema, hemorrhage, embolism, and pneumonic areas; in the brain, edema.

Uric-acid Diathesis. This is the foundation of gout, and is characterized by the deposit of uric acid and its salts in and about joints and other parts of the body, with severe inflammatory symptoms in the parts. Similar concretions may form in the renal tubes. (See Chapter XIII., B.)

Whether there is imperfect excretion of uric acid and urates by the kidney, or local causes determine its deposit, or the inflammatory symptoms follow the deposits in the joints or lead to it, are all unsettled questions. It is certain that heredity and residence in certain regions are both concerned in its development.



PART II.

SPECIAL PATHOLOGY.

CHAPTER VII.

DISEASES OF THE CIRCULATORY APPARATUS.

A. DISEASES OF THE BLOOD.

(a) Abnormalities of Quantity and Composition.

IN general the pathological conditions of the blood involve its total bulk or some of its constituents.

Simple increase in the amount of blood, without further abnormality—in other words, a hyperplasia of the blood—is called *true plethora*, and much doubt has been cast upon its real existence. Certain cases, however, of idiopathic cardiac hypertrophy, with marked congestion of all the organs, a pulse of high tension, and a tendency to hemorrhages without apparent cause, may be explained only by admitting that plethora exists (p. 100). This view is not disproved by the negative experimental attempts to cause plethora by transfusion in animals. In such experiments as much as 83 per cent. increase may be added to an animal from the blood of another without persistently high blood pressure, for the foreign blood is rapidly lost through excretion. But this rapid and artificial plethora cannot be compared to the slow increase in a subject's blood which takes place during months, and to which the vascular system gradually accommodates itself. In the newborn a more comparable plethora occurs when the umbilical cord is not at once tied after pulsation ceases, so that the placenta may be emptied by compression of the uterus, and its blood—varying in amount from 30 to 110 grammes—added to the system of the child. The extra blood is soon disposed of, frequently with more or less icterus neonatorum.

The serum of the introduced blood disappears first, and hence there is a temporary polycythemia as the result.

In contrast to true plethora a general lack of blood is called *anemia* or *oligemia*. This occurs after large, acute hemorrhages, and also after repeated small losses, and may be due to external or internal causes. Syncope may follow the loss of about 500 grammes of blood. When half the total amount is lost death usually occurs. After death by hemorrhage all portions of the body are remarkably pale, and even the veins which are usually full of blood appear empty. Because of the lack of blood the natural color of the organs is more evident.

In chronic anemias not only is the total amount of blood less than normal, but there are also abnormal relations in the single elements of the fluid. If the watery proportion is high a *plethora serosa* follows. This may result from the retention or introduction of enormous amounts of water; the former is noticed in kidney diseases and the latter with excessive ingestion of fluids.

An experimental serous plethora is as temporary as a plethora vera. Venous injections of salt solution are rapidly lost by excretion, and cannot be compared to the retention of fluid when the kidneys functionate imperfectly.

When the blood is rich in water and poor in albumins the condition is called *hydremia* or *hypalbuminosis*. Such a state may result from severe albuminuria, and hence is a symptom of nephritis. In these cases the percentage of albumin may fall from the normal (8 per cent.) to 4 or 5 per cent. When large amounts of water are removed from the blood the condition is called *anhydremia*, and a form of this is noted in cholera and other diseases with profuse discharges from the bowels.

Other qualitative changes in the blood occur when physiological elements are not excreted, and hence accumulate, as urea in renal disease; or when metabolic products are not completely reduced, as uric acid, sugar, and bile.

Hemoglobinemia is the name given to the solution of the blood-coloring matter in the serum. It results from the action of certain poisons, as chlorate of potash, toluylendiamin and fungi, after transfusion of blood from a species not closely related, and as the effect of severe burns. The pigment in many cases is also altered in its composition. *Hemoglobinuria*—the passage of blood-pigment through the kidneys—and hemoglobin infarcts in these organs often follow. (See Chapter XI.)

When bile pigment is dissolved in the blood it gives a yellow color to its foam. This condition, which is known as *cholemia*, appears with icterus neonatorum, acute yellow atrophy, pernicious anemia, and some other diseases, and there are present in the blood needle-shaped crystals of bilirubin.

The occurrence of corpuscular elements in the blood has been noticed under Metastasis (p. 45). Cells of various organs may enter the circulation, as from the liver after trauma, necrosis, and eclampsia, and these cells may cause embolism. Giant cells from the placenta may be found after eclampsia, and at times giant cells enter the blood from the bone marrow.

The presence of the malarial plasmodium in the blood results in the destruction of the red cells and the appearance of pigment in the plasma and organs. In such cases of *melanemia* hemosiderin is found in the spleen, liver, kidney, and marrow, so that the natural color of the part is changed by it, and iron may be excreted through the kidneys.

Blood Poisons. Together with a strong effect upon the nervous system, many poisons also destroy the blood cells. The pigment may be changed, new combinations may be formed with it, or it may simply be dissolved in the plasma by destruction of the red cells. Among such poisons may be mentioned cyanide of potassium, sulphuretted hydrogen, nitrobenzol, arsenuretted hydrogen, potassium chlorate, amyl nitrite, and others.

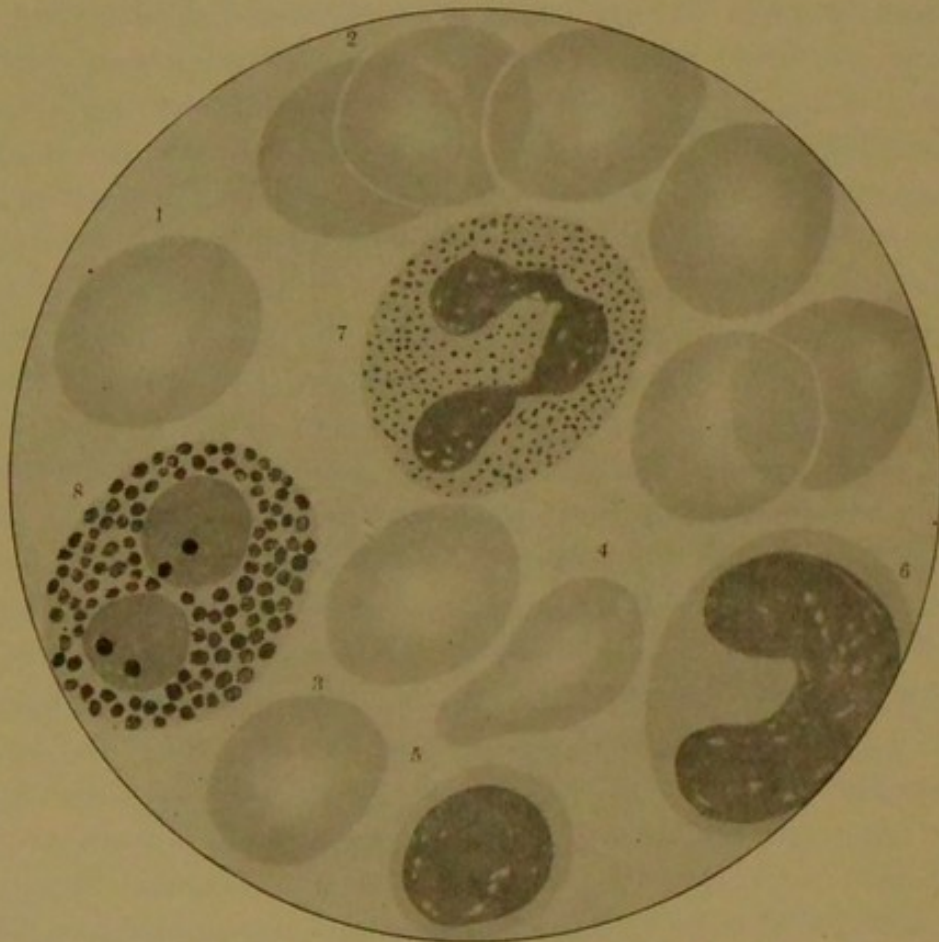
Poisoning by carbon monoxide occurs most often by respiration of coal gas or illuminating gas, which causes a firm chemical union between the hemoglobin and the CO. This may be discovered by the spectroscope, for the CO-Hb gives two absorption bands, which do not disappear after the addition of reducing substances. Moreover, when suspected blood is mixed with a double volume of NaOH it becomes of a cinnabar red instead of a dirty red brown. After poisoning by CO the blood in the cadaver is a peculiar bright cherry red, and remains fluid, and the post-mortem livores are also of a bright red. After hydrocyanic acid and its potassium salt the blood loses its power of taking up oxygen, and the cyanmethemoglobin formed gives the blood and parts containing it a bright-red color. Chlorate of potassium in large doses changes the blood pigment to methemoglobin, which has a brown color and shows in the spectrum four bands, only one of which is distinct. This poison causes also a hemoglobinemia, with destruction of the red cells. The post-mortem lividity has a peculiar dull-gray or violet hue. In the organs there

are spots of a sepia color, and in the kidney pigment infarcts occur, especially in the cortex, as brown spots and lines. (See Chapter XI.) Sulphuretted hydrogen forms sulphur methemoglobin, which turns the blood dark green or black, and the red cells are more or less destroyed. Slight degrees of this action are a regular post-mortem occurrence, noticed early in the intestinal canal and adjacent organs.

(b) **Changes in the Blood Cells.**

The cellular elements of the blood come in part from the marrow, in part from the spleen and the lymph nodes. The white cells are fewer than the red—about in the proportion of 1 to 500 or 800.

FIG. 164.



Normal blood (triacid stain). 1. Normal red cell, flatly spread and evenly stained. 2. Normal rouleau. 3. Normal red cells, varying slightly in size, thickly spread, showing central clear areas. 4. Normal red cell, of slightly altered shape. 5. Lymphocyte, medium size. 6. Large mononuclear leucocyte, incurved nucleus. 7. Polynuclear neutrophile leucocyte. 8. Eosinophile leucocyte. Separate nuclear lobes.

The red cells develop in the marrow, and during embryonic life in the liver and the spleen also. In the former place they are at first

nucleated erythroblasts. In these the hemoglobin appears, as in the later non-nucleated stages, as a distinct yellow color in the cell body.

The majority of the white cells—about three-fourths of all in the circulating blood—have irregular polymorphous nuclei, and by appropriate stains various granules may be discovered in the cell bodies (Ehrlich's neutrophile granules). A relatively small number have granules which stain with eosin (acidophile) or with basic stains (mast cells). These granules have a great significance in clinical examinations of the blood.

The polynuclear cells of every form of granules develop from the mononuclear cells of the marrow, with corresponding granules, and become polynuclear afterward.

The so-called lymphocytes—which arise in the lymph nodes and the spleen, and enter the blood by the lymph stream and the splenic vein—are in general smaller than the other white cells, and possess a single round nucleus; this may be slightly indented and so nearly fill the cell that it may appear as a free nucleus. Large cells with single nuclei are found, and, like the small lymphocytes, have no granules, and there are also polynuclear forms which are without granules.

1. Alterations of the Red Cells. The commonest change in the number of the red cells is a diminution, called *oligocythemia*, as occurs in anemia of all varieties, and may even reach a tenth of the normal. Thus in the cubic millimetre they may number 500,000 to 600,000 instead of 4,000,000 to 5,000,000.

Changes of form are of many kinds. That nearest to the physiological is the nucleated red cell, normal in size or much larger (*megalo-blast*). Abnormally small forms are called *microcytes*, and are probably normal red cells in process of disintegration. The irregular, pear, biscuit, and dumb-bell forms are called *poikilocytes*.

Changes in the shape and number of the red cells occur in all anemias, as in the secondary anemia after acute and chronic losses of blood (hemorrhagic diathesis), following acute general infections, chronic cachexias, and in some primary blood lesions (chlorosis). In the most pronounced form they are met with in pernicious anemia. In this, as in all severe anemias, there is fatty degeneration of the organs, as the heart, liver, kidneys, and especially of the vessel walls; and because of the latter lesion there may occur multiple small hemorrhages in various parts.

FIG. 165.



Poikilocytes.

With the destruction of the red cells the pigment accumulates in the various organisms. (See Hemosiderosis, p. 74, and Chapter X., D.) In severe cases the blood is pale red and even yellowish, and very thin.

Chlorosis is a disease in which there is a decrease in the hemoglobin of the single red cells, and usually they are also decreased in number. The loss of hemoglobin, or *oligochromemia*, may extend even to one-fourth of the normal. Chlorosis is commonly a temporary condition of young girls at puberty, but transitions occur to pernicious anemia. With the changes mentioned there is often a poikilocytosis, more or less marked. Hypoplasia of the circulatory apparatus and in later years dilatation of the heart are also common with chlorosis.

2. Changes in the White Cells. An increase in the number of the leucocytes, usually a secondary and temporary condition, is called leucocytosis. This occurs two to three hours after eating as a physiological leucocytosis. The condition is normal also in pregnancy. Puerperal leucocytosis is referable to the absorption of degenerating matters from the uterus and also to the loss of blood during parturition. Similar increase of the white cells follows hemorrhages, and may be caused by the introduction of bacteria or their proteids into the blood; hence it is a symptom of many acute diseases. Chronic forms are found in many cachexias and blood diseases. As in the normal blood, the polynuclear forms exceed the other white cells, but in chronic leucocytosis the eosinophiles may be increased.

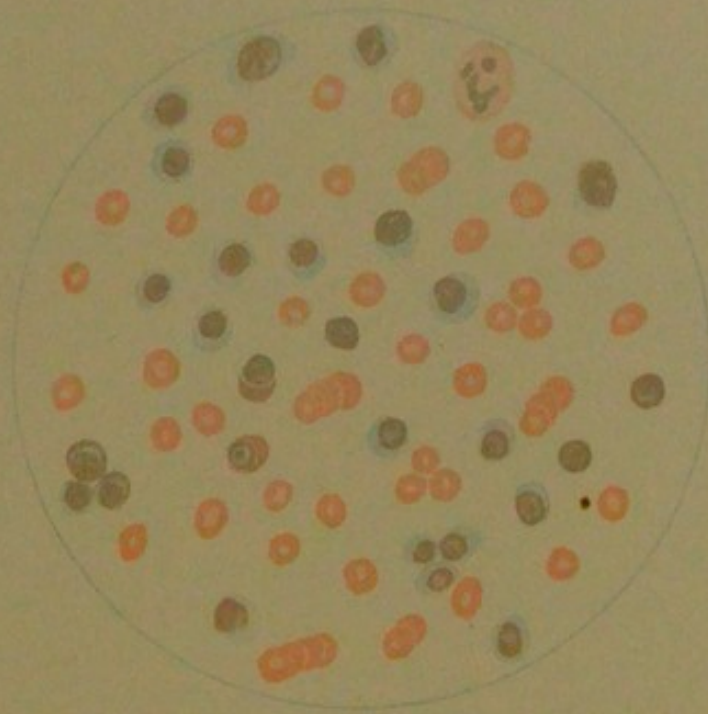
In contrast to the secondary leucocytosis there are progressive conditions of the blood, dependent upon lesions of lymphoid tissues, in which there are an increase of white cells and variations in their proportions. The condition is termed *leucocythemia* or *leukemia*. The cells most evidently increased are the lymphocytes, normally the fewest. According as there is marked hyperplasia of the spleen, the lymph nodes, or the marrow, three forms are distinguished, namely, the *lymphatic*, the *lienal* or *splenic*, and the *myelogenous*.

In the lymphatic leukemias the more numerous cells are the small lymphocytes, which have a single round nucleus and are formed in the nodes, which latter are hyperplastic.

In many instances the case is a combined splenic and myelogenous leukemia. The spleen and the marrow are hyperplastic, and in the blood there are eosinophiles and large myelocytes from the spleen and marrow, having one or two nuclei and large cell bodies. With these there may be also erythroblasts, mast cells, microcytes, leucocytes enclosing red cells, degenerated red cells, and Charcot-Leyden crystals.

PLATE XIII.

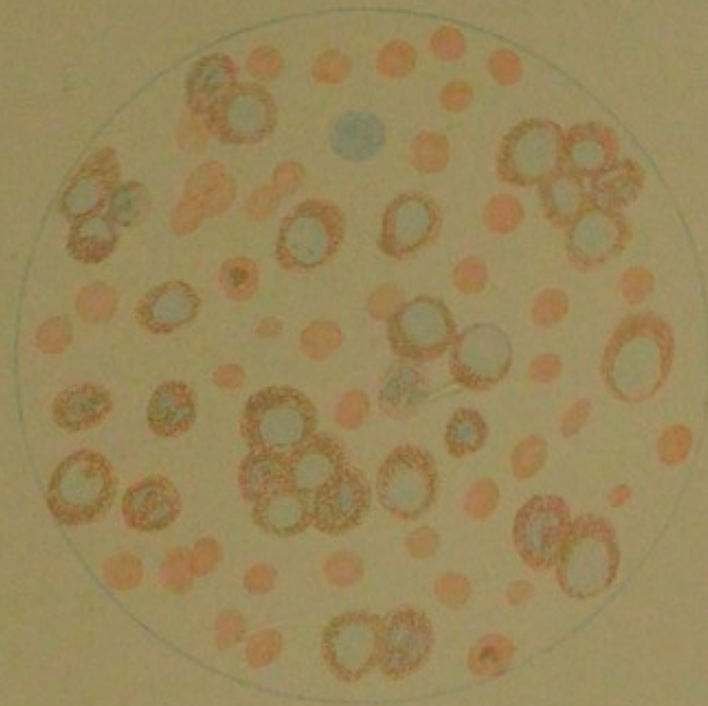
FIG. 166.



Lymphatic Leukemia.

Red cells, rose red ; white cells, mostly small and with single nucleus, blue. Hematoxylin-eosin. $\times 300$.

FIG. 167.



Mixed Leukemia; Myelemia.

Red cells, rose red ; left of the middle a nucleated red cell : most of the white cells with a single nucleus, which is very large in many of them ; some polynuclear forms. Three eosinophiles with dark red granules in the field. Hematoxylin-eosin. $\times 300$.



With the increase of white cells there is usually a decrease in the red, so that the proportion may sink to 1 to 40, or in severe cases the numbers may be equal or the white cells may be in excess.

Macroscopically the blood is light and raspberry colored, or even grayish yellow, or like pus. In the heart and vessels there may be a few light yellow clots which are covered by purulent material. The lesions in the marrow, spleen, and nodes will be discussed later. In the liver, kidney, lung, intestine, and elsewhere there may be swelling and hyperplasia of lymphoid tissue, lymphomata resembling granulation tissue, infiltrations with white cells, and white hemorrhages. The course of the disease is seldom acute.

A regeneration of the blood occurs after bleeding and in convalescence from anemias, and is due to the activity of the blood-forming organs. After hemorrhage the plasma is first renewed, then the white cells, and lastly the red.

Among the parasites occurring in the blood may be mentioned many bacilli, as anthrax, spirilla of recurrent fever, and also distoma hematobium and filaria. (See Chapter V.)

B. DISEASES OF THE HEART AND PERICARDIUM.

Malformations.

Abnormalities in the form of the heart depend partly upon restricted growth and partly upon an endocarditis which has occurred during fetal life.

In the first stage of development the heart is a straight tube which, by complicated bendings, slowly takes on its familiar form. As the septa between the auricles and ventricles and the separation of the pulmonary artery from the aorta depend upon complicated changes during development, defects in the formation of these parts quite commonly lead to cardiac malformations. Either the septum of the *truncus arteriosus*, or that from the auricles, or a third from the apex, which by their union complete the separation of the heart's chambers, may by defect leave a patent *foramen ovale* or communication between the ventricles or between the pulmonary and the aorta. The pulmonary may arise from the left and the aorta from the right ventricle (transposition of the great vessels), or both may arise from one ventricle. Congenital hypertrophy and hypoplasia of the heart occur, and the latter may involve the entire arterial tree. The valves may

vary in the number of their cusps, and the latter may be fenestrated. The commonest case is where more than one abnormality occurs, as stenosis or atresia of the pulmonary artery, with defect of the septum. With a patent *ductus Botalli* and hypertrophy of the right ventricle compensation may be established; in its absence cyanosis is pronounced in the earliest days of life. Anomalies dependent upon fetal endocarditis may appear, as valvular defects of the right side. (For other cases see Part I.)

Regressive Lesions.

Fragmentation of the Myocardium. Rupture of the muscle bundles in the papillary muscles and the septum may occur during the death agony, and to this the name *fragmentatio myocardii* has been given. The lesion occurs in a scattered way as microscopic transverse tears in the fibrillæ.

FIG. 168.

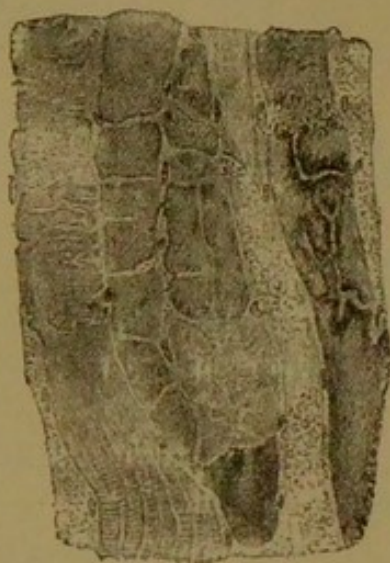


FIG. 169.



FIG. 168.—Necrosis of muscle fibres with hyaline and granular changes. Below, to the left, striation still preserved, but fibres split lengthwise; above, the splitting is transverse. $\times 350$.

FIG. 169.—Fatty degeneration of the heart muscle. $\times 350$.

Necrosis of the cardiac muscle is usually the result of a lessened blood supply, and appears as a loss of striation and a hyaline change in the fibre, with a later granular degeneration. (Fig. 168.)

Cloudy swelling occurs, as in other organs, during acute diseases, as typhoid, scarlet fever, diphtheria, etc. Microscopically, countless pale granules are found in the cells, which conceal the striation and the nuclei. These dissolve with dilute acetic acid. In the gross the myocardium is opaque, grayish red, and brittle.

Brown Atrophy (*atrophia fusca*). This name is given to an atrophic condition of the muscle in which there are granules of pigment within the fibrillæ, especially about the nucleus. The granules are yellowish brown, and distinguished from fat by their dark color and their insolubility in ether and alcohol and their less refraction, from albuminous granules by their insolubility in dilute alkalies and acids. Brown atrophy is partly a senile change, partly an accompaniment of cachexia, due to tumors and chronic anemias. The heart is smaller

FIG. 170.



Section from heart muscle with fatty degeneration. Treated with osmic acid.
× 40.

than normal, the coronary arteries are tortuous, the papillary muscles and the section of the heart wall are thin, dark brown red, relaxed, and brittle.

Fatty Heart. Two forms of this condition are recognized—the degeneration (*degeneratio adiposa*) and the true fatty heart (*obesitas* or *adipositas cordis*).

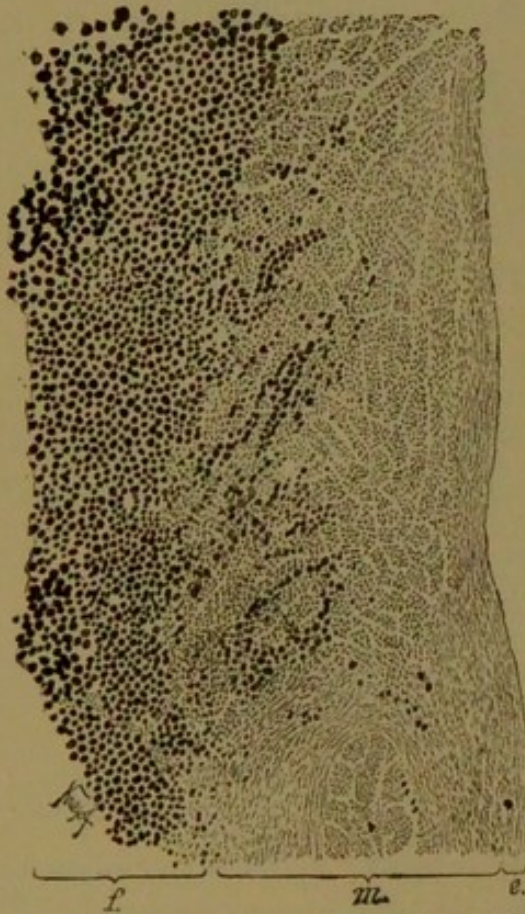
(a) **Fatty Degeneration.** Diffusely or in scattered points there appear small fat drops, which are recognized by their refraction and their solubilities; if abundant the fat hides the striation. Macro-

scopically the heart muscle is generally yellowish, with striated and spotted markings ("tiger heart"), and under both serous membranes the fat can be made out by the naked eye; or the organ is yellowish red, its cut surface is dull, and the muscle is generally soft and brittle.

Fatty degeneration begins as a cloudy swelling or is fatty from the start. It occurs with general albuminous degeneration, in anemia—especially pernicious—with arsenic and phosphorus poisoning, and acute yellow atrophy of the liver. It may develop when the cardiac vessels are stenosed, and also with chronic valvular lesions.

(b) **Cardiac obesity** is not a primary fatty degeneration of the heart muscle, but is due to the accumulation of subpericardial fat and its

FIG. 171.



Section through the wall of the right ventricle in *adipositas cordis*. *f.* Subpericardial fat passing deeper into the muscle, *m.* *e.* endocardium. Osmic acid. $\times 12$.

penetration between the muscle fibres; the muscle is then atrophied mechanically and replaced by fat. In this way the thin wall of the right ventricle may be more or less completely replaced by fat. When the fat reaches the endocardium it may be seen beneath this surface as yellow spots. This form of fatty heart occurs in drinkers, in general obesity, and at times with true fatty degeneration. In advanced age the fat becomes gelatinous.

Amyloid degeneration is rare in the heart, and occurs usually in scattered spots.

Circulatory Disorders.

Venous stasis gives the heart a peculiar blue look, and the coronary veins are distended. Some degree of hydropericardium is often associated with it.

In general anemia the heart is pale red, or it may be brown and atrophic.

Ischemia of smaller or larger portions occurs with disease of the coronary vessels, especially atheroma, which narrows their lumen, and

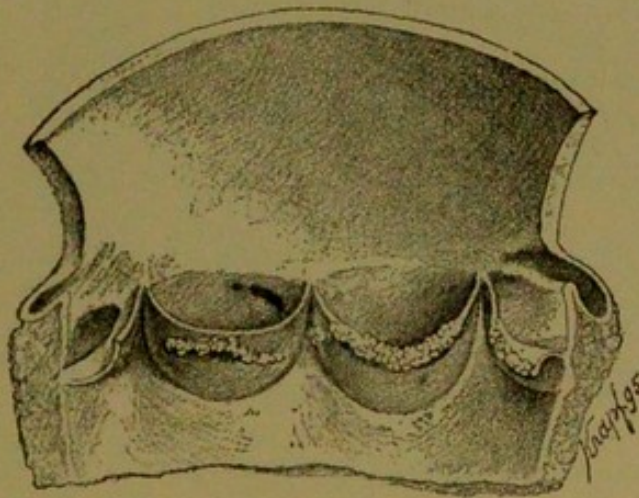
also with thrombosis and embolism of these vessels. The latter conditions may be due to atheroma or to syphilitic arteritis, and the emboli may come from such lesions or from the valves of the heart. When a vessel is closed its corresponding muscle fibres become necrotic, lose their striation, and form a homogeneous mass (infarct), which appears whitish and striped or dentate in form. At first the area is hard; later it may soften (myomalacia) and be replaced by fibrous tissue. In such conditions and with inflammation of the heart and general septic conditions small bleedings and hemorrhagic infarcts may be found in the heart muscle.

Inflammation.

Exudative and productive inflammations involve especially the epicardium and the endocardium, seldom the myocardium.

Endocarditis. Apart from this lesion during fetal life, its commonest site is the endocardium of the left ventricle, especially of the

FIG. 172.



Endocarditis verrucosa on the aortic valve

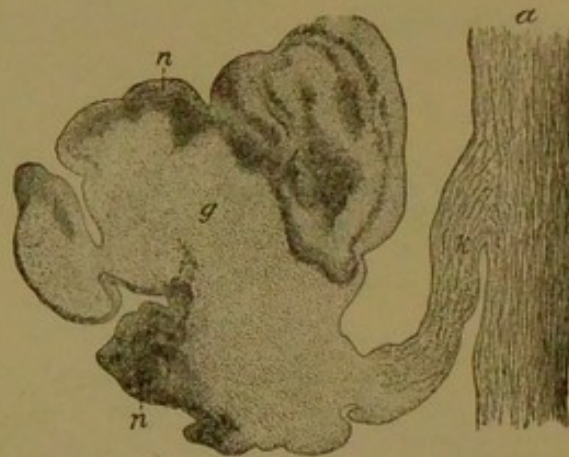
mitral and the aortic valve. If it attacks the endocardium of the ventricle or the auricle it is usually near the valves or in the tendons of the papillary muscles. Three chief forms are distinguished, which may pass into each other, namely, the acute verrucous, the chronic fibrous, and the ulcerating or diphtheritic endocarditis.

1. In **endocarditis verrucosa** there are formed—usually on the under side of the line of contact of the cusps—small warty or papillary projections, often arranged in rows, which may be so small as hardly to be visible, or may reach a relatively large size. In color they are grayish yellow, or by imbibition of blood pigment they may be red-

dish, and in consistence they are usually soft. On their surfaces there is commonly a layer of fibrin, thrombotic precipitates from the blood, which may easily be lifted off. Microscopic examination shows corresponding layers superficially, which are granular or thread-like, and consist of fibrin and plates, with leucocytes. The remainder of the wart consists of cellular granulation tissue, and in older cases there may also be many vessels and leucocytes. The upper layers may become necrotic and fuse with the fibrinous deposits.

Because of the soft, gelatinous nature of the verrucous formations they are liable to be broken off and carried as emboli to the kidneys, spleen, or brain, where they cause infarcts, and in the last-mentioned place areas of softening. Verrucous endocarditis is less malignant than the ulcerating form, and it causes fewer infarcts, and they less often ulcerate.

FIG. 173.



Section of a verruca on the aortic valve. *a*. Wall of the aorta. *k*. Valve cusp. *g*. Granulation tissue. *n*. Necrotic tissue with fibrin deposits. $\times 6$.

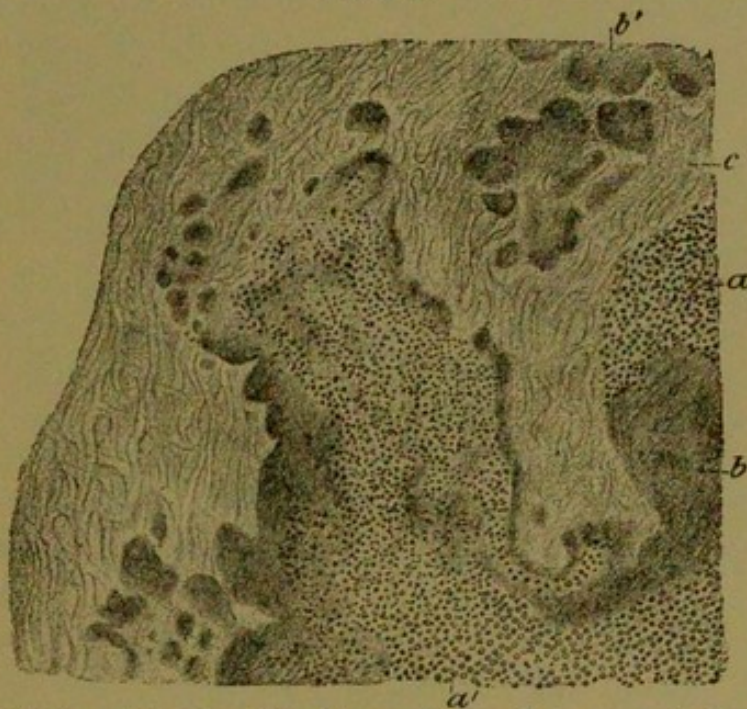
The lesion localized on the valves usually heals by conversion of the exudate into fibrous tissue, and owing to the subsequent contraction of this there may be marked deformity of the valves, with resulting functional disturbances.

2. Chronic Fibrous Endocarditis. Similar lesions to those which result from the verrucous process may begin as chronic changes from the first, and lead to the same distortion of the valves. This process is called chronic fibrous endocarditis. In the course of the disease, with or without a previous acute stage, there may be exacerbations of the lesion—a recurrent endocarditis—which have the same functional and anatomical results in the valves; and the atheromatous deposits in the aorta, which are common as a senile change, may occur in the valves also. Thus the cusps become callous and thickened, and

regressive changes begin in them which lead to fatty softening and defect or to atheroma. Upon the calcified and thickened portions coagula deposit, and functional disorders occur as before.

3. **Endocarditis Ulcerosa, seu Diphtheritica.** This is called malignant endocarditis because of the ulcerative destruction of the parts involved and the severity of the clinical course. The valves are found covered with a mass of detritus made up of coagula and the destroyed cusp. The valve may be perforated or separated entirely by this process; or the thinned valve may bulge in the direction of the flow of blood, and so form an acute valvular aneurism. Similar ulceration takes place

FIG. 174.



Stronger magnification of the edge of Fig. 173. *a, a'*. Granulation tissue. *b*. Necrotic portions. *b', c*. Thrombotic and fibrinous portions. $\times 350$.

on the wall of the cavities, especially in the vicinity of the valves, and when the chordæ tendineæ are affected they may be broken through.

Embolism is very common in the course of malignant endocarditis, and as the emboli carry pyogenic organisms in them, they produce abscesses wherever they lodge. Pyemic ulcers may be found in various organs without actual infarct formation.

The etiology of the different forms of endocarditis is not constant, and, moreover, one variety may blend with another. In the verrucous and chronic fibrous lesions bacteria are seldom found, perhaps because they rapidly die and are removed. In the ulcerating form they are constant and of several varieties, including staphylococci, streptococci,

pneumococci, and others. Endocarditis occurs independently and also with other diseases, the verrucous form with articular rheumatism especially, and sharing its tendency to return. Ulcerating and verrucous forms occur with typhoid, puerperal fever, and pyemia, partly as the result of the causes of these affections and partly as the source of a new distribution of pyogenic organisms by metastases.

Defects of the Valves. Endocarditis causes three varieties of valvular defects, as follows:

1. The cusps may be wholly or partially thickened as the verrucae are absorbed, their edges being stiff and indented, or hard projections may remain on them, so that the surfaces no longer fit exactly upon each other, and the valve is called insufficient.

2. The cicatricial contraction of the new fibrous tissue produces shortening in the cusp and retraction of the chordæ tendineæ and the edges of the ostium. The result is here also an imperfect closure or insufficiency.

3. Adhesions may form between neighboring parts of cusps, or a cusp and the wall of the heart or a vessel, so that with the opening of the ostium the cusps can not retire and leave the lumen free; hence a permanent narrowness occurs, which is called stenosis. All these lesions may be combined.

When such valvular defects are marked they produce functional disorders which increase the work of the heart and a resulting hypertrophy of the muscle (p. 99). Other cases of insufficiency depend upon distention of the valves, with involution of the edges of the cusps, rupture of the tendons; and at times great dilatation of a cavity produces a relative insufficiency. This is seen in the left ventricle with atheroma and aneurism of the aorta, in the right as the result of emphysema, and in both with pericardial adhesions. Regurgitation of the blood stream causes thickening of the valves and fibrous changes in the heart muscle.

In the bodies of infants there often appear small, soft, and reddish nodules on the edges of the valves which simulate acute endocarditis, but are only the remains of fetal mucoid tissue. In both infants and adults other thickenings may be found on the mitral and aortic cusps, which occupy the free edge of the cusp, but are separated from it by a kind of seam, and on the opposite side gradually fade into the valvular tissue. These are anomalies of development.

Acute Myocarditis. An acute inflammation of the heart muscle may arise from similar lesions of either serous surface or by emboli,

especially from ulcerative foci. In the fresh state the part affected is in granular or fatty degeneration, or necrotic, and the tissue between the fibrillæ is infiltrated with leucocytes. If it originated through the vascular system there may be emboli in the arteries and anemic or hemorrhagic infarcts. In other cases the infarcts are purulent and may be multiple, as in the course of pyemia.

When such an acute myocarditis heals a granulation tissue forms in the focus and organizes into a fibrous scar, which resembles that resulting from a primary infarct and necrosis (p. 275). Such callous

FIG. 175.



Chronic myocarditis. *m.* Muscle fibres still preserved. *b.* Fibrous scars. $\times 150$.

scars may stand in evident relation to similar fibroses in the endocardium and about the valves. This process is called fibrous myocarditis, and it may arise from acute inflammation or simply from closure of an artery.

In other cases there is a diffuse fibromatosis which produces many small cicatricial lines and spots throughout the muscle, so that the myocardium is very hard, and even with the naked eye may be irregularly sclerosed. Such conditions are due to the degeneration of countless fibrillæ, whose places are taken by fibrous tissue. It may follow atheroma of the coronary arteries and consequent disturbance of the

nutrition of the myocardium, or it may follow certain poisonous influences (tobacco, alcohol, lead), or in some cases it depends upon straining and stretching of muscle fibres from strong overdistention of the dilated or hypertrophied wall, with valvular defects. The apices of the papillary muscles often are thus affected.

Cardiac Aneurism. In consequence of weakening of the heart wall the blood pressure may produce a bulging of a certain part, with thinning, and this is called a cardiac aneurism. The acute form follows ulcerative endocarditis or simple myomalacia, especially when an inflammatory process attacks the myocardium, and in such cases there may be actual perforation of the organ. In a similar way the chronic aneurism develops, because of lessened resistance in parts which are the seat of fibrosis or infarct. Most often the chronic form occurs in the distribution of the left coronary artery (descending branch). On the internal aspect there is usually a deposit of fibrin, which may adhere closely to the wall.

Hypertrophy and Dilatation.

The origin of hypertrophy has been already mentioned in Chapter III., B. and VI. Simple dilatation causes an increase in the capacity of the chambers, without thickening of their walls, which involves flattening of the trabeculæ, lengthening and thinning of the papillary muscles, and thinning of the wall. Hypertrophy combined with dilatation is called eccentric; by itself it is called simple. Dilatation alone may occur in greatly weakened conditions, with blood diseases and after severe bodily exertion; and in the latter case it may be temporary or persistent, followed by hypertrophy or developing in a heart already hypertrophied.

When the right ventricle is chiefly involved the heart becomes broader, and the apex is formed in part by this ventricle instead of wholly by the left, as is normal. When the left ventricle is dilated and hypertrophied the heart becomes longer and of a more conical form, and the septum bulges toward the right.

The clinical picture of cardiac insufficiency can develop from simple degeneration of the myocardium; from valvular defects which are uncompensated; from other mechanical conditions, as *synechia pericardii*; from loss of compensation in the hypertrophied organ, imperfect nutrition of the muscles, with coronary sclerosis, and from closure of these vessels and fibrous changes in the myocardium.

Infectious Granulomata.

Tubercular lesions occur in the heart most commonly as a pericarditis (see below). In general tuberculosis there may be small tubercles under the endocardium. Tubercular endocarditis is extremely rare. On the valves there are small excrescences, often polypoid, with caseous centres, and tubercle bacilli may be found in them.

Syphilitic lesions are not common in the heart. Gumma of the muscle, syphilitic pericarditis, and arteritis with myomalacia and fibrosis, are the usual forms encountered.

Tumors. Fibroma, myxoma, and rhabdomyosarcoma have been noticed in the heart, and metastatic sarcoma and carcinoma, but all these are unusual. The pericardium may become involved when tumors invade the mediastinum or the pleuræ.

Injuries. Perforating wounds are usually followed by rapid and fatal hemorrhage, but cases of healing are known. Occasionally rupture of the heart has followed the action of a blunt external force.

Lesions of the Pericardium.

In the pericardial cavity a small amount of serous fluid is normally found—about 4 to 5 c.c.—but with a protracted death agony this amount may be 100 c.c. or more. Larger amounts are called *hydro-pericardium*, and follow general venous stasis. The fluid is either clear, or contains a few fibrinous flakes, or becomes turbid in the air.

Hemopericardium, or effusion of blood into the cavity, follows penetrating wounds of the heart, rupture of the heart wall or of coronary aneurisms. In hemorrhagic pericarditis there may be so much blood in the exudate that it appears to be nothing but fluid blood. Small petechiæ and ecchymoses occur in the pericardium with inflammations, in certain cachexias, and commonly after death by asphyxia.

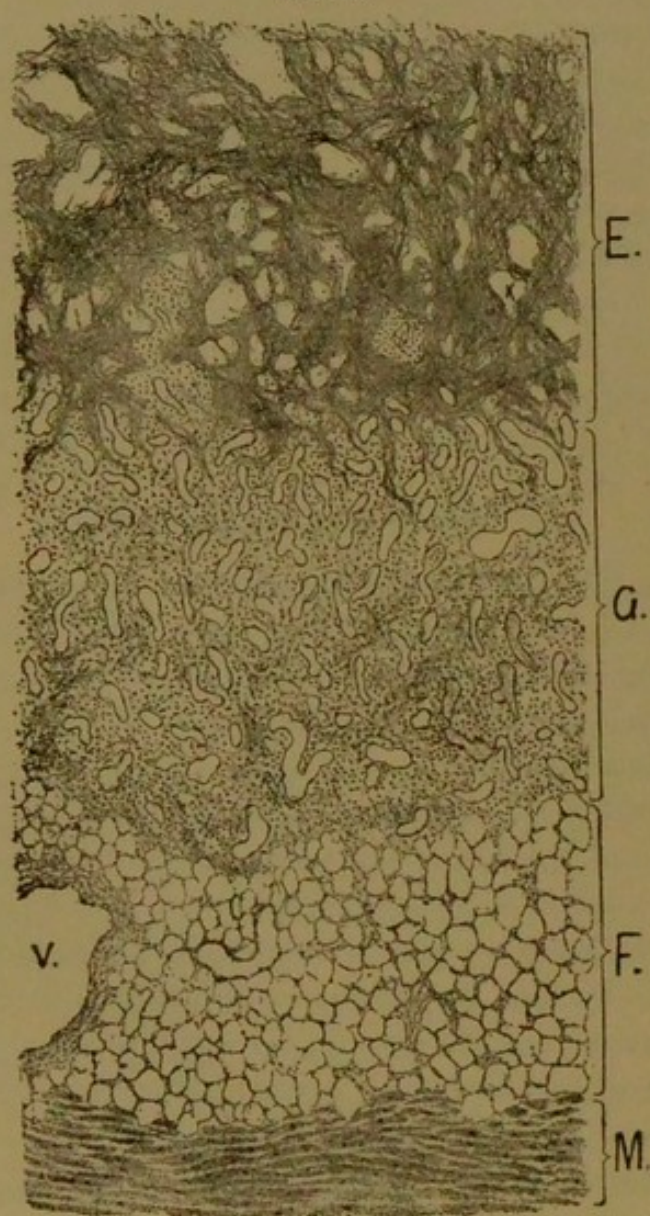
Very rarely air gains entrance to the pericardium (*pneumopericardium*) by trauma or ulceration of adjacent hollow organs, as the stomach, esophagus, and lung. When putrefaction occurs in a pericardial exudate there may be a collection of gases in the cavity. During the progress of an autopsy an artificial emphysema of the outer layer of the pericardium occurs as the sternum is lifted off.

Inflammation.

1. **Serofibrinous pericarditis** begins as a clouding of the more or less hyperemic membrane, with the addition of a small petechiæ. In

the early stage the normal shiny look of the surface is lost, and then there occurs a satiny clouding and an exudate of grayish-yellow color, which is made of fibrin and can be stripped off as a net-like membrane. With more exudate the fibrinous masses are thick and cover both layers of the pericardium. When this is very marked it gives the

FIG. 176.



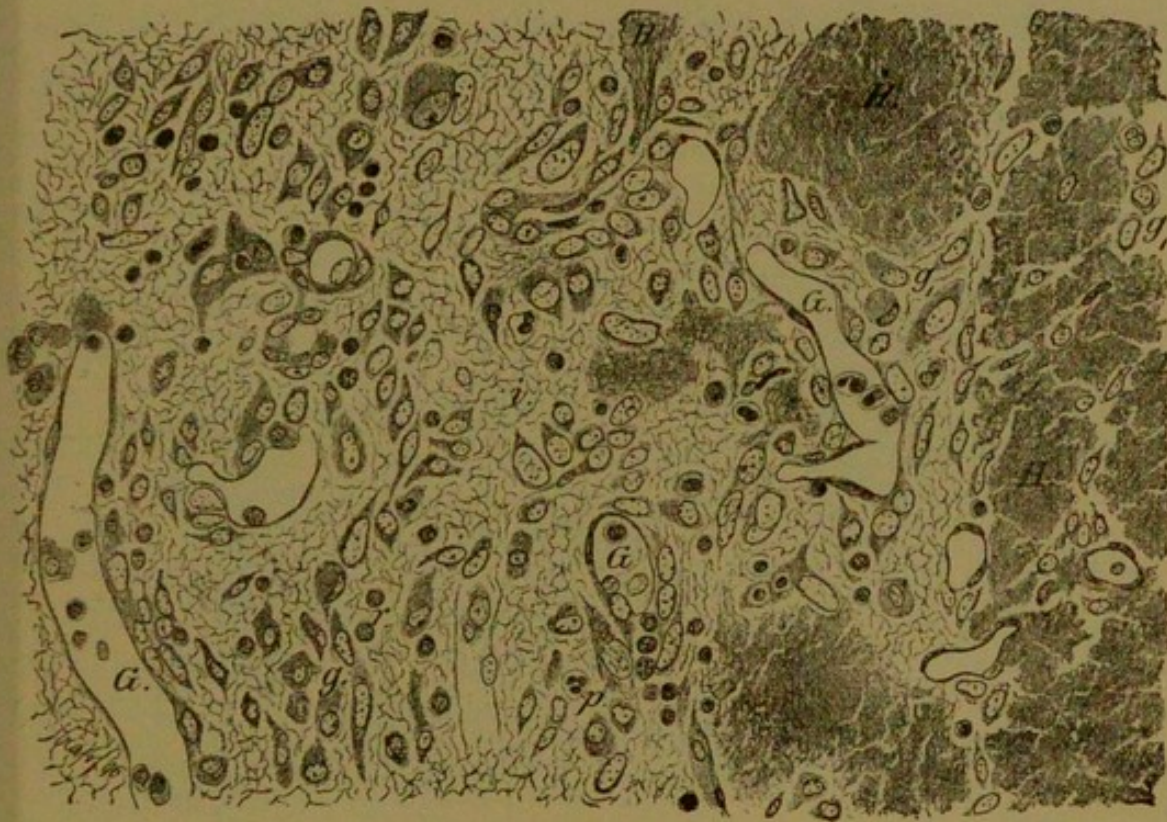
Fibrinous pericarditis. E. Fibrinous exudate. G. Granulation layer. F. Subepicardial fat. V. Veins. M. Wall of the heart. $\times 250$.

heart a shaggy appearance, which has been termed *cor villosum*. A serous exudate usually accompanies the fibrinous, and this contains much albumin, flakes of fibrin, and is turbid—characters which distinguish it from hydropericardium. If the serum is scanty the lesion is called *pericarditis sicca*.

After the exudation of fibrin there is a development of granulation tissue, which becomes organized, and under the fibrin forms a layer, which is at first grayish red and then firmer and more gray. The process results in the formation of fibrous scars, which are known as tendinous thickenings (*maculæ albidæ*), on the surface of the organ.

It is not uncommon to find the two layers of the pericardium adherent by the fibrin, and when this becomes organized the fusion

FIG. 177.



Granulation tissue from a deposit on the epicardium following fibrinous pericarditis. *g, g'*. Granulation cells. *r*. Lymphocytes. *p*. Polynuclear leucocytes. *i*. Fibrillar intercellular substance. *G*. Vessels. *H*. Hyaline fibrin. $\times 350$.

may be permanent. It may involve the entire cavity, obliterating it (synechia), or only certain areas (adhesive pericarditis). In the latter case the movement of the heart stretches the adhesions into bands, which may interfere with the function of the organ, and this is more marked in proportion to the extent of their attachments. An external pericarditis causes such fibrous bands in the mediastinum.

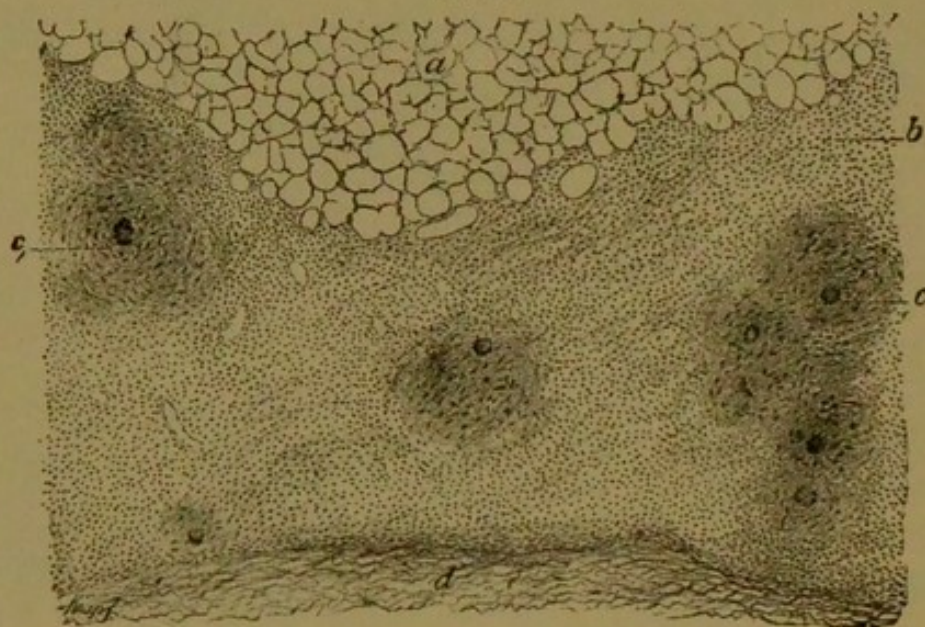
Serofibrinous pericarditis may be primary, or accompany infectious diseases, or arise by contiguity from pleural and mediastinal inflammations.

2. **Productive pericarditis** may follow the first variety or begin independently. The results are practically the same as given for the former.

3. **Suppurative pericarditis** is unusual. It may follow an ulcerative endocarditis or purulent myocarditis, or similar inflammation in neighboring tissues, or the pleura; or it may occur from pyogenic emboli and in the course of pyemia. It is usually fibrinous and hemorrhagic as well as purulent. If not fatal the lesion may heal, as in fibrinous pericarditis, by granulation and organization. Exudate which is not absorbed may thicken and be infiltrated with lime salts.

Pericarditis externa affects the outer layer of the parietal pericardium, and follows extension of inflammation from the mediastinum or the pleura, etc.

FIG. 178.



Tuberculous pericarditis. a. Subepicardial fat. b. Granulation tissue with tubercles. c. The same with giant cells. d. Fibrin. $\times 250$.

Tuberculosis of the pericardium occurs as part of a general miliary disease, with the formation of small nodules, which undergo caseation, as elsewhere. The name tubercular pericarditis usually implies that tubercles occur together with the lesions of an ordinary pericarditis. This may be exudative, of any form, or productive, and in the first case the exudate is apt to be hemorrhagic. With the productive form the tubercles may be difficult to find, or large masses of granulation tissue may become caseous. The lesion develops as a hematogenous infection or spreads from similar disease of the pleura and lung or the mediastinal nodes.

C. DISEASES OF THE VESSELS.

Regressive Changes.

A series of regressive lesions in the vessels may be observed as part of a general condition, and also connected with arterio-sclerosis and other diseases. Thus atrophy may affect the vessels either with general atrophy or as the result of local processes, as aneurisms, fibrous changes in the media, calcification, etc.

Fatty degeneration occurs in the intima and media of large vessels, and also in capillary walls, with atheroma, in anemias and cachexias, and acutely with many poisonings.

When the intima is fatty the stellate cells may be completely permeated by fat droplets, so that the form of the cells is evident without further preparation. (Fig. 179.) When the media is fatty the granules are found in the muscle cells. In the smaller vessels such changes may result in rupture.

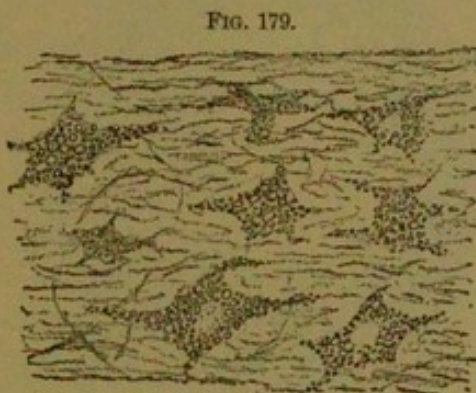


FIG. 179.

Fatty stellate cells from the aortic intima.

Calcification occurs, apart from atheroma, as a senile change in the arteries, and the fine particles of lime in the muscle cell appear as fine, circular lines on the wall. When very marked this process converts the vessel for a distance into a hard, inelastic, brittle tube.

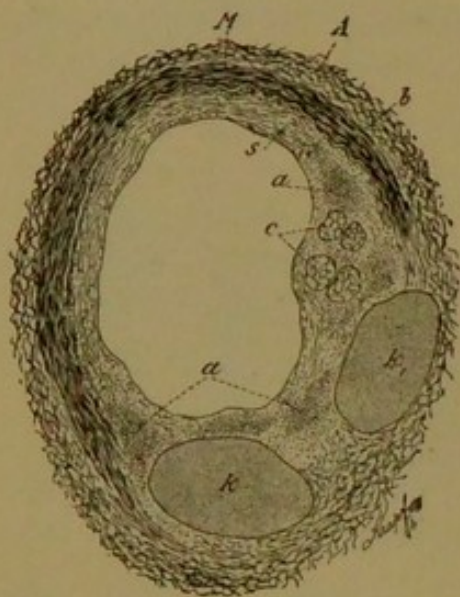
Amyloid degeneration, like the hyaline, begins in most cases in the vessels of various organs (pp. 65, 67).

Atheromatosis (Arterio-sclerosis).

This lesion involves a region or the greater part of the vascular system, and consists in thickening and proliferation of the intima, which varies according to the size of the vessels attacked. In the large vessels, like the aorta, and sometimes in smaller ones, there are flat and slightly prominent yellowish plates on the inner surface, especially common about the origin of branches from the main trunk. In other cases there is a diffuse thickening of large sections of the intima. Very soon there is a spotted yellow look in the thicker parts, caused by partial fatty degeneration. A similar change affects the endothelia over the plates, which up to that time may have been smooth and

clear. Microscopically there are many round or fusiform cells in the intima, together with a fibrillar basement substance, which later becomes firmer, more sclerotic and less cellular, and finally a uniform, homogeneous, softened mass. (Fig. 25.) As long as the cell structure is appreciable the fat is found especially in the stellate cells already mentioned, and may be demonstrated by stripping off a layer of intima with a forceps and examining it under the microscope. Incision into

FIG. 180.



Atheromatous mesenteric artery. A. Adventitia. M. Muscularis; to its inner side is the intima, which is fibrillated at *s*, infiltrated with small cells at *a*, *a'*. *c*. Vacuoles from softening. *k*. Calcified parts.

such an area discovers beneath it a mass made up of detritus, often colored with blood, which contains fat and cholesterin. On the surface of the intima there are rough places from loss of endothelia or perforation of a deeper, softened portion. In the latter case there may be ulcerative defects of some extent, with undermined edges and particles of detritus clinging to the base. These may be the seat of fibrinous deposit. Infiltration with lime salts is common both in the hyperplastic parts of the intima and also in the ulcers, either as granules or in larger plates.

In the small arteries the sclerotic part of the process is more pronounced than the fatty or calcific, which latter

practically disappears in the smallest. The thickening of the intima is also commonly diffuse. Normally there is almost no intima tissue in the smaller arteries, like those of the Sylvian fissure, but the endothelial cells lie directly upon the elastic layer; but when they become the seat of atheroma there may be a proliferation of endothelia, which supplies a comparatively broad layer between endothelium and elastic lamella.

The adventitia and media of atheromatous arteries suffer regressive changes, either fatty or calcareous or atrophic.

The results of atheroma in small arteries are those of occlusion by the process or by fibrin and thrombosis. In the larger vessels, as the aorta, the weakening of the wall permits great dilatation. Middle-sized arteries show stenosis in places and dilatation in others. The hyperplastic tissue is far less elastic and pliable than the normal, and

hence the blood pressure may lead to rupture at the site of the lesion, especially as the other layers have undergone regressive changes. Many of the important hemorrhages in the brain are explained by the rupture of such diseased arteries. When the distention of the vessel is more gradual, aneurism may be the result, and in time this also ruptures.

With general atheromatosis the loss of vascular elasticity causes general circulatory disorders, for the work of the heart is increased by removal of the adjuvant elasticity of the arteries. Embolism is common in these cases, from the fibrin deposited on rough places and from the breaking of softened foci into the blood current, which latter may cause multiple capillary embolism.

General atheroma of most of the arteries is the rule in old age; but it may be specially marked in certain sections, as the coronary arteries and the aorta, and from the latter site the process often extends to the aortic valve.

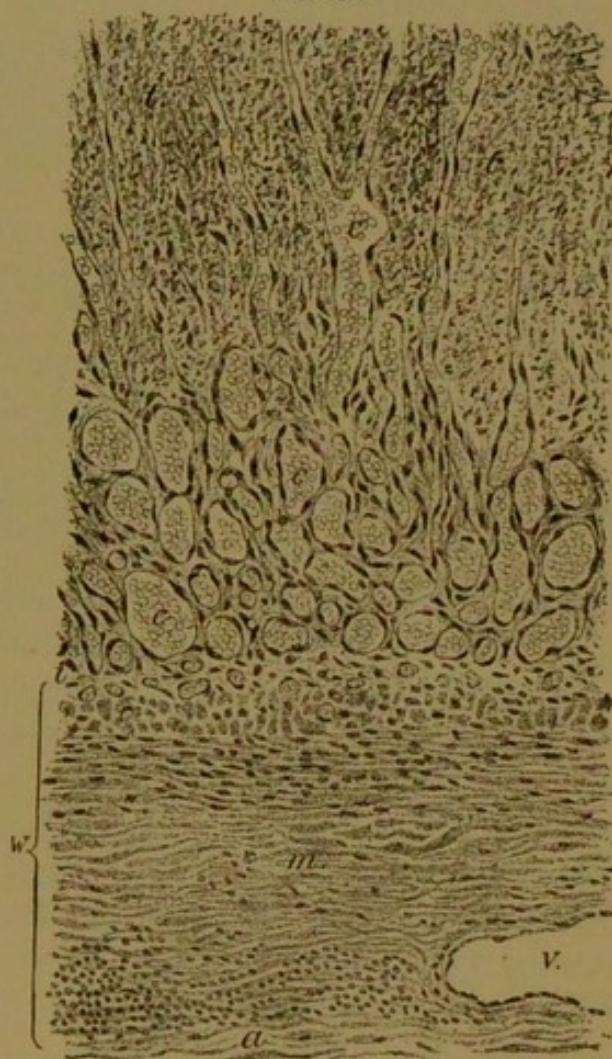
Other cases of atheroma occur when there is permanent increase of the blood pressure, with hypertrophy in valvular lesions, or with kidney disease. Dilatation of the diseased vessel may then be due to the repeated increases of intravascular pressure as the heart functions, and even the capillaries may be distinctly larger than normal. The thickening of the intima may be regarded as a reparative prevention of extreme dilatation, but its degenerative changes directly lead to this. When the arterial system is generally thickened, as occurs in some cases of chronic renal disease, the name arterio-capillary fibrosis has been given to the condition. (Gull-Sutton.) When the lesion of atheroma occurs in early life it is spoken of as presenile atheromatosis, and certain of these cases may be referred to syphilis; probably many have a causal relation to aneurism formation. When the disease attacks the media and the adventitia (mesarteritis, periarteritis) the outer layers of the vessel are marked by fibrous scars in the line of the vasa vasorum; and since both elastic and muscular elements are lost in such places, it is probable that the weakened wall is specially liable to aneurism, as is seen most often in the aorta.

In some cases, beside the fibrous hyperplasia about the vasa vasorum there is a small-cell infiltration, which later becomes caseous, and the intima is usually thickened and dimpled over such adhesions. The process is syphilitic, and occurs most often in the thoracic aorta; and when the origins of the coronary arteries are affected they may be closed off, and sudden death may result.

Periarteritis nodosa is the name given to a rare arterial disease in which the arteries of various organs present many nodules in their course. These are made up of cellular infiltration and proliferation of the three layers, and the normal elements disappear. Thrombi and aneurisms are common. The disease is probably due to acute infection.

Proliferation of the intima occurs in other conditions, at times as a physiological process. All these have in common a thickening of the

FIG. 181.



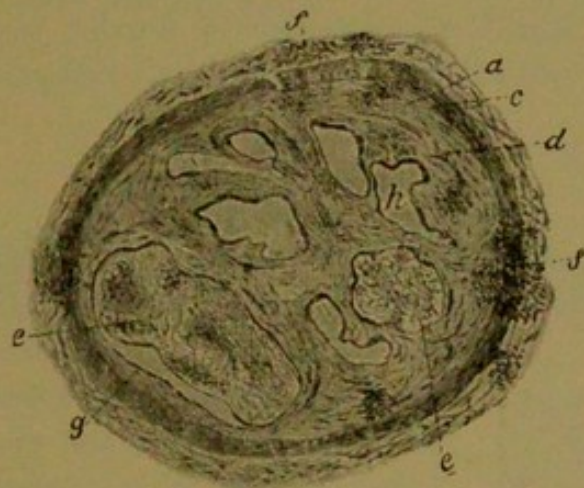
Organization of thrombus in a vein. W. Wall of vein. a. Adventitia. m. Muscularis. v. Vessel of the wall. i. Intima. t. Thrombus. c. Young capillaries entering the thrombus. $\times 250$.

intima, and are grouped as *endarteritis obliterans*, since the lumen may be wholly destroyed, but their origin is not always the same. The physiological instances are obliteration of the umbilical vessels and the *ductus Botalli*. According to Thoma, thickening of the intima always occurs when there is a disproportion between the lumen of a vessel and the amount of blood passing through it, and this proceeds

until the condition is remedied. Thus in the cases mentioned the process ends in complete occlusion, for the vessels carry no more blood. In other cases the endarteritis (or endophlebitis) is a reparative process after wounds or is the result of productive inflammation, which prevents the entrance of destructive processes into the vessels. The new tissue may become vascular, and is thus protected from degenerations.

Apart from the physiological cases, similar obliterating processes occur after ligation of vessels or lesions of their walls—in the latter case after the wound has been closed by a white thrombus. In both cases the vessel is closed definitely. When small vessels are entirely divided the two ends retract, the muscle fibres narrow the lumen, the intima is folded together, and the folds adhere.

FIG. 182.



Old canalized thrombus. *a*. Thrombus altered into connective tissue. *c*. Media. *d*. Small-cell infiltration in the organized portion. *e*. Remaining part of thrombus, not yet organized. *f*. Infiltrate in media and adventitia. *g*. Endothelium. *h*. Canals through the thrombus.

Obliterating arteritis occurs also in the organization of thrombi, tissue springing from the intima and growing through and replacing the thrombus. As this new tissue shrinks, fissures and spaces form, and the thrombus is said to be canalized.

In many interstitial and indurative processes in various organs there is an accompanying endarteritis, due to the irritation of the original lesion. Either or all of the arterial coats may take part in the thickening. Examples are found in interstitial renal and pulmonary disease.

Productive arteritis occurs, finally, in organs which are the seat of tubercular, syphilitic, or purulent processes. The intima becomes thick in proportion to the danger of perforation from the destructive process, and is properly a protective measure. If the attack is slow a

large section of the vessel may be thus protected before the outer coats are destroyed by the external process, and in the case of malignant tumors this prevents metastasis through the blood, and also erosion and hemorrhage.

Purulent Inflammation of Vessels.

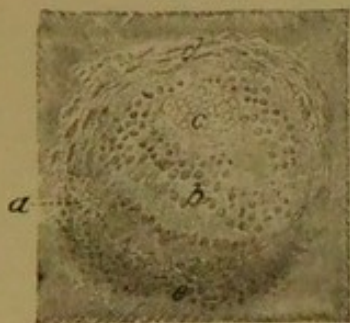
When included in a focus of inflammation the vessels suffer a small-cell infiltration of their walls. If the inflammation is suppurative the artery may undergo purulent softening, though in general very resistant to such processes. The veins are more liable to be involved in suppurative lesions, but the lumen may be obliterated and entrance of pus prevented. When the wall is much affected a thrombus may form in the vein, and as this breaks down metastatic abscesses develop.

The converse of this is noted when suppuration passes from a vessel to the vicinity, as with septic emboli in arteries, large thrombi, and thrombophlebitis extending centripetally, and subsequent periphlebitis.

Infectious Granulomata.

Within tuberculous foci in various organs the vessels undergo a tuberculous inflammation by direct infection of their walls. In

FIG. 183.



Tuberculous arteritis. Caseous destruction of adventitia and media. *a*. Muscularis. *b*. Thickened intima infiltrated with cells. *c*. Lumen filled with red cells. *e*. Caseous mass.

the adventitia and then in the media there are single or confluent tubercles, which destroy the wall. At first the intima is protected by obliterating inflammation, but soon it also becomes tuberculous, usually after the lumen is closed. In general, the resistance of vessels to the tuberculous process is strong, and thus in areas otherwise wholly destroyed by caseation we find strands of fibrous tissue formed from obliterated vessels.

Primary hematogenous tuberculosis of vessels is typically seen in tubercular meningitis. On the vessels appear many round or fusiform thickenings, made up of epithelioid, small round, and giant cells; and, as elsewhere, these collections suffer caseation. If the focus projects inwardly the lumen of the vessel is narrowed or closed.

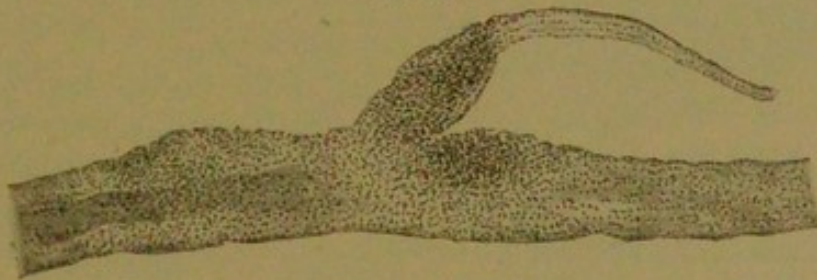
In rare cases there are large, prominent plaques on the intima of the aorta, which may even be polypoid, made up of tubercular tissue, and due to hematogenous infection. Such an aortitis tuberculosa may

be the starting point for general infection, like the large tubercles of the venous intima.

The importance of venous tubercle as a source of acute miliary tuberculosis has been treated in Part I. (p. 128). The general infection occurs either when the intima becomes infected through the blood, or when a lymph node or other tuberculous process directly attacks the vein wall. The foci appear as flat or pedicled or thrombotic masses on the intima, and may show superficial ulceration. The ulcer may then be covered by new thrombi.

Such tubercular phlebitis should be distinguished from the acute miliary tubercles which are found in the conus pulmonalis, endocardium, and veins of the lungs as part of a general miliary infection. Occasionally tubercles develop in the intima of the pulmonary vessels in chronic pulmonary tuberculosis.

FIG. 184.



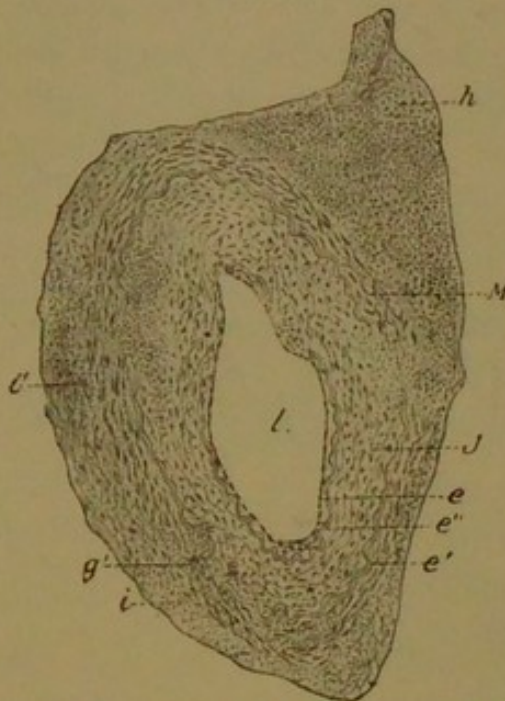
Tubercle in the vessels of the pia. Fresh teased preparation. (From ASCHÖFF-GAYLORD. *Cursus d. pathol. Anat.*)

Syphilis. Vessels which are exposed to syphilitic lesions undergo a thickening of their walls, especially of the intima, which is not itself syphilitic; but both arteries and veins may be the seat of syphilitic lesions by direct infection or by extension from adjacent tissues. In contrast to atheroma, syphilitic arteritis begins in the adventitia as a marked cellular proliferation. Similar changes may be found in the media, especially about the vasa vasorum. Very soon there is a more or less fibrous or hyaline thickening of the intima, and this new tissue may be vascular. The cell multiplication in the adventitia may be circumscribed or extend diffusely over long sections of the vessel. In the former case there are many small nodules sessile on the vessel (arteritis gummosa), but even the diffuse form shows places of special thickening and consequent diminished lumen.

In both the circumscribed and the diffuse forms of syphilomata there occurs either a caseous or a fibrous change. The intima usually remains thickened, with partial or complete loss of lumen.

As in atheroma, syphilitic disease of the vessels causes a loss of their elasticity and resistance, and hence may lead to rupture, with hemorrhage, or to slow dilatation and aneurism. The thickening of the intima may lead to thrombus formation and embolism, and in the brain often causes areas of softening in the territory supplied. (See Chapter XII.) The cerebral vessels, especially at the base of the brain, are peculiarly liable to syphilitic lesions in all forms, and a large percentage of softenings of the brain are to be thus explained, especially those occurring in youth. Analogous lesions may be found in the spinal cord.

FIG. 185.



Arteritis syphilitica. *c.* Lumen. *e.* Endothelium. *J.* Intima, much thickened, partly fibrous, partly infiltrated with cells. *e'* Elastica, destroyed in places. *e''* Newly formed elastica. *M.* Muscularis. *i, i'* Infiltrate in the adventitia. *h.* Small-cell infiltration in adjacent tissue. *g.* Infiltration of the media. $\times 45$. (After OBERMEIER.)

According to late investigations, syphilis may produce a simple endarteritis which has nothing characteristic about it. It is unwise, on the other hand, to make a diagnosis of syphilis merely from the lesions described above, for they are found in other conditions.

A certain diagnosis of syphilis based upon vascular changes appears at present to be impossible.

Dilatations of Bloodvessels (Aneurism; Varix).

Aneurism is the name given to a circumscribed dilatation of an artery. It occurs where a weakened portion of the wall is distended by the blood pressure, and if this is on one side the aneurism is called sacculated; if over the whole circumference it is called diffuse. The condition precedent is loss of elasticity and resistance in the vessel wall. Many causes may lead to such a condition. Against the natural supposition that atheroma predisposes to the formation of aneurism it may be objected that in general these dilatations occur earlier in life than atheroma usually appears; hence atrophy and thinning of the media have been suggested as a cause, which will explain both the loss of power in the vessel and also the compensatory

proliferation of the intima already noticed. Mesarteritis has also been considered as a cause, and in this relation syphilis has been considered very important. Probably aneurisms may follow several anatomical processes, and among these traumatism must be included.

The further behavior of the aneurism depends upon the coats of the vessel. In the simplest case—so-called *dilatation aneurism*—all three coats are distended, but these soon show secondary changes. The atrophy of the media continues until only traces of its muscle fibres remain, and there is a fibrous hyperplasia which tends to oppose the thinning of the wall, and at last converts it into a fibrous tube in which the original three layers can hardly be recognized. Similar connective-tissue formation occurs in the neighborhood. As a result of the stretching and degeneration of the wall it may finally rupture, either the intima, the media, or the adventitia also being torn. When the two former coats are torn the dilatation is called an *aneurism by rupture*. If the intima alone breaks, the blood may dissect below it for a distance, making a *dissecting aneurism*; or the two outer layers are pushed forward, making a *sacculated rupture aneurism*. When the media also is torn the adventitia and the perivascular tissue prevent hemorrhage for a time. In the lumen of such aneurisms there are deposits of fibrin, which may organize in part. In the brain dissecting aneurism may be simulated by absorption of blood from the neighborhood into the perivascular spaces when the vessel passes through a focus of hemorrhage.

Bursting of an aneurism may be followed by death if a large vessel like the aorta be involved, or the bleeding may cease and an arterial hematoma form. Even smaller vessels may cause death when ruptured, as in the brain and in cavities in the lungs.

Aneurisms by dilatation and rupture are most common on the aorta, especially the arch, the carotids, popliteals, and radials. Dissecting forms are most common in the aorta and the small arteries of the brain.

Large aneurisms may have a destructive effect upon neighboring organs, as when the vertebræ or the sternum are eroded by an aortic aneurism. Healing occurs only in the smallest aneurisms.

A special form of aneurism is called embolic, and is due to the entrance of pointed objects, like bits of calcified thrombi, into vessels, and consequent lacerations of their walls. If the embolus is infected the aneurism is both embolic and mycotic. The embolic form is most common in the basal vessels of the brain, where they cause subdural and meningeal hemorrhages.

In the arteries of the brain, and at times also in those of the lung and intestine, small aneurisms occur, which are hardly visible; these are called miliary.

Cirroid or *serpentine* aneurism forms a transition between true aneurism and diffuse dilatation of the vessels, a large number of branches of an artery being widened and tortuous.

Racemose aneurism (*tumor vasculosus*) is formed by the dilatation, thickening, and tortuosity of an entire vascular region, so that a tumor-like tangle of vessels is formed. This is most common about the head.

FIG. 186.



Miliary aneurisms in a cerebral vessel. (After LÖWENFELD.)

Dilatation of Veins (*phlebectasia*) may be diffuse, cylindrical, fusiform, or sacculated. In the latter form it is called *varix*. If the vein is also lengthened it becomes tortuous. Almost always such

FIG. 187.



Dissecting aneurisms on a cerebral artery. (After LÖWENFELD.)

dilatation involves an entire plexus of veins, which lie then in a prominent mass of thickened strands. By pressure the contiguous walls of the veins may atrophy, and thus a cavernous arrangement results. The dilatation may be due to mechanical obstacles to the venous flow, either local or general in nature. Among the general are cardiac weakness, diseases of the lungs, and the action of gravity; among the local are thrombi and pressure, as from tumors or the gravid uterus.

The dilated veins become thicker, and fibrous tissue replaces the elastic, and the lumen may be partly or quite closed.

Beside the causes mentioned there must be changes in the wall of the vein, as may follow inflammation, which lessen the elasticity and resisting power of its walls. As these dilatations appear to be inherited, there may be also a congenital weakness in the veins. Although varix may occur anywhere, the usual places are in the lower limbs,

about the rectum, and along the spermatic cord, whence arise varices of the legs, hemorrhoids, and varicocele.

Within the dilated place a thrombus may form, and when this calcifies it is called a *phlebolith*. Atrophy of the wall may lead to rupture and hemorrhage from a varix. In the organ whose veins are affected various ill consequences may follow, as catarrh of mucous membranes, atrophy and eczema of the skin, edema and lymphatic stasis, hypertrophy of the skin and subcutaneous tissue, and also of the periosteum (*elephantiasis phlebectatica lymphatica*). Mechanical injuries and inflammations easily cause obstinate ulcers to develop, and from rupture of the stiff and brittle veins there may be severe bleeding. (See Chapter XV.)

When aneurism and varix coexist and communicate there may be (1) *aneurisma varicosum*, by rupture of an aneurism into a vein, which later becomes dilated; or (2) *varix aneurismaticus*, when both vein and artery are wounded at the same time and the arterial blood streams into the vein and dilates it.

Capillary ectasis may be congenital, as in vascular nevus, or acquired, as in stasis and chronic inflammatory conditions.

CHAPTER VIII.

DISEASES OF THE SPLEEN, LYMPH NODES AND VESSELS, AND MARROW.

A. THE SPLEEN.

THE spleen is provided with a capsule which is covered by peritoneum, and from its inner side trabeculae of fibrous tissue pass into the organ, dividing into fine branches in their course. On the cut surface there are follicles or Malpighian bodies, macroscopically visible, and the remaining tissue is the spleen pulp.

The structure of the pulp is not wholly understood. Examination of pencilled normal spleen, or acute splenic tumor, reveals many different cells. There are plenty of red and white blood cells and a varying number of large round cells with one or more large nuclei; the latter are called pulp cells. They often enclose red cells, pigment from the blood and other sources, and fat granules. Slender sickle shapes are also nearly always found, which have a prominent nucleus about their middle, and are considered as endothelia from blood spaces.

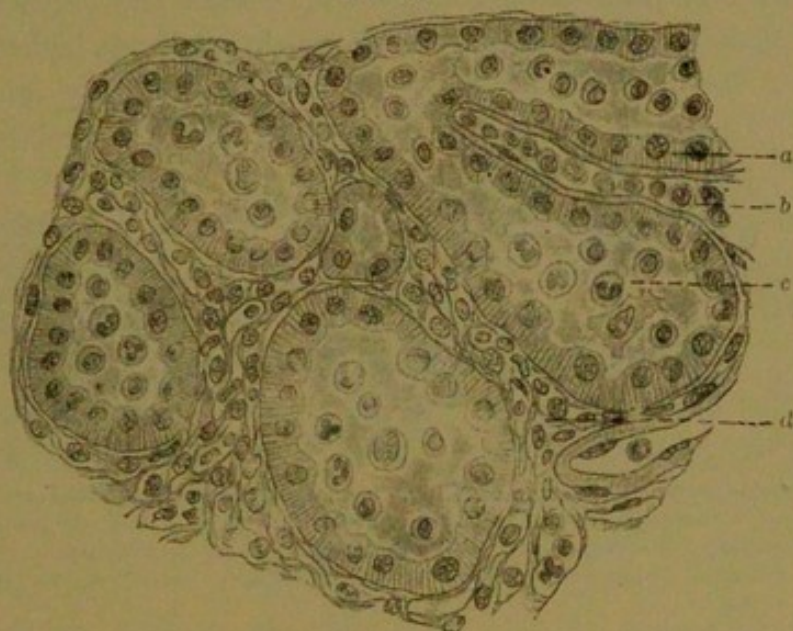
In sections the pulp presents many arteries and veins in which a remarkable tall and cubical endothelium may be found. These may pass into thin-walled tubes with spindle-shaped endothelia, between which there are stomata that allow the blood to pass into the tissue of the gland. There are also the so-called pulp cavities, which are lined with high cubical epithelia and filled with red blood and other cells. The epithelium in many places is finely striated. The rest of the pulp is traversed by a reticulum of fine mesh, which is connected with the coarser reticulum of the organ, and contains in its strands various kinds of cells.

The reticulum can be recognized only in pencilled or very thin sections. A similar reticulum is found in the Malpighian bodies, which are connected with the branches of the splenic artery, and in its meshes are lymphoid cells like those of the lymph nodes. The follicles are among the places where leucocytes form, and from them these cells enter the pulp and then the blood. The cells which contain red corpuscles and pigment suggest that physiologically there is a

destruction of red cells in the spleen. In the embryo they are also formed here.

The relation of the spleen to the lymphatic organs and to the blood appears from its histology. In the latter relation the organ stands as the lymph nodes to the lymph, characterized as it is by slow circulation, direct contact between the blood and tissue, long stay in the organ, opportunity for deposit of transported matters and for intense chemical action. All these features dispose the spleen to secondary affections from the blood, as the nodes from the lymph. Hence the spleen shares in blood disorders and in general diseases.

FIG. 188.



Section from human spleen (sublimite fixation). a. Striated epithelia. b. Bloodvessel. c. Blood space. d. Reticulum. $\times 350$. (After BÖHM-DAVIDOFF.)

As the organ filters particles out of the blood, deposits of pigment occur in hemoglobinuria and melanemia, so that the organ may be black in color, and particles of coal-dust may have the same effect. With *icterus neonatorum* the spleen contains hematoidin crystals, which form post-mortem.

Bacteria also are filtered out of the blood, and toxins act very strongly here. In various infections, as typhoid fever and anthrax, the spleen presents a swelling, from congestion and cellular hyperplasia, which is characteristic. The volume of the organ may be two, three, or many times the normal. This is called acute splenic tumor.

In the spleen swollen by congestion the capsule is stretched, the pulp is swollen and granular, and hides both the trabeculae and the

follicles, and is intensely red. Hyperplasia of the pulp cells and follicles is soon added, and many of the former are in fatty degeneration. The sickle-shaped elements are numerous and swollen. The appearance of many cells containing red cells and pigment is evidence of the rapid destruction of the erythrocytes in the organ. From the cellular hyperplasia the color becomes of a darker red, and the consistence of the pulp lessens until it is semifluid. In the most severe forms the capsule may burst, with fatal hemorrhage into the peritoneum. Infectious material held in the spleen often causes localized necroses, and these lead either to fibrous scars, like those of infarcts, or to softening, and with pyogenic organisms to abscesses in the organ. When such soft and infected foci break, a fatal peritonitis may be the result. Rarely a suppuration in the vicinity of the spleen passes to

FIG. 189.

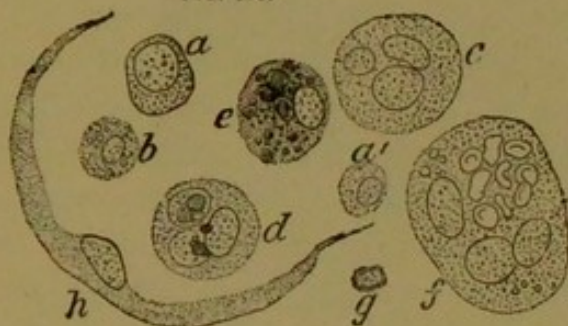


FIG. 189.—Cells from acute splenic swelling. *a, a'*. Pulp cells with one nucleus. *b*. The same, with fat drops. *c*. Polynuclear pulp cells. *d, e*. Pigmented cells. *f*. Polynuclear cells enclosing red blood corpuscles. *g*. Lymphocyte. *h*. Endothelial cell from a blood space. $\times 250$.

FIG. 190.

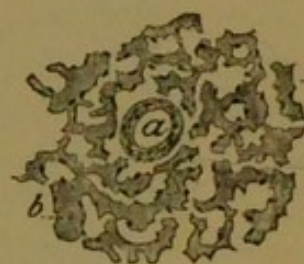


FIG. 190.—Amyloid degeneration of the splenic reticulum. *a*. Vessel. *b*. Thickened amyloid reticulum. $\times 250$.

the organ. In certain diseases, as diphtheria and scarlet fever, the hyperplasia especially affects the follicles, which appear as large and prominent gray spots on the section; and in diphtheria there may be fibrin and necrosis about them.

When a swollen spleen remains in this condition for a long time a chronic induration of the organ follows, accompanied by atrophy of the cellular and hyperplasia of the fibrous elements. This interstitial increase affects first the trabeculae which enter the organ from the capsule, as well as the capsule itself, the adventitia of the vessels, and the reticulum. Owing to such fibrous increase the pulp atrophies, the organ becomes small and hard, until a size less than the normal may be attained. On the cut surface the fibrous bands are plainly recognized dividing the organ as if by numerous septa, and the pulp between appears dry, hard, and sunken, and often deeply pigmented. The

capsule may be uniformly or locally thickened, and the fibrous spots may be cartilaginous in hardness, as is common in the perisplenitis fibrosa of old age. Such chronic indurations may follow the acute splenic tumor or gradually develop in the course of many chronic diseases, especially tuberculosis and syphilis.

The highest grade of splenic hyperplasia is observed with certain diseases of the blood and lymphatic organs, as in malaria, when the organ may reach a size many times the normal. The distinguishing characteristic of these cases is the massive deposit of pigment in the organ, which gives it a black or slaty color, across which run the gray lines of the thickened trabeculae.

The lymphoid elements of the spleen may undergo hyperplasia analogous to that observed in the lymph nodes, both in cases of splenic leukemia and, apart from this, in so-called splenic anemia (pseudo-leukemia). The follicles may swell and be of the size of peas or cherries. Afterward an induration may blot out the structure of the pulp and follicles and make the organ very firm, though it continues to enlarge. Pigment of a brown or black color and anemic or hemorrhagic infarcts also are observed in these cases.

Other circulatory disorders include stasis and infarction.

Splenic swelling from stasis, in the majority of cases, is due to general stasis with valvular cardiac lesions or to obstacles in the portal circulation. It may also occur from compression or occlusion of the splenic vein. In any case there is a swollen and cyanotic organ.

After persisting a time the condition leads to cyanotic induration, and as a consequence the organ may become somewhat smaller. Swelling of the spleen is constant with hepatic cirrhosis, and this has been referred entirely to the portal congestion. Lately it has appeared as if the splenic enlargement in cirrhosis were more independent, for it may occur early in the disease, before there is much congestion; and the increase is more dependent upon cellular hyperplasia than upon excess of blood, although the latter is of some influence.

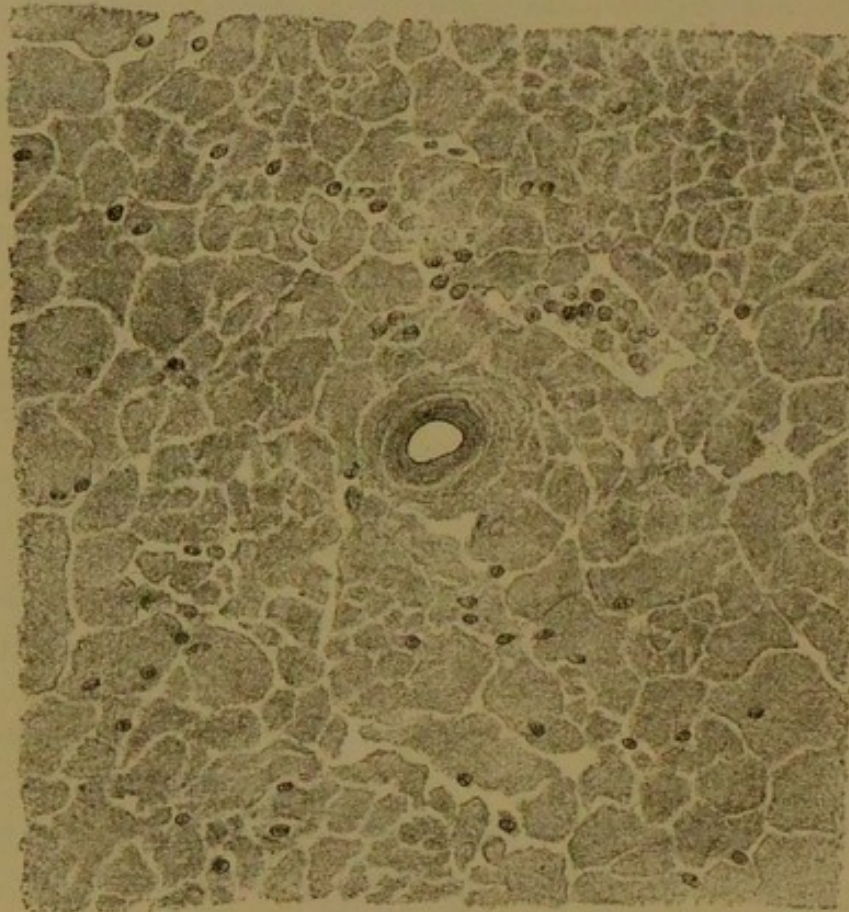
Embolie and thrombotic infarcts of the spleen are either anemic or hemorrhagic. In the former case the affected spot is yellow, firm, surrounded by a hyperemic or hemorrhagic margin, and of a wedge-shape, with the base superficial. The hemorrhagic forms are at first dark red, and then their color fades more and more. The resulting necrotic foci heal and are replaced by fibrous tissue, which may be pigmented after hemorrhagic infarcts, and the capsule over them is

thick and depressed. With infection there may be small abscesses, which perhaps heal, or large ones, which break.

Simple **atrophy** of the spleen may be part of a general atrophy, and is common in old age. The organ is small, its capsule is thick and wrinkled, the trabeculae are thick and prominent, the pulp is pale, smooth, and sunken, and the follicles are indistinct.

Among the *degenerations* amyloid changes are common in the spleen, and appear early in general conditions of this nature. Two forms are

FIG. 191.



Marked amyloid degeneration in a splenic follicle. In the centre there is a vessel with thickened amyloid walls. But few lymphocytes preserved. Between the amyloid masses narrow spaces remain. $\times 250$.

distinguished. In one—the “sago spleen”—the follicles are prominent and appear homogeneous and glassy, like grains of boiled sago. When the degeneration chiefly affects the pulp the section appears smooth and translucent in places or generally, and has a firm consistence and a peculiar color, like raw bacon or ham; in the diffuse form the organ may be enlarged.

Microscopically, in both forms the reticulum and the walls of the vessels are involved. The cells atrophy, so that at last only thick,

glistening masses remain, which stain brown with iodine and correspond in arrangement to the reticulum, whose interspaces are reduced to the minimum.

Tuberculosis occurs in the spleen as miliary and as conglomerate nodules, the former as countless small nodules in general infection. The tubercles are smaller than the follicles and are prominent above the cut surface, are not easily scraped off, and have a yellow color from caseation. Microscopically they have the characteristic structure. Single large nodules—conglomerate tubercles—may be as large as peas, and are common in children in the course of tuberculosis of other organs.

Syphilis often causes hyperplastic induration of the spleen, and rarely gummata. In congenital lues the organ is large and two or three times as heavy as normal. The fibrous tissue is thickened, and there is a cellular infiltration of the vessel walls.

Tumors are uncommon in the spleen. They may be metastatic sarcomata, or carcinoma of neighboring organs may invade the spleen.

Of the animal **parasites**, *echinococcus* and *cysticercus* are occasionally found in the spleen.

Injuries. An extremely swollen spleen, especially when the pulp is fluid or there is an abscess, may rupture and cause fatal hemorrhage or purulent peritonitis. Small tears in the capsule allow the pulp to protrude, and give rise to so-called hernias of the spleen. These appear as small brown projections, often along the anterior border, and from them cysts may develop, with clear contents. Traumatism may rupture a swollen organ.

Deformity and Dislocation. The spleen may be lacking, or it may have a false position (*situs inversus*, *hernia*). In chronic enlargement the heavy organ may stretch its ligaments and lie more deeply in the abdomen. Small accessory spleens are common.

B. LYMPH NODES.

In the lymph nodes three elements are distinguished: 1. The supporting tissue, made up of capsule, trabeculae, and reticulum. The trabeculae pass from the capsule into the node, and divide into finer branches. The reticulum is clothed with endothelium, and permeates the whole node. 2. The follicles and the follicular strands (cortex and medulla), made up of lymphoid tissue, and the site of manufacture of the lymphocytes. 3. The lymph spaces, occupying the intervals

between the other structures, connected with the afferent and efferent lymph vessels, and containing the lymph.

The roots of the lymph vessels are found in the tissue spaces, and from here all injurious materials are carried to the nodes. Thus in the lungs inhaled dust is carried to the bronchial nodes, and from suppurating wounds and foci bacteria are taken to adjacent nodes. In this way the vessels and the nodes may become diseased. The transport of such material is carried on partly by phagocytes. Foreign material is laid down first in the lymph sinus and later in the follicular structures. Similarly, chemical materials, as toxins, may enter and affect the nodes. Hence bacteria and other noxious substances have opportunity to cause inflammation and disease of lymph structures; and, on the other hand, the latter protect the body from these injurious influences, though some infections, like syphilis, pass freely through the nodes.

From these relations it is evident why secondary lymphatic lesions are so often regional and why special groups of nodes are often involved. With diseases in the mouth the cervical nodes are affected, from the lungs the bronchial, and from the genitals the inguinal groups are attacked. Less often the lesion is carried in the other direction by way of the blood. Such lesions of the nodes are observed in general infectious diseases.

Access of inflammatory agents or products may cause an acute *lymphadenitis*, as already mentioned. The node becomes hyperemic, there is a cellular emigration from the capillaries, and also a hyperplasia of the cells of the follicles. In the sinus there is an accumulation of the proliferated lymph cells and a strong multiplication of the endothelia, which also desquamate. Macroscopically packets of nodes are uniformly swollen, and their cut surfaces are succulent and perhaps marked by small hemorrhages. In many infections, as anthrax, the bleeding is copious. Acute inflammation of the nodes may resolve or become chronic. The abdominal nodes in typhoid fever are much swollen and soft, and may undergo necrosis, softening, and perforation.

Resorption from a purulent process fills the spaces of the nodes with polynuclear pus cells, which may be recognized from the single nuclei of the lymphocytes. This resorption of pus should not be confounded with purulent lymphadenitis, which may follow it or start in the nodes after access of pyogenic organisms. Added to the lesions of acute lymphadenitis we then have the formation of purulent collections in the node as yellow points, which enlarge by fusion until the

tissue of the node is completely melted into an abscess and neighboring tissues are perforated. If the pus is lost on the surface the abscess heals, with scar formation. According to the nature of the cause the lymphadenitis may be necrotic or gangrenous. In diphtheria this is more common than suppuration.

When injurious material is carried to a node in a chronic manner, as from long-standing catarrh or slow ulcerative processes, a chronic form of hyperplastic lymphadenitis develops. Cellular hyperplasia is accompanied by fibrous, the trabeculae thicken, the cells finally atrophy, and the tissues become hard, small, and fibrous.

Similar changes follow the absorption of dust and other corpuscular matter, and the nodes acquire a characteristic pigmentation. This is seen in the bronchial nodes with anthracosis. In many cases the deposit of finely divided material leads to the softening of the node, so that anthracotic nodes may break into vessels and their coal-dust pigment be scattered to other parts, especially the spleen. With slight degrees of pigmentation the induration may not be marked. Discoloration of the nodes follows tattooing, resorption of blood (hematoidin), various skin diseases, and *morbus Addisonii*.

Tuberculosis of nodes is usually secondary to similar disease of the lungs, bones, intestine, etc. The bacilli reach the nodes which correspond to the site of the lesion. In some cases the disease appears to develop primarily in the nodes, as in the neck and the mesentery, without apparent disease of the intestine. Probably the bacilli enter by the mucous membrane, but are carried to the nodes before they have time to cause lesions at the place of entry. In other cases small foci which may be missed in ordinary examinations may be the original starting-place. Primary disease directly passed from the mother to the fetus cannot be excluded as impossible.

Tuberculosis of the lymph nodes may be circumscribed or diffuse, but in either case it tends to caseous degeneration. In the first form the tubercles occur as a few small, grayish nodules, which increase and multiply to larger caseous masses. They may become hyaline and fibrous or calcareous. In the latter form there is an infiltration with small and large cells diffusely through the tissue, which may calcify or soften. Large groups of nodes may be attacked, and extensive abscesses may result.

The process may spread from node to node until almost the whole system becomes involved, or there may be an encapsulation, which confines it and ends in healing.

Serofulous lymphomata are due in part to chronic hyperplasia, in part to lymph stasis, and in other cases to tuberculosis.

In the course of **syphilis** swelling of the nodes is an important feature. Large, hard, indolent buboes form, which are grayish red on section, and are either regional, corresponding to the initial lesion, or spread over larger portions of the lymph system. They are due to cellular hyperplasia in the sinus and the follicles, to which fibrous growth is added later, and degenerative changes may follow this.

Malignant **tumors** may enter the lymph channels and infect the vicinity. Carcinoma especially is apt to spread from separation of its cells and their transport through the lymph ways. They are arrested in the sinus of the node, and form new tumor nodules. In metastatic carcinoma the stroma is formed from the fibrous portions of the nodes, while the cellular are lost.

Among the primary tumors of lymph nodes the most important occur in leukemia (p. 149). Other primary tumors are sarcoma, angiosarcoma, and endothelioma.

Among **degenerations**, amyloid and hyaline lesions may be mentioned. The latter involves the reticulum, converting it into a homogeneous, glistening substance, and the cells disappear. The former attacks both the reticulum and the vessels, and gives the node a firm consistence. Calcification may follow suppurative and caseous changes.

C. LYMPH VESSELS.

The commonest lesion is acute *lymphangitis*, as the result of material or organisms absorbed from inflammatory foci. The vessel may carry the inflammation to the node and remain unaffected, or itself become inflamed. The wall of the lymph vessel is infiltrated with small cells and frequently hemorrhagic in the adventitia. The endothelia are swollen and desquamate, and lymphatic thrombi may fill the lumen. These changes appear as red lines on the skin when the superficial vessels are involved.

Purulent lymphangitis may follow absorption of pus (septic lymphangitis). The wall of the vessel is infiltrated with pus and the lumen filled with pus and fibrin, softening thrombi, and detritus, and consequently it is swollen, nodular, and of a yellow color. Abscesses may follow in the course of the vessel and in the node, and entrance of the pus into the venous system may cause septic or pyemic conditions.

A chronic productive inflammation may follow other chronic inflammations, especially of serous membranes, with proliferation of endothelia and occlusion of the vessels (lymphangitis obliterans).

Tuberculous lymphangitis is common in the neighborhood of similar lesions in the organs. The wall of the vessel is thickened and contains small nodules, and between occluded points it may be slightly dilated. In the largest trunks, as the ductus thoracicus, larger masses of tuberculous tissue may be found in the intima, and from here a general infection may take place through the blood.

Tumors. Carcinoma grows for long distances along lymph vessels. Endothelioma and lymphangioma occur.

Dilatation of lymph vessels (*lymphangiectasis*) follows stasis after occlusion of a vessel by scars, tumors, and tubercles when collateral lymph channels do not compensate. Lymphorrhagia may follow closure of a large vessel. Frequently dilatation of lymph channels and chronic inflammation stand in relation to each other as cause and effect. The dilatation may be uniform or sacculated. Here belong *pachydermia lymphangiectatica* and *elephantiasis Arabum*—the latter due to filaria—and also cases of *macroglossia* and *macrocheilia*, which may depend on congenital dilatation of the lymph channels. The lacteals may be dilated, thickened, and tortuous when their contents become inspissated and caseous.

D. BONE MARROW.

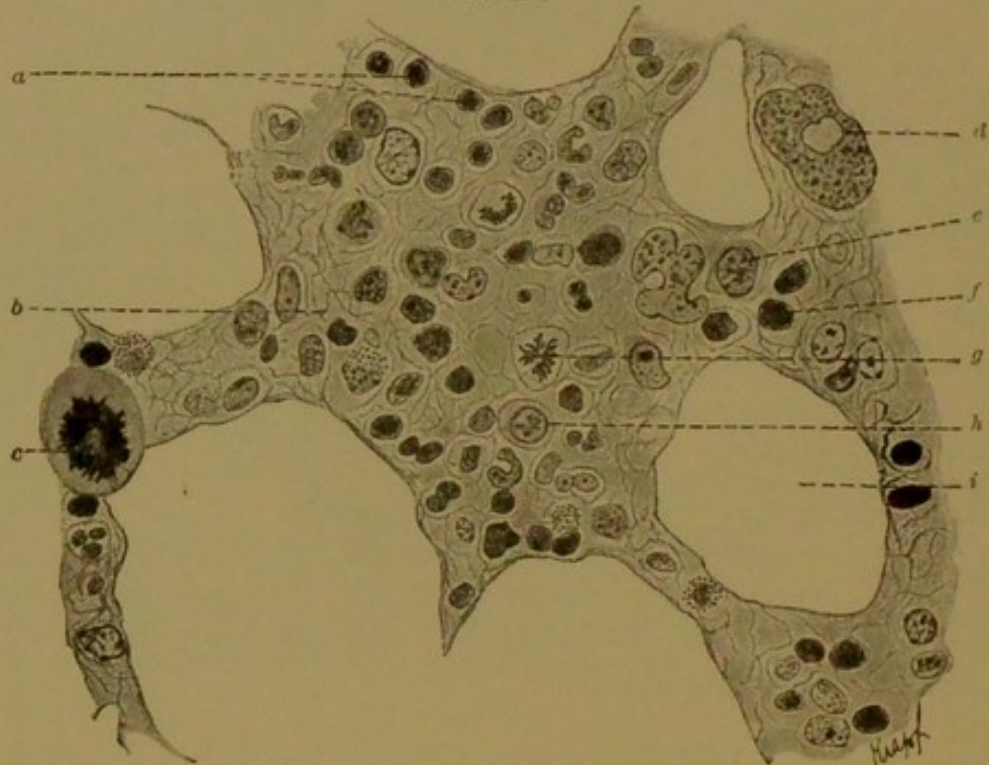
In the red marrow there is a fine reticulum, which contains various cells: 1. The true marrow cells, which are round, larger than a lymphocyte, and have a single nucleus, often indented; from these come the polynuclear leucocytes. 2. Ordinary leucocytes. 3. Erythroblasts—nucleated cells with hemoglobin, making red blood cells. 4. Giant cells—large elements with many small nuclei or large polymorphous nucleus, serving as osteoclasts in the physiological resorption of bone.

In the growing individual the marrow, up to puberty, is red or lymphoid; then in the long bones it becomes fatty, but in the short and flat bones it remains red. Fatty marrow shows many cells which contain fat, but is generally poorer in cells than the red. In advanced age and in cachexias fatty marrow becomes changed into mucoid material.

Hyperplasia of the marrow, in which fatty and gelatinous marrow becomes again lymphoid, occurs after acute hemorrhages, oligemia,

pernicious anemia, leukemia, and many infections. In pernicious anemia the marrow is dark red, cellular, and under the microscope shows degenerating red blood cells, macrocytes and microcytes, and nucleated forms (normoblasts, megaloblasts). Many red cells and their products are enclosed in white cells.

FIG. 192.



From a section of human red marrow. *a*. Nucleated red blood cell. *b*. Reticulum. *c*. Mitosis in a giant cell. *d*. Giant cell. *e*. Marrow cell. *f*. Nucleated red cell. *g*. Mitosis. *h*. Marrow cell. *i*. Space in which there was fat. $\times 680$. (After BÖHM-DAVIDOFF.)

In leukemia the marrow is also red, raspberry color, or because of the cellular proliferation it may be grayish red, or yellow, or even purulent in color. There are many nucleated red cells, cells with pigment and red cells enclosed, and Charcot-Neumann crystals, and hemorrhages.

Changes in the marrow, with diseases of the bones, will be treated in Chapter XIII.

CHAPTER IX.

DISEASES OF THE RESPIRATORY ORGANS.

A. NOSE AND ADJOINING CAVITIES.

THE commonest disease of the nasal mucous membrane is acute catarrh, due to the various elements which cause acute pharyngitis and laryngitis, as will be mentioned later. *Coryza*, or acute nasal catarrh, is a typical inflammation of a mucous membrane, and presents several stages. Hyperemic swelling of the membrane is followed by a stage with mucoserous exudate and then by mucopurulent discharge, with rapid desquamation of the epithelium. With severe purulent catarrh the cavities opening into the nose are apt to be similarly affected, and the purulent collection is called empyema of the antrum or frontal sinus. Croupous and diphtheritic inflammation invades the parts from the pharynx. Occasionally there is a fibrinous rhinitis, without epithelial necrosis. This form is of obscure etiology, but diphtheria bacilli may be found in the membranes.

Chronic nasal catarrh occurs with scrofula, and causes hypertrophy at first, later atrophy of the mucosa. Erosions and ulcers are constantly found, on which the exudate dries to crusts. The secretions may be fetid in odor, perhaps because of the micro-organisms contained (*ozena*). In the course of the disease there may be a formation of multiple polypoid growths.

Tuberculosis of the nasal mucosa is rare. It is accompanied by erosions and development of tubercles. Lupus may pass from the face to the interior of the nose.

Syphilitic lesions are common in the nose. In the earlier stage there may be a syphilitic catarrh, with marked *ozena*; and, later, papules and erosions, gummata, and infiltrations in the mucosa, the periosteum, and the perichondrium of the parts may be found. The result of these changes may be necrosis and caries of cartilaginous and bony tissues. In the latter case there will be malformation of the nose.

Glanders is unusual in the human nose. It causes nodular infiltrations and ulcers.

The commonest neoplasms in the nose are mucous polyps as circumscribed hyperplasias of the mucosa. They consist of a cavernous tissue like that of the mucous membrane, or contain glands also. Polypoid fibroma and adenoma are also found.

Of the malignant tumors, epithelioma (squamous celled) of the nostril, sarcoma, chondrosarcoma, and others may occur. The so-called fibrous pharyngeal polyp is a fibrosarcoma starting in the periosteum of the basis cranii and growing into the nasal and pharyngeal cavities.

B. LARYNX, TRACHEA, AND LARGE BRONCHI.

Larynx and Trachea.

As a congenital anomaly the epiglottis may be slit or the larynx may be hypoplastic.

In the laryngeal mucosa simple circulatory disorders with increased excretion may be hard to separate from inflammatory lesions. Both may occur with the clinical symptoms of edema of the glottis, in either an acute or a chronic form. The mucosa is then the seat of an extreme accumulation of serous fluid, and where it is loosely connected to the tissues beneath it swells so that the lumen of the tube is closed, and death by asphyxia may occur. The parts most swollen are the ary-epiglottic folds and the space between them. In the cadaver the swelling may have partly disappeared, but in this case the tissues are loose and lie in folds, and we conclude that during life the edema was more marked.

At times the swelling is a simple edema, at times a serous inflammation; and it may be due to venous stasis, especially from compression of the cervical veins, or less frequently, to a general stasis from diseases of the heart and kidneys. Erysipelas also may cause simple edema of the larynx. With other inflammatory processes in the larynx or near it edema laryngis may be developed. Among these are diphtheria, ulceration of any kind, inflammation in the larynx and affecting the cervical spine, carcinoma, and as the first stage of phlegmonous laryngitis. Certain drugs, as iodine and mercury bichloride, may have a similar effect.

Acute catarrh of the larynx (*laryngitis catarrhalis*) may be part of a general inflammation of the respiratory passages or develop with certain acute exanthemata, and it may either be primary in the larynx

or descend from the pharynx or ascend from the bronchi. Cold, inhalation of irritating material—as dust, gases, hot air, etc.—and excretion of chemicals—as iodine and sublimate—may also be the cause.

Laryngitis is common with influenza. With acute laryngitis the mucosa presents the stages of similar lesions in any mucous membrane—redness, swelling, at times marked edema, and a secretion corresponding to the stage, either mucoserous or mucopurulent.

A similar etiology exists for **chronic laryngitis**. Frequent repetitions of causes for the acute form may result in the chronic inflammation, as is noticed in certain trades where contaminated air is constantly respired. A large percentage of the cases is connected with stasis, analogous to the similar lesions of the bronchioles and lungs (brown induration). Overuse of the voice and excess in alcohol and tobacco may produce the same result.

The entire larynx with adjoining parts of the trachea may be involved, or certain areas of the mucosa, as over the vocal cords or the epiglottis, may be the seat of the lesion. The swelling and the irregular injection of the vessels will usually involve the aryepiglottic folds and commissure and the false cords, where the tissue is loose, and the true cords may be concealed by the former. The swollen mucosa may present folds and wrinkles.

Pachydermia diffusa is the name given to one result of chronic inflammation, by which the epithelium and even the connective tissue of the mucous membrane become thickened in various sections of the larynx. It follows chronic abuse of alcohol, and tobacco especially.

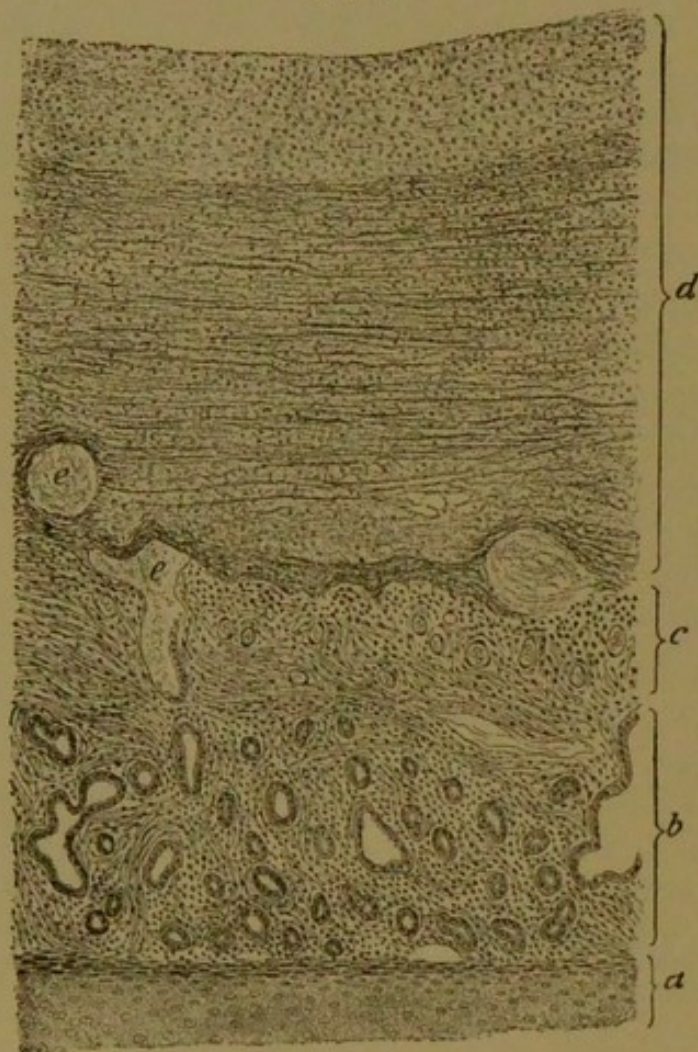
The epithelium becomes thick, white or gray, opaque, and may be stripped off as a single layer. It is composed chiefly of cornified cells, and the cylindrical may become squamous. A verrucous form of the lesion results from inequalities in the thickening. Laryngitis tuberosa may occur as small projections on the vocal cords. A chronic hyperplasia of the parts just below the cords is known as *chorditis inferior hyperplastica*.

Pseudomembranous (diphtheritic) inflammations of the larynx occur with a variety of acute infectious diseases, especially in the course of the disease clinically known as diphtheria. (Bretonneau.) Commonly the disease spreads downward from the pharynx, but it may begin either in the larynx or trachea. The characteristic feature is the formation of a false membrane (p. 113). Such a false membrane may usually be stripped off, and the epithelium below it is found to be absent, the parts injected, but otherwise unchanged. On the sur-

face of the epiglottis and the vocal cords the membrane is more firmly attached. Deeper inflammations, with sloughing of the entire thickness of the mucosa, develop on the edges of tracheotomy wounds and about the erosion produced by the lower end of the intubation tube.

The membrane may cover the interior of the larynx as small and scattered white spots, or form thicker masses, which reproduce the

FIG. 193.



Croup in the trachea. *a*. Cartilage. *b*. Submucosa with many mucous glands. *c*. Mucosa. *d*. Layer of fibrin. *e*. Plugs of mucus.

cavity as a cast when coughed out. The latter may close the lumen of the part. Such membranes are removed by coughing or undergo softening as the disease improves. (See Chapter X.) Similar pseudo-membranes occur in the course of scarlet fever and variola, and in typhoid circumscribed ulcerations of the mucosa follow necrosis and desquamation of the epithelium.

Phlegmonous laryngitis is a much deeper process than catarrhal laryngitis, and consists in purulent infiltration of the mucosa and sub-mucosa. It is usually secondary to severe catarrh, croup, and diphtheria, or occurs with endocarditis, pyemia, and erysipelas. It may also result from injury to the part. Usually a circumscribed portion of the larynx is thickened and swollen, and within this is a collection of pus, which may open later into its lumen. The lesion and its preceding stage of edema are often localized about the aryepiglottic folds and the false cords.

Purulent perichondritis leads to the accumulation of pus between the cartilage and its investing membrane, the latter being stripped up and necrosed. The pus may perforate into the larynx or outwardly through the skin. This lesion follows deep ulceration and other severe diseases of the part, and is preceded by edema of the glottis.

Tuberculosis of the larynx and trachea occurs in about 30 per cent. of cases of phthisis, and in the majority of cases follows infection by the bacilli in the sputa passing over the laryngeal surfaces. As on all mucous membranes, the lesion begins with the formation of small nodules under the epithelium, which are surrounded by a tubercular granulation tissue; and to this area of reddened and prominent surface the name tuberculous infiltration is given. Caseous changes soon convert the part into an ulcer, and on its base and about it new tubercles develop.

The commonest sites of the lesion are between the arytenoid cartilages and the vocal cords, and about the posterior commissure, where papillary excrescences form, and following their destruction irregular, gray, crater-like ulcerations remain. The vocal cords are at first red and swollen, and then may themselves suffer ulceration, and the result of the latter may be longitudinal fission of the cord. When several ulcers along their edges become merged they give the part a peculiar thick and dentate appearance. On the epiglottis and other portions of the larynx similar ulcers may form and become confluent, and thus produce widespread destruction.

Together with the ulcers, miliary and submiliary tubercles are seen in the mucous membrane under the epithelium, and especially about the ulcers. Parts which are not ulcerated present the swelling and wrinkling of chronic laryngitis. Edema of the glottis, perichondritis, and necrosis of the cartilages, especially the arytenoid, may occur with tuberculous laryngitis.

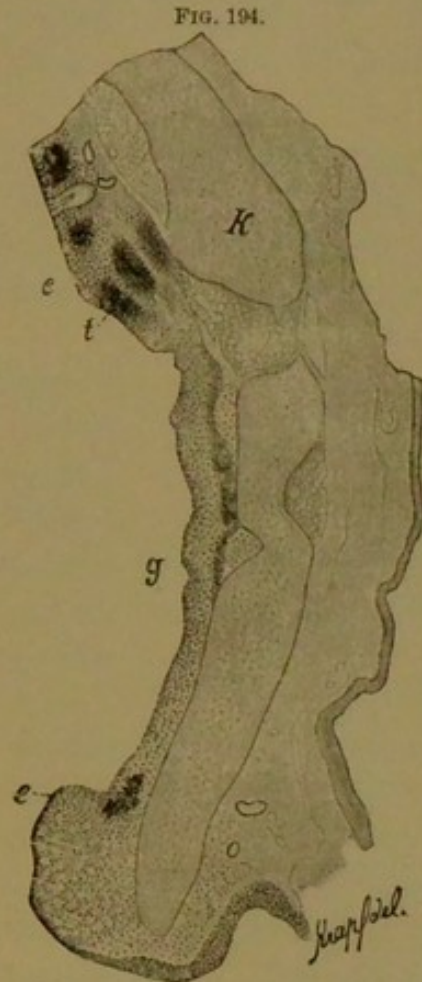
In the trachea there are usually flat, lenticular ulcers, which may join and cause large defects.

Lupus in the larynx resembles the same lesion in the pharynx, and is said to have occurred here primarily.

Syphilis of the larynx is either secondary or tertiary. In the former there may be an inflammation which is not specific, or mucous plaques may be added. The latter are mucous papules caused by cellular infiltration and hyperplasia of the papillæ and proliferation of the epithelium over them, and appear as whitish or gray, round and prominent spots. The central portion becomes eroded and of a dark-red color. Mucous patches usually spread from the pharynx to the epiglottis, the interarytenoid region, and ary-epiglottic folds and vocal cords.

In tertiary syphilis there develop diffuse infiltrations or multiple circumscribed nodules. Both of these may break down and leave ulcers with thickened edges, a raw base, and sharp limitation from the healthy tissue; and by their rapid perforation to the deeper structures perichondritis, necrosis of the cartilages, and phlegmonous laryngitis may result. The portions not involved in the ulceration may become hyperplastic and prominent, and further deformities result from the scars left by the ulcers. These are shiny fibrous bundles, often projecting from the wall, and by their contraction the form of the larynx may be so changed as to cause marked stenosis.

Tuberculous ulcer of the tracheal mucosa. Section through the tracheal wall. *k*. Cartilage, over which are sub-mucosa and mucosa. *e*. Epithelium. *t*. Tubercles in the mucous membrane and below it, cellular infiltration also. *g*. Ulcer. $\times 10$.



In the course of typhoid fever simple or croupous laryngitis may occur, or infiltration and ulceration and diphtheritic necrosis of the mucosa. It is uncertain how much of this is due to the typhoid bacillus. (See Chapter X.)

Rhinoscleroma (see Chapter XV.) produces a slow inflammatory process in the laryngeal mucosa and submucosa, with atrophy and contraction; and these changes are usually accompanied by simple chronic catarrh.

Of the benign *tumors*, papillary fibroma is common in the larynx, especially invading the vocal cords. It appears as wart-like nodules, as large as grapes at times, or smaller and multiple. Chronic laryngitis always accompanies it, and stenosis may result from the swelling. Cystic tumors are at times found on the epiglottis and the false cords.

Of the malignant forms carcinoma is the most common. As a rule, it begins on the false vocal cords, and is an epithelioma. Stenosis and more or less destruction of the larynx are usually the result, and adjacent tissues are apt to be involved. Secondary carcinoma may extend from the esophagus.

Calcification and *ossification* of the larynx sometimes occur as a senile change or after chronic inflammation, especially in tuberculous subjects. Ossification may produce ankylosis of the joints, and slight trauma may result in fracture. Injuries and luxations of the laryngeal articulations may lead to stenosis, and the latter may be caused also by foreign bodies. Compression of the larynx and trachea by enlarged thyroid, tumor of the esophagus, and aortic aneurism may occur, and a "sabre-sheath" deformity result.

C. DISEASES OF THE BRONCHI.

Lesions of the small bronchi are so closely connected with those of the lung that they will be treated together. Remaining diseases of the bronchi do not need extended mention. Inflammation and tuberculosis are practically the same as similar affections of the trachea.

Acute catarrhal bronchitis follows causes like those mentioned for laryngitis. The mucosa is swollen and red and covered with mucoserous or purulent exudate, in which mucous corpuscles and degenerated epithelia are found. When the secretion is copious the case is called *blennorrhœa*.

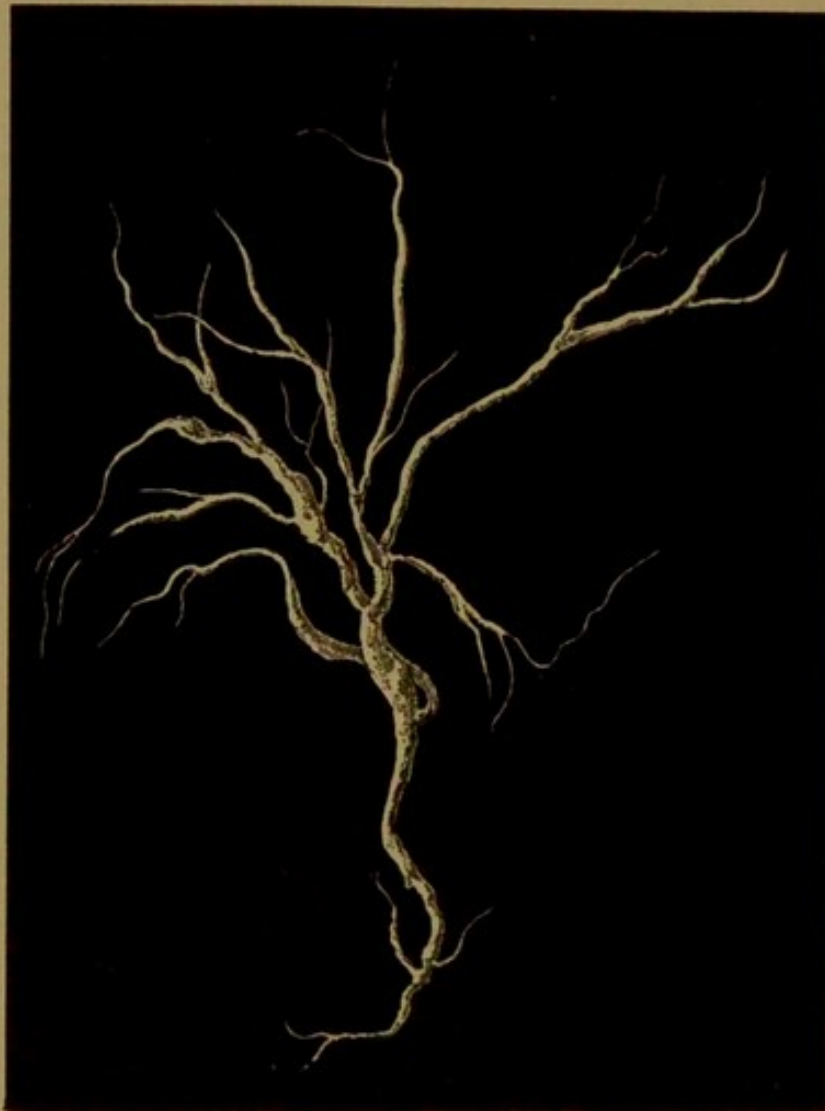
Inflammation in the finest divisions of the bronchi is called *capillary bronchitis*. It occurs primarily or with general diseases, especially acute exanthemata, and is of importance because of the relation of these bronchi to the parenchyma of the lung. (See Catarrhal Pneumonia.)

Chronic catarrhal bronchitis follows the acute or is secondary to various lung diseases, especially emphysema and tuberculosis. In many cases it is associated with stasis and brown induration and chronic edema of the lung, with copious sputa (*blennorrhœa*). The

mucosa affected is swollen, hyperplastic, and then atrophic, and the muscular coat is thickened. Atrophy lessens the resistance of the bronchial wall and leads to dilatations and emphysema.

The thickened sputa may remain in the bronchi a long time, and undergo putrefaction from the access of saprophytes. This is called

FIG. 195.



Large fibrinous coagulum from the bronchi in a case of croupous pneumonia. (After KAATZER.)

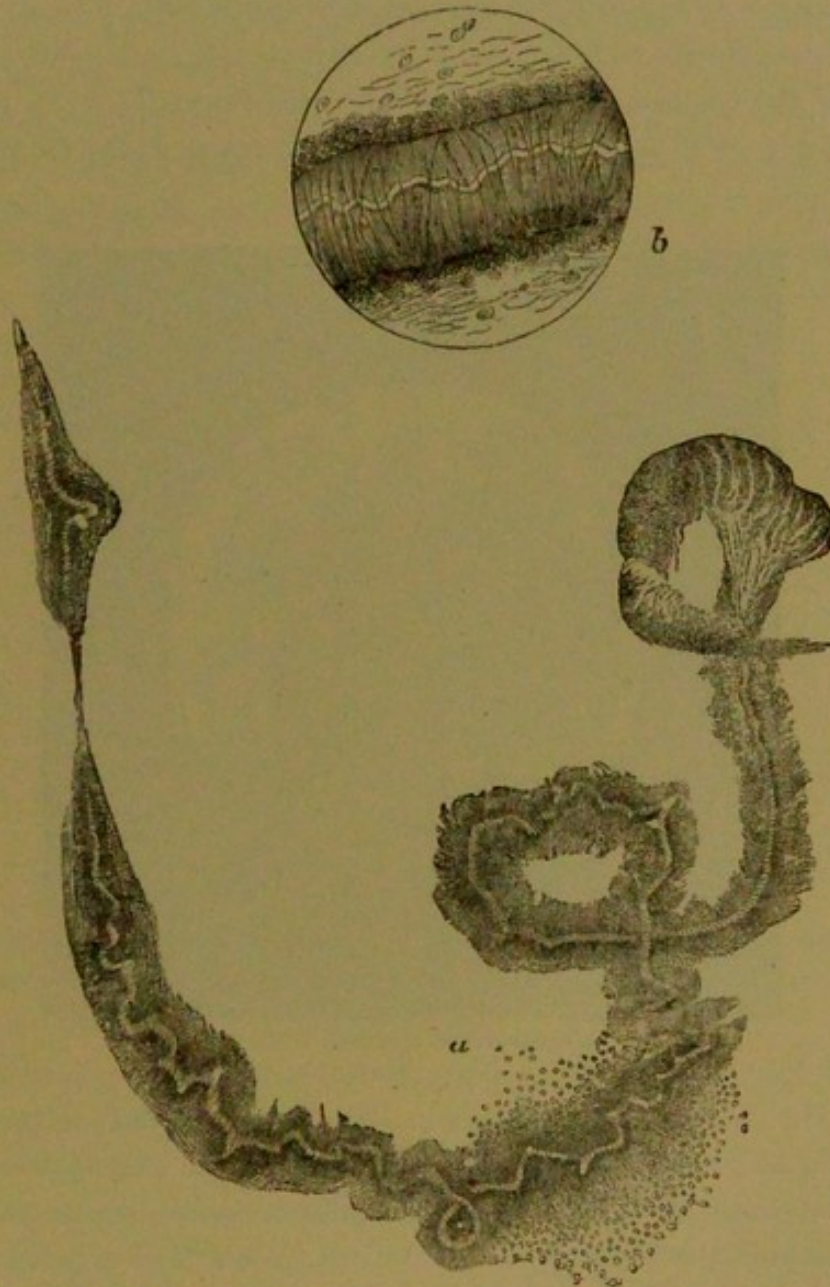
fetid bronchitis, and when a collection of sputa in a dilated bronchus thus decays it may be the starting point for gangrene of the lung.

In contrast to the trachea, croupous inflammation of the small bronchi is uncommon, but a croupous inflammation may descend to the finer divisions of the tube. Pseudomembranes in the large bronchi are common. Fibrinous exudates may form in the smaller during croupous pneumonia.

Croupous exudates in the bronchi must be distinguished from the casts of the smaller bronchi, which are known as Curschmann's spirals. With the latter octahedral "asthma crystals" are common.

Tuberculosis affects the bronchi as the trachea, making flat, lenticular, and confluent ulcers.

FIG. 196.



Curschmann's spirals. a. Magnified 80 times. b. Magnified 300 times. (After LEYDEN.)

Bronchiectasis. Dilatations of the bronchi may be either circumscribed or diffuse. At times they are vicarious when a part of the lung is unable to functionate and the rest takes on its function. The entire inspiratory pressure then acts upon certain branches of the

bronchi, and their walls, especially if diseased, yield more or less. This is seen in small bronchi in atelectatic parts of the lung, when the air pressure acts only on the bronchial wall. Difficult breathing and increased expiratory pressure, as in emphysema, may also cause bronchiectasis. According as such influences are exerted on a larger or smaller portion of the lung, the dilatation is circumscribed, or diffuse and uniform. Circumscribed sacculated bronchiectasis follows indurating and contracting lesions, as in chronic phthisis and collapse, because of the traction on the bronchial wall, especially when the lung is adherent to the thoracic wall so that the force works from a fixed

FIG. 197.



Asthma crystals from sputum. (KAATZER.)

point. The largest dilatations are called bronchiectatic caverns, and in them putrefaction of secretions may lead to putrid bronchitis, pulmonary gangrene, and tuberculosis. Such cavities are distinguished from tubercular cavities by the fact that they are lined with mucous membrane.

Appendix. Thyroid and Thymus.

As a congenital malformation the isthmus of the thyroid or a lobe may be lacking, or, on the other hand, the isthmus may be large enough to form a middle lobe reaching up over the larynx, and making

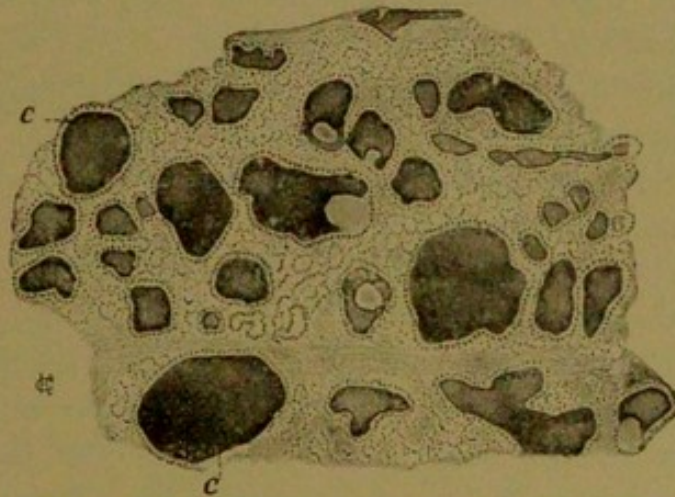
tracheotomy difficult. The gland as a whole may be large, and accessory glands are found.

Hyperemia may enlarge the gland for a short period, making a transitory struma.

Inflammation in the gland is unusual. Purulent thyroiditis may follow trauma with wound infection or extension of the inflammation from near-by processes, as in diphtheria, or arise by metastasis in endocarditis and pyemia.

The most important lesion in the thyroid is hyperplasia, of many kinds, and all grouped under the name struma. It may be congenital or acquired, and attacks the whole gland or a part of it; in the latter case there are various nodules through it. Nothing is cer-

FIG. 198.

Colloid struma. c. Colloid masses within the widened acini. $\times 40$.

tainly known as to the cause of struma except that it is endemic in many places. It occurs frequently with cretinism and idiocy.

The varieties of struma are as follows:

1. *Struma parenchymatosa*—simple hyperplasia affecting the whole gland or as nodules.
2. *Struma colloides*, or *gelatinosa*, in which the acini contain large quantities of colloid material and are distended by it.
3. *Struma cystica*, in which the walls of acini break down and large cavities form, which may contain clear or gelatinous or hemorrhagic fluid.
4. *Struma fibrosa*, in which there is hyperplasia of the fibrous tissue and atrophy of the glandular.

All these forms may be combined. Calcification of the stroma gives a form called *struma ossea*; dilatation of the vessels makes

struma vasculosa, which has other names, according to the vessel, as *struma aneurismatica* and *struma varicosa*.

True tumors occur, as adenoma, sarcoma, carcinoma, fibroma, and various combinations of these.

The thymus, according to the newest views, is an organ of epithelial origin, which later becomes transformed into one of lymphoid character. The concentrically marked Hassal's bodies found in the gland are probably remains of the original epithelium. After puberty the thymus gradually atrophies.

The pathology of the thymus is but little understood. Abscess may occur in it (Dubois' abscess) in syphilitic newborn children as peculiar pus-like masses; they may occur in other cases also. At times these foci appear to be only very rapid cadaveric softening, which here and there assumes a purulent look; and in other cases there is a growth of lymphoid tissue into the remains of epithelial tissue or an actual accumulation of pus. With umbilical phlebitis and pyemia abscess of the gland may follow.

In many cases of leukemia and pseudoleukemia the thymus becomes large. Gumma and tubercle have been observed in it. In death from phosphorus poisoning and after asphyxia relatively large bleeding may occur in the thymus.

Sarcoma and lymphosarcoma and endothelioma are the commoner tumors of the gland, and perhaps some of the diffuse sarcomas of the mediastinum take their origin here. Dermoid cysts have also been found in it. In some of the tumors starting from the gland Hassal's bodies occur.

D. DISEASES OF THE LUNGS.

The lungs consist of numerous subdivisions (lobules) separated by septa, and into each a small division of the bronchus leads. On the finest branches of the bronchiole there are lateral sacs, called alveoli, and the tube is here called a respiratory bronchiole. This widens to a pyriform cavity, on the walls of which there are alveoli, the whole called an infundibulum; while the portion of the bronchiole leading into this infundibulum—like the stem of the pear—is called the alveolar passage.

In a section of the normal lung (Fig. 199) we therefore see these various parts. The septa are fibrous. The wall of the infundibulum is made of homogeneous connective tissue in which there are elastic

PLATE XIV.

FIG. 199.



Section of Normal Lung.

A. Lobule, bounded by the pleura, *P*, and the septum, *S*; in the latter are lumina of bronchi and vessels. *B.* Bronchiole. *G.* Vessels in lobule. *r, r*₁. Respiratory bronchiole. *i-i*₄. Infundibula with alveoli. $\times 25$. (Orcein stain.)



fibres, especially collected about the entrance into the infundibulum. The bronchioles carry cylindrical epithelium; the infundibula and their alveoli are entirely covered with flat epithelia. Two varieties of flat cells are found—small, nucleated forms, and larger cells without nuclei. Within the lobules the lymph vessels begin, which enlarge as they run in the septa by the side of bronchi and vessels.

Malformation of the lungs is unusual. The commonest is variation in the lobes, as two for the right or three for the left lung. Dermoid cysts sometimes occur.

Changes in the Content of Air.

When the whole lung or a portion of it is deprived of its air the condition is called collapse, or *atelectasis*. Fetal atelectasis is a physiological state during intra-uterine life, for the supply of O and the removal of CO₂ are not provided through the lungs. With the first inspiration of the newborn the old order ceases, but if this is prevented by collections of mucus in the air passages or lack of stimulation to the respiratory centre the lung remains collapsed. It is then dark bluish red, of the consistency of flesh, and fills but a small part of the thorax. In water it sinks immediately. Partial fetal atelectasis occurs when only some of the lobules receive air after birth. The collapsed portions make bluish spots throughout the parenchyma, and are sunken below the surface. Acquired atelectasis is of three main varieties:

1. **By Compression.** When the available space within the pleural cavity is lessened by large quantities of fluid, tumors, hypertrophy of the heart, or any pressure on the lung directly, the air may be driven from the organ. It looks then like the fetal undilated lung except that it contains less blood, for the bloodvessels have also suffered from the pressure. Part or the whole of the organ is tough, small, and without the usual crepitation on pressure or incision.

2. **By Collapse.** After catarrhal and other inflammations of the bronchi, in the course of which secretion lies for a long time within them, they may be impermeable for the air. If this condition persists for a time the air in the lobules corresponding may be gradually absorbed, and the tissue may collapse from its elasticity. According to the size of the bronchus occluded the atelectatic part of the lung varies in extent. As there is no pressure on the part it is dark red and livid.

3. **Marantic Atelectasis.** With imperfect respiration and weakness of the heart this form may arise. When the respiratory intake

does not suffice to dilate all parts of the lung, the lowest and most posterior portions gradually collapse. As the heart is weak, a hypostatic congestion occurs in the same portions of the lung. The air may be nearly but not entirely lost from the part, it is full of blood and usually edematous, and dark in color.

A collapsed portion of the lung after a time may undergo induration, splenization, and bronchiectatic changes.

A lung recently collapsed is still capable of being reinflated, in life and also at the autopsy; but after a time the alveolar walls become adherent, there is a proliferation of fibrous tissue in the part, the epithelium is lost, and the part becomes tough, pale, pigmented with blood and anthracotic pigment, and wholly airless. To this condition the name induration is given.

Splenization occurs when edema affects the collapsed part, so that it swells and has a peculiar dark-red color and resembles the spleen. This may occur in the marantic form or also with hypostatic congestion.

In the bronchi which lead from the atelectatic region there frequently develop bronchiectasæ, because they support the entire pressure of the air in the part. Such dilatations occur also in the fetal form.

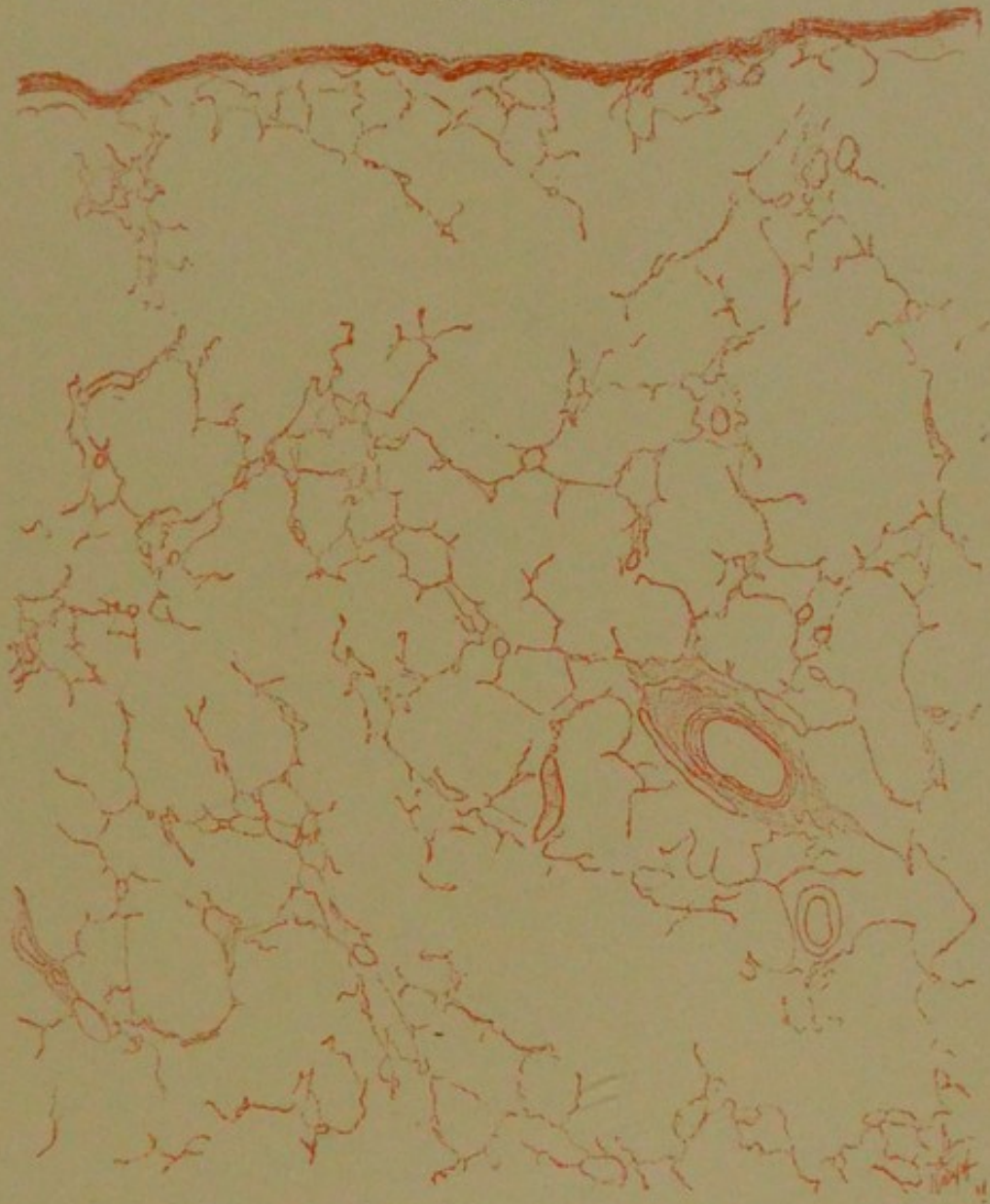
Emphysema is exactly the opposite condition from atelectasis, the alveoli being abnormally inflated and dilated. This may occur in a short time from forced inspiration—a condition called acute vesicular emphysema—and as a partial affection of the lung it occurs when a large region of the organ is suddenly put out of function.

Chronic emphysema is accompanied by more or less atrophy of the lung tissue. In chronic bronchitis, if the secretion is viscid and copious it hinders respiration and expectoration, and the efforts at coughing increase the expiratory pressure, so that the infundibula dilate to large vesicles, which may be visible in the gross. Because of this stretching the alveolar septa are shortened, the alveoli flattened, the septa then atrophy, and only a few low prominences on the wall suggest their former sites. In higher degrees of emphysema the infundibular walls disappear, so that neighboring ones join, and large cavities result. Such continued rarefaction of the lung tissue produces emphysema bullosum.

These changes make the volume of the organ large, and it is inflated and lessened in actual amount of tissue. It is soft, and on section is far more crepitant than normally. Pressure of the finger leaves a

PLATE XV.

FIG. 200.



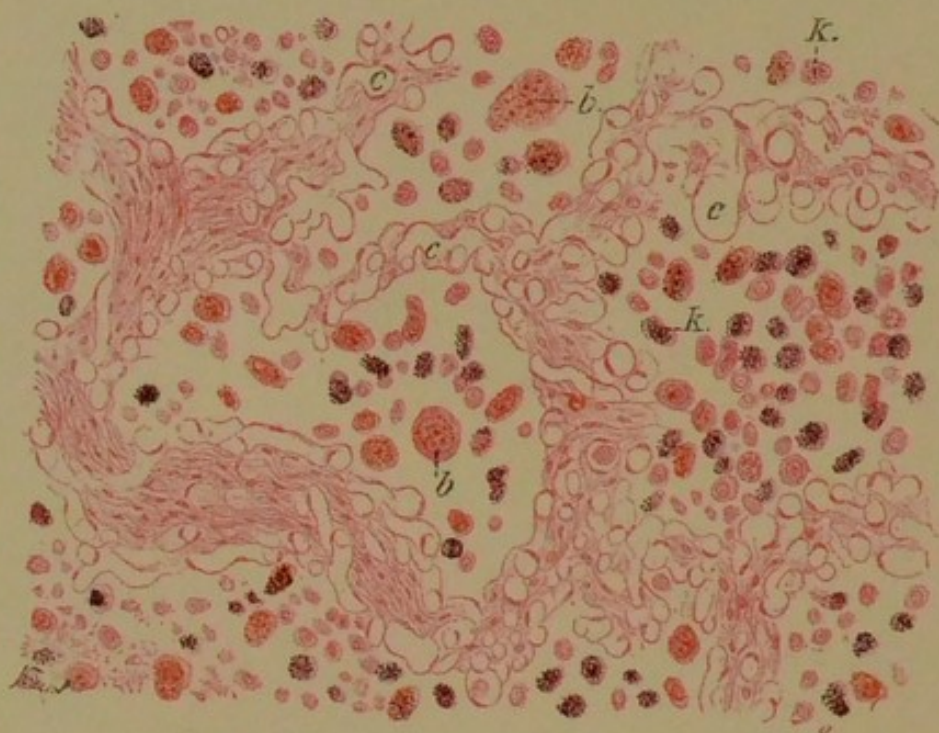
Emphysema of the Lung. Infundibula dilated, alveoli flattened, lung tissue rarefied by atrophy of many spots. $\times 25$.





PLATE XVI.

FIG. 201.



Brown Induration of the Lung.

Septa thickened, strongly dilated capillaries in them, *c*, projecting into the lumen of the alveoli.
b, k. Cells in the latter containing pigment from blood and from dust; these cells are partly epithelial, partly leucocytes. $\times 300$ (Carmin stain.)

dimple in the lung because of the loss of elasticity. With the atrophy of septa there is a loss of bloodvessels which run in them, so that the lung is pale and anemic, of a leaden gray color, and very dry on section. Desquamation and fatty changes in the alveolar epithelia are common. Such a condition throughout the whole lung is called general substantive emphysema.

The destruction of the bloodvessels causes an increase in the work of the right ventricle, and hence hypertrophy of its wall.

As an idiopathic condition some degree of emphysema is common in old age, and is called *senile emphysema*. It affects the whole lung, and is doubtless due to atrophic changes in the organ.

Partial chronic emphysema occurs as a vicarious change in parts which assume the work of diseased tissue. It is often seen along the edges of the lungs. This is called consecutive, collateral, or *vicarious emphysema*.

In the varieties so far described the air is in the alveoli of the lung, and hence all these kinds are grouped as alveolar emphysema. An interstitial form exists when the air is found in the septa and interlobular tissue from bursting of alveoli. It appears then as bubbles in rows under the pleura, arranged in a meshwork along the septa. This may be post-mortem, due to putrefactive gases.

Disorders of Circulation. *Anemia* of the lung is chiefly a part of general anemia or occurs locally from pressure or occlusion of vessels.

Brown induration is a name given to the effect of chronic stasis, for instance, from obstacles to the flow of blood into the left auricle. Usually there is a defect in the valves of the left side of the heart or else general cardiac weakness. The distention of the capillaries, which in the lung is accompanied by a tortuous condition, diminishes the lumina of the alveoli, for the capillary ectasis projects strongly into them. A constant change is the deposit of quantities of brown pigment, due to the numerous small hemorrhages in the alveoli and interstices of the lung. This pigment gives the organ a characteristic brown color, even though it be anemic. The coloring-matter lies as free granules in the alveoli or is enclosed in cells, and these cells are so constantly found in such conditions that they have received the name of heart-disease cells. Wandering cells and red blood cells are commonly found, and usually free desquamation of epithelia with the chronic catarrh which is found with the stasis; the latter cells are distinguished from the wandering cells by the larger body and large, light nucleus.

With the thickening of veins and capillaries the fibrous stroma suffers a hyperplasia similar to the cyanotic induration of other organs. A chronic edema is often associated with these lesions, and then the lung is of a peculiar tough and swollen appearance.

Pulmonary edema is a very frequent condition, which may be found in varying circumstances. Because of the transudation of fluid the organ is imperfectly aerated, and on section a slight pressure squeezes out a copious grayish-yellow fluid. The bronchi, large and small, and the interstices of the lung, are filled with it; hence the lung is heavy, voluminous, inelastic, and doughy.

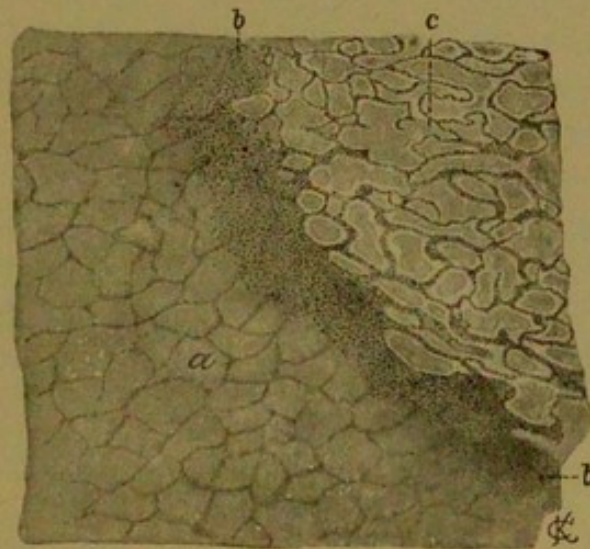
The importance of the condition is dependent upon the cause and other considerations. Some of the cases are due to stasis, developed as the result of cardiac weakness, so that the negative air pressure in the alveoli collects the blood in their capillaries. This blood is greater in amount than the left side of the heart can receive, and it is imperfectly emptied by it. A combination of hyperemia and edema begins, therefore, in the dependent portions of the lung. With some cases there is probably an early paralysis of the left ventricle, while the right continues strongly contracting. When the main air passages are closed, as by edema of the glottis, the chief element in the production of edema is forced inspiration, by which the negative pressure in the alveoli causes the blood to collect in the capillaries. Pulmonary edema is often developed shortly before death or during the agony. In the cadaver a serous condition of the lung may develop, but it differs from the edema described in not being foamy; the fluid is quite free from air. Other forms of edema occur about foci of inflammation, and are certainly developed before death, and with lesions of the brain it may occur in some unexplained way.

Hemorrhages may occur in the lung in certain diatheses or with stasis, but these are usually small. Larger hemorrhagic infarcts may be due to occlusion of a vessel by thrombosis, or embolism, or to vascular erosion. Emboli and thrombi commonly do not cause infarcts, because of the free anastomoses between the capillaries and the bronchial and pulmonary arteries. In conditions leading to brown induration infarcts are fairly common where the pressure in veins and capillaries is raised, so that a return flow may occur after an artery is occluded and also where the vessels are disposed to bleed, as is evident from the quantities of pigment present. Hemorrhagic infarcts are of the size of a hazelnut or larger, wedge-shaped or irregular, and usually the embolus is found in the part farthest from the pleura. On the

surface of the lung they appear as slightly prominent, firm, dark-red areas; on section the color is the same, they are wholly non-aerated, sharply marked off, and from the surface much blood can be scraped.

The commonest cause of pulmonary infarcts is marantic thrombosis in the right side of the heart, from which large pieces are at times broken off and carried as emboli into the lung. The thrombus from which the emboli come is found between the papillary muscles on the right side. An embolus may come also from any part of the venous system. It usually lodges at the bifurcation of a vessel, in what becomes the apex of the infarct, and part may project into each branch, the embolus riding on the angle between. The further changes in the infarct have already been treated (p. 96 ff).

FIG. 202.



Hemorrhagic infarct of the lung. *a*. Infarcted area, the alveoli filled with blood; all nuclei have lost their staining power. *b*. Septum. *c*. Adjoining part of lung, in which the alveoli contain some blood, but the cells are not necrotic. $\times 40$.

In other cases the infarct is due to rupture of vessels in the lung from increased pressure, or with ulcerating processes, as in tuberculous cavities, or with wounds of the lung, as when the sharp end of a broken rib penetrates it; and at times bleeding of the lung occurs with cerebral hemorrhage. When bleeding occurs in the bronchi the blood may easily be drawn deeper into the lung by inspiration. Small hemorrhagic foci appear scattered through the organ, though actual pulmonary hemorrhage has not occurred.

A special form of embolism is caused in the lung by transport of fat into its vessels, as happens often after fracture of the bones, and less frequently with contusions of the subcutaneous fatty tissues.

Slight degrees of the lesion are common and unimportant. With large amounts of fat pulmonary edema and death may be the result. Microscopically the fat is found in the capillaries.

Embolism of air in the vessels of the lungs occurs with similar conditions in the right side of the heart.

Inflammation.

1. **Fibrinous** (*croupous* or *lobar*) **Pneumonia.** With inflammation of the actual parenchyma of the lung there is an exudate within the infundibula and alveoli. This condition is called hepatization—a term which refers to the resemblance of the solidified lung to liver tissue in the gross. In the form of pneumonia called fibrinous or croupous this hepatization is distributed over large sections of the organ, as an entire lung or one of its lobes, in a more or less uniform manner; hence it is spoken of as lobar hepatization, and its consistency is firm, depending on the nature of the exudate.

Three stages are usually distinguished in the course of such a pneumonia—those of *congestion*, *red hepatization*, and *gray hepatization* or *resolution*. In the first there is a severe inflammatory congestion, with marked edema, and the lung is large and contains less air.

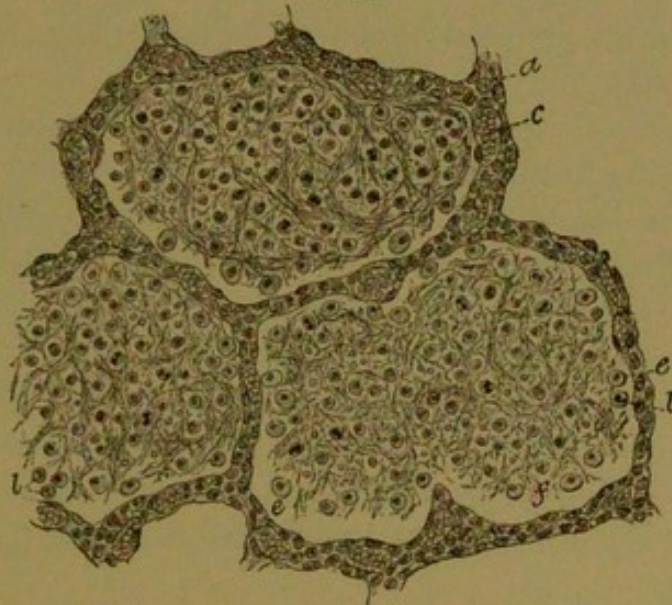
In the red stage the characteristic exudate is formed in the air spaces. This is fibrinous and coagulates, with the formation of countless reticular threads through it. The alveolar epithelia suffer necrosis and a hyaline change, and are desquamated, singly or in groups, as pseudomembranous layers. In the exudate there are large numbers of leucocytes and red cells. These cells are entangled in the solid exudate, and with it form casts of the air spaces in which they lie, so that the section has a typical granular appearance, and from it the fibrinous plugs may be scraped away by the knife. Examined with a low power these plugs have a lobulated form corresponding to the infundibula and their alveoli. Since the air spaces are completely filled in this way the lung is wholly unaerated; and when the pleura is opened the organ cannot collapse, as it usually does. It is voluminous, distended, firm, and friable, and on section of a dark brownish red in which the grayish plugs are noticeable.

More careful microscopic examination shows that the hepatization is not so uniform as it appears in the gross. In the central parts of the lobule the exudate is more cellular, and there are groups of cocci; in the peripheral alveoli there is more fibrin. These conditions depend

upon infection through the bronchi, for parts of the alveoli nearest the bronchiole are most severely affected.

The red stage lasts, on an average, from one to three days, and then the gray stage begins, and with it the decline of the process. Resolution consists in the conversion of the exudate to a soft, and later fluid, mass of fat granules and detritus, which is either absorbed or expectorated, while the alveolar epithelia are regenerated. In the alveoli the leucocytes are increased. The cut surface has a grayer color, and as the capillaries of the hepatized portion are bloodless the anemia adds to the lighter tint. The granular look of the section is lost as the plugs soften, the alveoli become freed and again receive

FIG. 203.



Croupous pneumonia. Three alveoli filled with fibrinous exudate disposed in a meshwork, *f*, in which are the cells of the exudate, *e*, *l*. *a*. Alveolar septum with capillaries, *c*. $\times 250$.

air, and their epithelium is renewed, so that a normal condition is attained.

It is probable that resolution may occur during the first stage without the lung passing through the gray hepatization.

Death usually occurs on the sixth to the eighth day, during the change from red to gray, and is due to the gravity of the infection, insufficiency of the lung from the amount involved, to complications as pericarditis and meningitis, and especially to cardiac weakness. A very important element in a fatal case is the oligemia resulting from the copious exudation from the blood, and this may be the direct cause of the cardiac failure and the edema of non-hepatized lung. Other results of the disease are suppuration, carnification and gangrene.

Carnification occurs when the exudate becomes organized, like a thrombus. When the exudate is not removed by expectoration and resorption, a fibrous hyperplasia may start in the septa, and particularly about the peribronchial connective tissue, and the latter pushes the bronchial epithelium before it into the lumen. It also follows the course of the bronchi to the infundibula, renders the exudate vascular, and replaces it with young connective tissue. The bronchial epithelium is lost, the fibrous growth passes from alveolus to alveolus, and at last the section affected is converted into lobules filled with granulation tissue. From the alveolar septa a similar process aids in the vascularization of the exudate. In the gross the lung is then red, tough, and like muscle, and hence the name *carnification* is employed. The new cellular fibrous tissue becomes poorer in cells, and contracts, and the end of the process is complete induration and usually pigmentation of the part.

Certain cases of fibrinous pneumonia vary from the type as discussed, especially in children and the aged. In the child the inflammatory process may be distributed over scattered lobules and not uniformly through a lobe, so that the gross appearance resembles that of catarrhal pneumonia. The distinction from the latter is made by the firmer hepatization, the complete absence of air, and the granular surface, and microscopically by the coagulated exudate. Another variation is due to very scanty exudate, as is common in old age. The cut surface then presents a diffuse, more yielding hepatization, the part is moist, and its air is not wholly absent. This form is common in influenza.

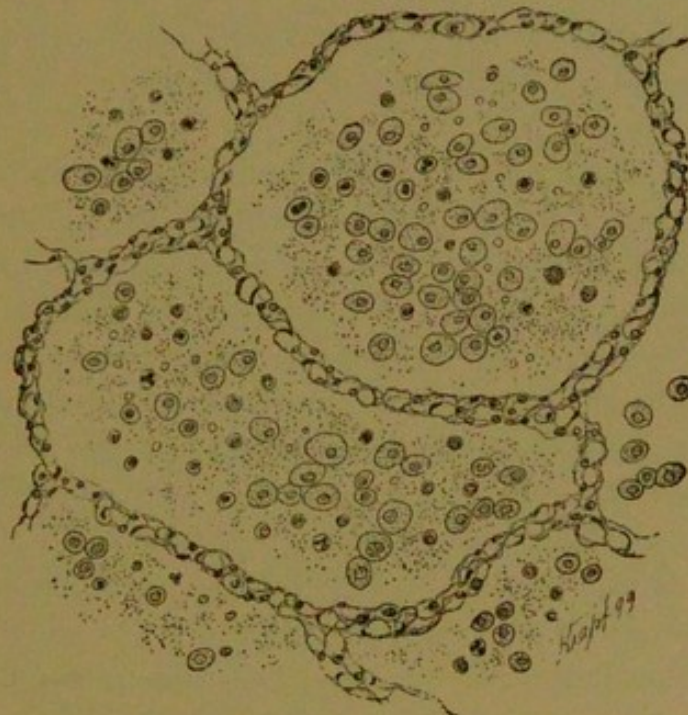
In most cases croupous pneumonia begins in the lower lobe and progresses upward, and more often on the right side than on the left. It may pass from one lung to the other. Almost always there is a complicating serous or fibrinous pleuritis, and this may be purulent. Catarrhal and fibrinous inflammation of the large bronchi is usual. Fibrinous pericarditis may occur.

Whether all cases of the disease are due to a single micro-organism has not been proved, but the typical clinical and anatomical nature of the disease and the almost constant presence of the Fränkel-Weichselbaum diplococcus suggest this belief, and this bacterium is generally accepted as the specific cause.

2. Capillary Bronchitis and Catarrhal Pneumonia. When catarrhal inflammation involves the finest divisions of the bronchi it is called *bronchiolitis catarrhalis*, or capillary bronchitis. The swell-

ing, infiltration of the bronchial wall, and increased secretion are similar to the same features in larger bronchi when inflamed. Pressure on the cut surface of the lung causes the protrusion of scattered drops of turbid mucous or purulent fluid from the cross-sections of the bronchioles. The exudate may close the tubes affected, and the atelectatic parts corresponding appear as slightly sunken bluish areas in which the consistence is firmer than normal, and there is no air. Vesicular and interstitial emphysema may be associated with this condition.

FIG. 204.



Catarrhal pneumonia. In the lumen of the alveolus there are desquamated epithelia as large cells with a light nucleus; and leucocytes, small cells with dark and in places polymorphous nuclei. Hardening methods have caused a granular precipitate in the albuminous exudate. $\times 250$.

In many cases the bronchiolitis passes directly to the lung parenchyma, and the result is a catarrhal pneumonia. In this way areas which correspond to the divisions of a lobular bronchiole are functionless, firmer than atelectatic lung, and red and hyperemic. Hence the other name sometimes employed for this condition is lobular pneumonia. The exudate consists of albuminous fluid, desquamated and fatty epithelial cells, and few or many leucocytes. Fibrin may be found in it, but it is not so copious as to form plugs and casts of the alveoli. Aspiration from the bronchi may introduce mucus into the alveoli also. The red color soon turns to grayish red or yellow, because of the fatty changes which begin in the central parts of the

exudate. From the cut surface a turbid yellowish fluid may be scraped. The hepatized portions differ from the croupous lesion in being less firm and having a smooth surface because of the absence of plugs in the alveoli.

Together with the hepatized parts there are always atelectatic sections, from occlusion of bronchioles, and these are distinguished by their dark cyanotic color, and their slight depression below the surface. In such collapsed portions other causes of inflammation develop, and thus they may become hard and voluminous in subsequent pneumonia.

The variation in color between the fatty and paler parts of the diseased lung, and the hyperemic margins about these, with foci of recent inflammation between and dark atelectatic spots, is described as marbled.

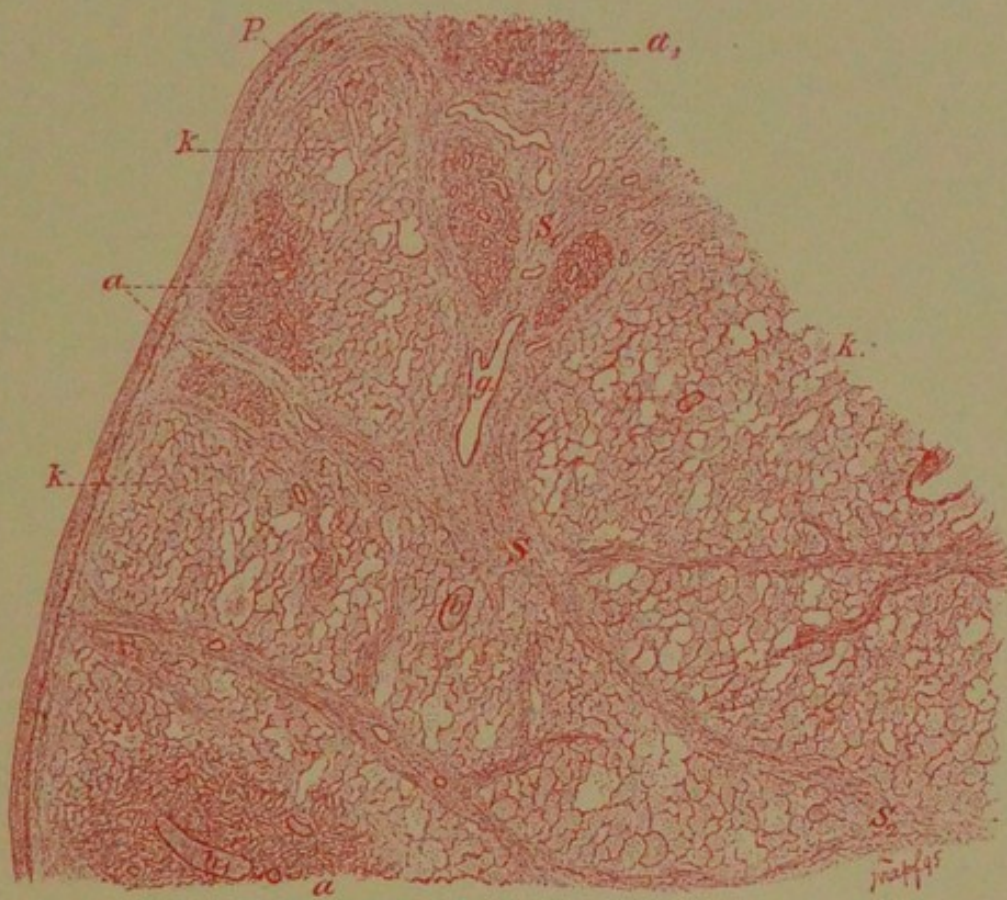
The more numerous the affected lobules are, the more neighboring lobules are infected through their bronchioles, and thus large parts of the lung may be inflamed, so that a lobar rather than a lobular distribution of the lesion occurs. Circumscribed or general pleurisy may accompany the lesion, and the pleural exudate may be large.

The usual result of catarrhal pneumonia is resolution by fatty degeneration, and expectoration or resorption of the exudate. When the respiration is weak, or the exudate is not removed, or becomes itself chronic, an indurative process is apt to develop in the septa, as has already been discussed. Bronchiectasis and emphysema, both vicarious and interstitial, are also noted, and the pneumonic process may be the starting point for suppuration, gangrene, and tubercular lesions.

Capillary bronchitis and lobular pneumonia may occur primarily or in the course of another disease, and most commonly they accompany exanthemata in childhood, as measles, scarlet fever, and diphtheria. At both extremes of life there is a great disposition to catarrhal diseases of the lungs, especially in chronic forms. The cause of the catarrhal variety of pneumonia is probably not always the same. Pneumococci (Fränkel), diplococci of pneumonia (Friedländer), staphylococci, and streptococci have been found in the lesions, and the disease occurs with influenza. A chronic form is common with pneumoconiosis, and in the course of tuberculosis of the lungs. Diffuse catarrhal inflammations follow hypostatic and marantic congestion and splenization. When the dependent parts of the lungs are filled with blood and there is an exudate in the alveoli with desquamation of the epithelium, the process is called a hypostatic pneumonia.

PLATE XVII.

FIG. 205.



Catarrhal Pneumonia, with Atelectasis and Induration.

P. Pleura. *S, S₂*. Thickened septa. *g.* Vessel. *b.* Bronchi. *k.* Places with exudate in the alveoli.
a, a₁, a₂. Collapsed parts. Orcein stain. $\times 50$.



The hepatization is not complete, the cut surface is dark or grayish red, smooth, and much softer than in croupous pneumonia.

3. **Purulent pneumonia** begins with the formation of an exudate which is at first catarrhal or fibrinous, but at the same time rich in cells, and which later becomes purulent, and the tissue at the same time is destroyed. The causes of the suppuration may enter the lung in three ways: by the bronchi, the bloodvessels, or the lymphatics from adjacent foci.

(a) Through the bronchi a suppurative pneumonia may begin by the entrance of foreign bodies, as bits of food, stomach contents, pieces of croupous membranes from the upper air passages, and tissue from neoplasms which are breaking down. This gives rise to aspiration pneumonia. When a patient is unconscious, or the mechanism of swallowing is disordered, such infection is easily produced, and after section of the vagus it follows paralysis of the larynx. The lower lobes are the usual seat of the lesion, and the amount of material aspirated determines whether it shall be discrete or in larger groups of lobules. At first the foci are grayish red and hyperemic, later on they melt into a purulent mass, and about them is a zone of hemorrhagic infiltration. They may empty into bronchi or the pleura, setting up empyema in the latter case. As a rule, together with abscess cavities, there are freshly invaded lobules of a grayish-red color which somewhat resemble croupous pneumonia. The pyogenic organisms are staphylococci and streptococci which enter the lung with the foreign body, and if putrefactive organisms also are included in it gangrene of the lung may arise.

A lung which is already the seat of inflammation may become infected with pyogenic organisms through the bronchi and become purulent, and this is seen often with stagnant bronchial secretion in chronic catarrh, with caseous tuberculous foci and about dilated bronchi.

(b) Purulent pneumonia arises through the bloodvessels when septic emboli enter the lung from thrombi in purulent softening or vegetations in endocarditis; the former may produce infarcts which later break down.

(c) The lymphatics bring pus from adjacent organs, as carious vertebræ and ribs, and hepatic abscess, and in empyema a pleurogenous form is described, though the cause of the suppuration may have come at first from the lung to the pleura. The suppuration follows chiefly the lines of the lymphatics in the pulmonary septa, and from there attacks the parenchyma. It may follow the bronchi and involve them, producing a purulent peribronchitis.

4. **Productive (interstitial) Pneumonia.** This process, already mentioned in connection with collapse, is at times a reparative and at times a progressive lesion, causing organization of exudates which cannot be removed or extending over more and more of the lung as a form of chronic pneumonia.

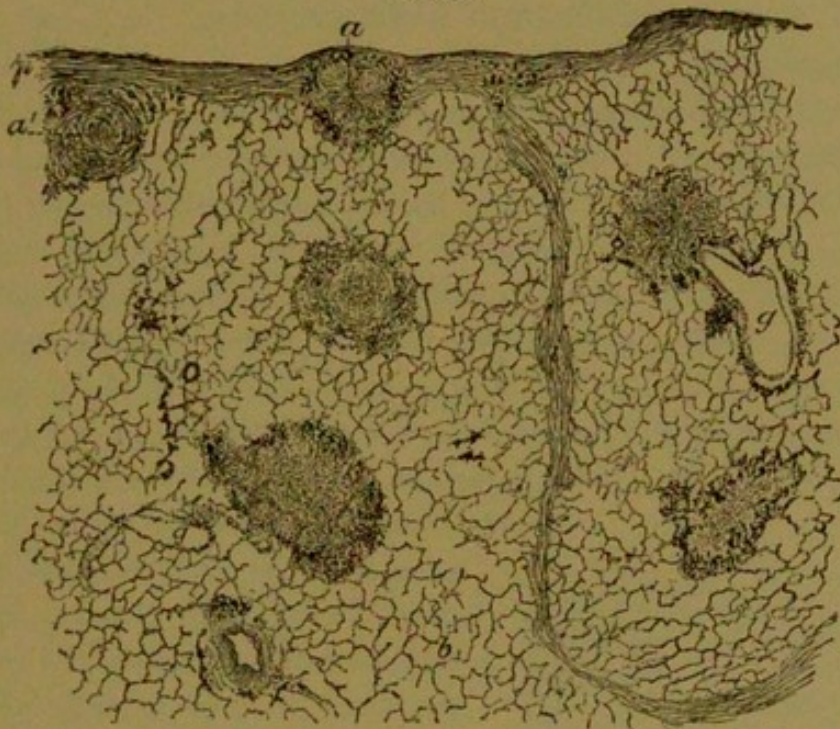
The induration involves both the interstitial and the parenchymatous elements in the lungs. In the former it begins with the growth of a richly vascular granulation tissue which gradually becomes cicatricial and converts the septa into thick bands of connective tissue. In the parenchyma it may begin with a collapse and subsequent induration, or as an organization of retained exudate. The indurated parts of the lung are small, firm, non-aerated, scar-like, and usually of a slaty pigmentation.

Emphysema and bronchiectasis are frequent consequences, and constant repetitions of catarrhal inflammations, to which the lung is particularly disposed, produce new atelectasis and induration until the entire lung may be cirrhotic.

Processes of this variety are common with prolonged inhalation of dust—pneumoconiosis. Small quantities of dust are taken into the lungs by everybody, and in general are without serious effect. Large amounts of dust may be caught in the air passages and never deposited in the lung itself, or portions of the foreign material may be taken up by lymph vessels and deposited in the nodes at the hilum of the organ, and, as a rule, these nodes are deeply pigmented in the adult. Alveolar epithelium and white blood cells take up particles of dust, and thus it may be expectorated or laid away in the lymphoid tissues. Certain kinds of dust, as calcium carbonate, may be dissolved in the lymph, and thus are without effect. When large quantities of dust are breathed in for long periods chronic catarrhal bronchitis and chronic catarrhal pneumonia result, the pigment is found in the strongly thickened fibrous portions of the lung, and the whole organ is subdivided by a reticular fibrous hyperplasia reaching to the pleura, where the limits of the lobules are clearly marked out. Atelectasis, induration, interstitial pneumonia, emphysema, and dilatation of the bronchi are often associated with the condition. Healing is peculiarly difficult in such a lesion, because the chronic irritation of the dust continually disposes the organ to new catarrhal inflammations. Tuberculosis is a very frequent complication, but the variety of dust inhaled seems to play a part, for phthisis is more common with stone-cutters than in simple anthracotic lungs.

Diseases of this variety are usually connected with occupations in which air contaminated with various finely divided materials is breathed for long periods. *Anthracosis*, or pigmentation with coal-dust, is common to all dwellers in cities, less frequently found in those who live in the country, and of all dust, that from coal seems least harmful. In the lung the septa and certain tough nodules are black from the coal, the bronchial nodes are black, but the parenchyma of the lung is but little colored. It appears as if larger quantities of coal-dust were inhaled when other kinds of dust, more irritating to the organ, are taken in at the same time, and we conclude that a lung

FIG. 206.



Induration of the lung from lime-dust; chalicosis. *p.* Pleura. *a a'*. Fibrous nodules below pleura; similar nodules occur in the lung, and about the vessel, *g.* *i.* Thickened septa. $\times 30$.

with but little anthracotic pigment has inhaled but little other dust. The most severe grade of anthracosis is found in coal-miners' lungs, workers in powder factories, chimney-sweepers, and those who use graphite in trades. Tuberculosis affects about 13 per cent. of all anthracotic lungs.

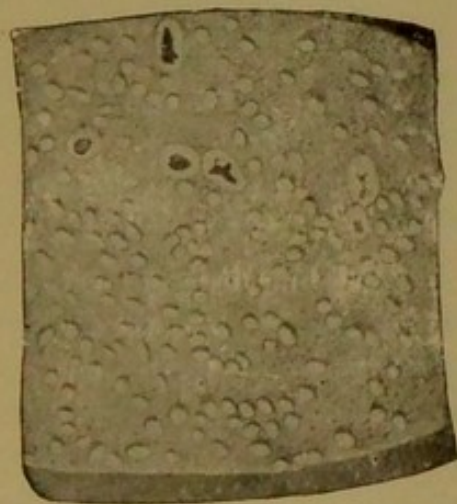
Workers in dust from stone, glass, and pottery have *chalicosis* of the lung. In the fibrous septa and on the pleura small nodules form, of tough consistence and grayish-white color, about the size of a small seed, and these are full of small grains of dust. Anthracosis is always present, and the coal-dust may be disposed in margins about the other nodules. Tuberculosis occurs in 8 to 16 per cent.

Siderosis is the deposit of iron in the tissues of those who work in it, as filemakers, smiths, and locksmiths. Those who sharpen iron or steel by grinding have a mixture of stone-dust and iron particles. The color of the iron lung depends upon the chemical compound present; red oxide gives a red lung, black oxide and phosphate of iron a black lung. The induration is diffuse and not nodular, and the disposition to tuberculosis is marked, about 62 per cent. of cases showing such lesions. The lung may contain 1.45 per cent. of iron. Workers in copper and other metals, and inorganic material, as feathers, cotton, tobacco, etc., have other forms of the disease.

Infectious Granulomata.

Tuberculosis. Two chief forms of pulmonary tuberculosis are recognized. In the acute form large numbers of bacilli enter the lung in a short time and produce many disseminated nodules; for this the names hematogenous, or acute miliary, or acute disseminated tuberculosis, are employed. In the other form there is a much slower spread of the disease by bronchi and lymphatics, and larger and smaller foci develop of various characters; this is called chronic pulmonary tuberculosis.

I. Acute Miliary Tuberculosis. Infection of the lung by many tubercle bacilli through the bloodvessels may proceed from lesions elsewhere which up to that time had been localized, and may be either direct or indirect. In the former a softening focus breaks into a vein, in the latter a large lymph channel is entered by bacilli, and from here they pass to the blood and to various organs. In both cases countless tubercles develop, especially in the lungs, of the size of a millet seed or a little larger, and the lung lesion is but part of a general infection which clinically is of short course and fatal.



Acute miliary tuberculosis. Natural size.

The single nodules lie in the fibrous tissue about vessels, bronchi, and lobules, as well as under the pleura, and in the parenchyma of the lung. Those in the fibrous tissue correspond to tubercles in any organ. Those in the parenchyma are evidently due to circumscribed

cell proliferation, or resemble the results of exudative inflammation, and others are made up of both pneumonic and proliferative products. In all, giant cells and caseous degeneration are common.

On the cut surface the tubercular foci are prominent gray nodules, as numerous in the lower as the upper lobes, and between them the lung tissue is unchanged, or slightly hyperemic and edematous. About the larger tubercles there may be a rim of congestion and exudation into adjacent alveoli. As the nodules begin to be caseous they appear as yellow centres with gray margins.

II. Chronic Tuberculosis of the Lungs. In adults the chronic forms of pulmonary tuberculosis are usually referable to inhalation of bacilli, and the lesion is most often begun in the apex of the right lung. This local disposition is, perhaps, to be explained by the smaller excursion of this part in breathing, and hence its imperfect ventilation, and also by a relative anemia because of its high position. In many cases, especially in children, the first lesions are found in the bronchial nodes.

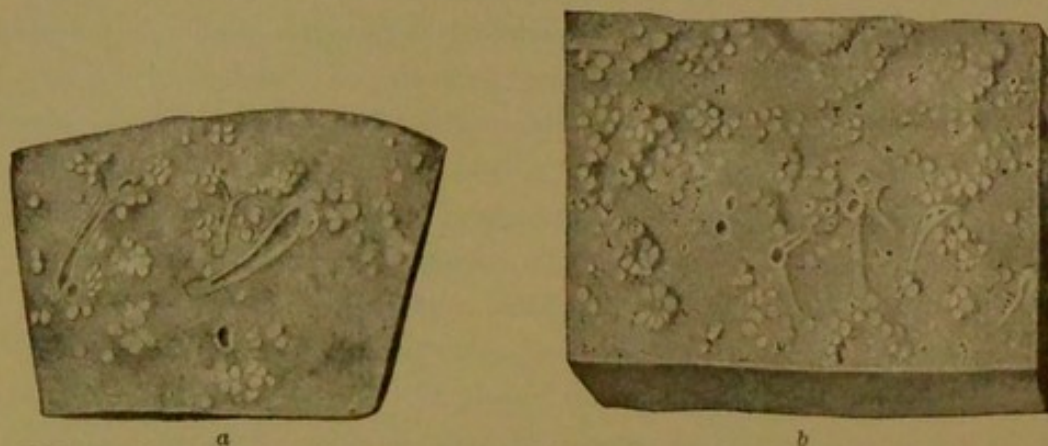
The anatomical appearances are manifold and hard to understand, because tuberculosis produces various changes on the various elements of the organs, because complicating and resulting lesions accompany the tubercular, because both old and recent lesions occur together, and lastly, because tuberculosis may cause either circumscribed or diffuse proliferation or exudative inflammation. The nodules occurring in the course of a chronic pulmonary tuberculosis are not all strictly tubercular, but in part due to simple inflammation, though they may afterward undergo caseation. The earliest stages are not often available for study, and hence the description must refer to lesions already somewhat advanced.

I. Tubercular Bronchopneumonia. Small tubercles form on the finest end branches of bronchi, singly or in series, and follow the bronchus proximally, remaining sharply defined or invading the vicinity as well, and then leading to resorption tubercles. (Figs. 209 to 211.)

In a lung with chronic tuberculosis areas of recent eruption of tubercles are found, as small round or clover-leaf deposits, about as large as a pin's head, at first gray and later yellower and caseous. In contrast to the general miliary infection these nodules are grouped about the final distributions of bronchi, like the crown of a tree about its branches. The tubercles may form in or about bronchioles whose walls and lumen can be seen by the unaided eye. The commonest location is at that point of the bronchiole where it begins to be an alveolar passage. The parenchyma between the tubercles at first is

unchanged and contains air, unless the tubercles are so crowded that they are confluent and leave no lung tissue between them. In other cases the parenchyma is sunken, non-aerated, collapsed, and pigmented.

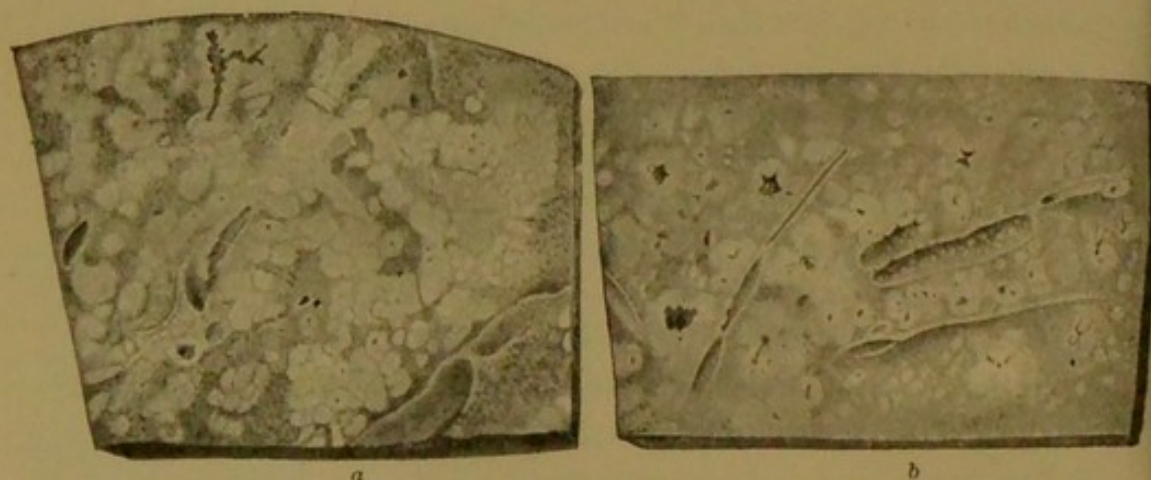
FIG. 209.



Nodular tuberculous bronchopneumonia. The grouped arrangement of the tubercles is evident, and in *a* there are nodules on two bronchioles which are divided longitudinally. Compare Fig. 211.

While the first tubercular foci are seated upon the finer branches of the bronchi, later the process invades the bronchial wall as a caseous inflammation, and nodules thus form which may converge from neighboring branches and fuse, as can be recognized in sections that contain

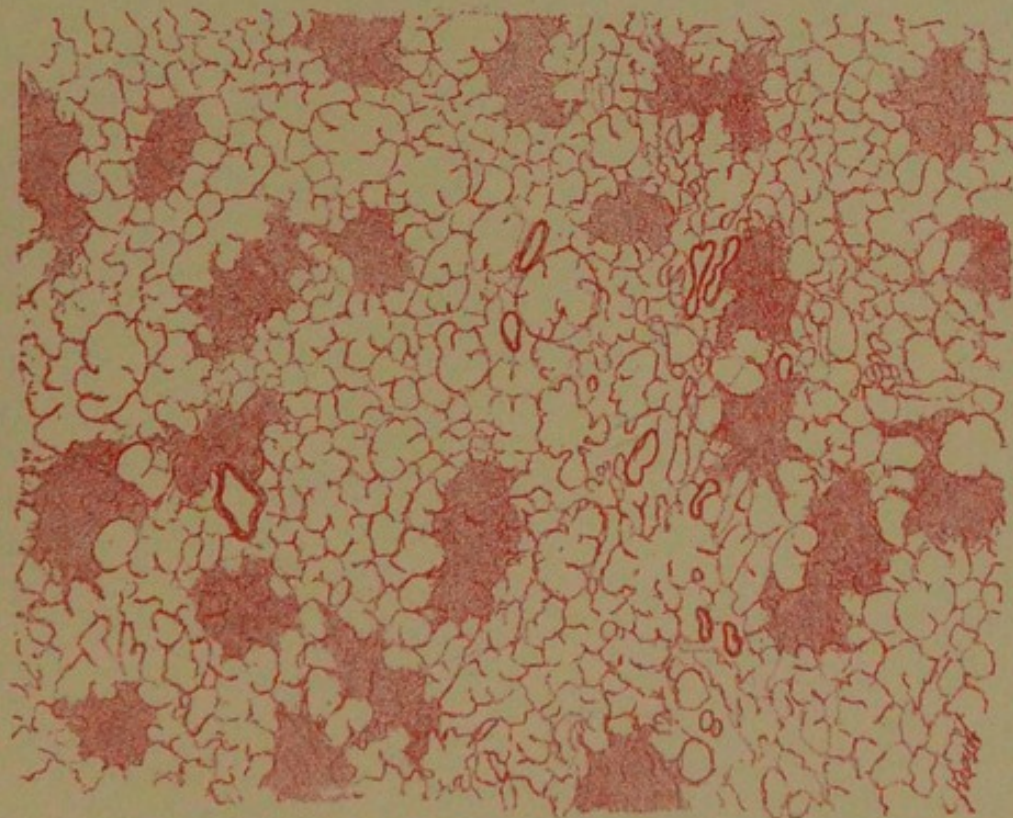
FIG. 210.



Tuberculous bronchopneumonia, spreading superficially, with partial confluence of the foci. Natural size. In *a*, near the middle, transverse sections of caseous bronchi; above, a longitudinal section with the lumen irregularly widened by softening. In *b* many small cavities and bronchi with tubercles on the inner wall.

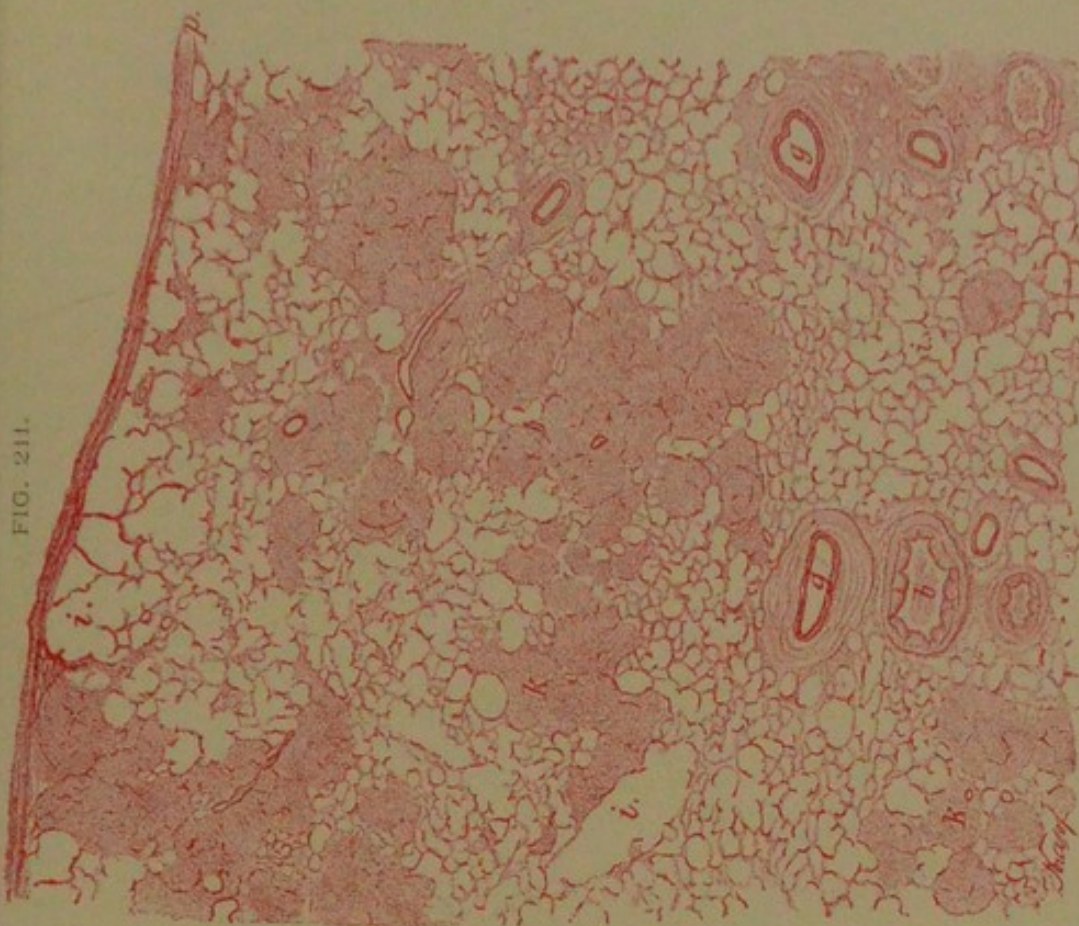
the air passages in longitudinal division. Cut transversely the tubercular areas appear as rings surrounding a lumen filled with caseous material, the former being the wall of the bronchus and the latter its

FIG. 208.



Acute Miliary Tuberculosis of the Lung. Disseminated Tubercles. Orcein Stain. $\times 20$.

FIG. 211.



Tubercular Bronchopneumonia.

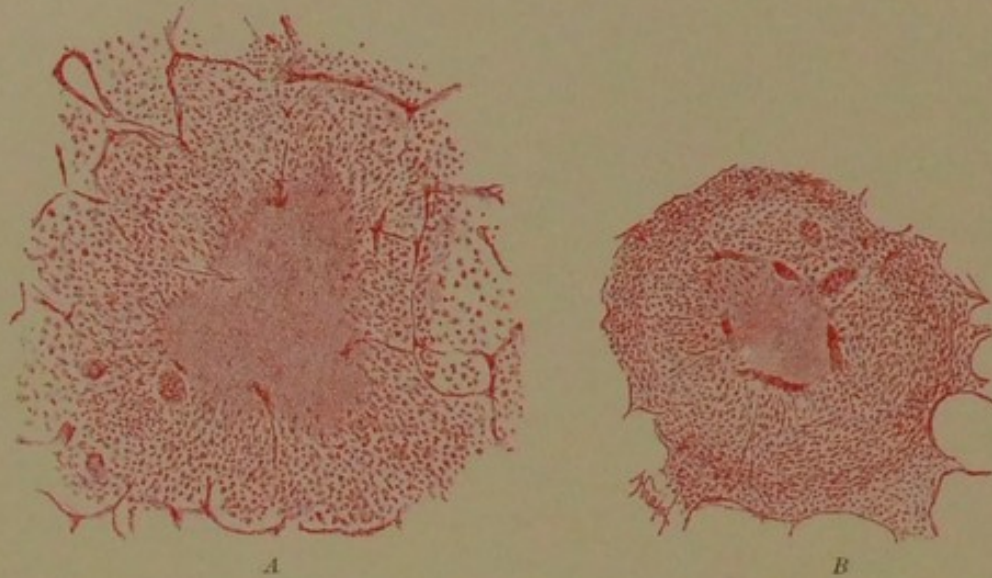
The foci are partly bronchopneumonic, partly resorption tubercles. Nodules about the bronchi, in places confluent, as at *k*. *g*. Aerate parenchyma. *b*. Large bronchiole. *g*. Vessels. *p*. Pleura. Orcein stain. $\times 20$.





PLATE XIX.

FIG. 212.



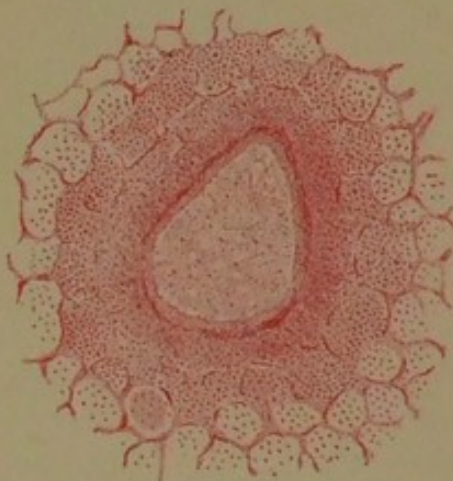
Bronchopneumonia, more Highly Magnified.

A. Alveolar passage filled with exudate which is caseous; the alveoli contain cellular exudate not yet caseous. B. Respiratory bronchiole, its elastic tissue-wall interrupted by exits of alveoli; caseous exudate in its lumen and about it a cellular exudate which is becoming fibrous, the whole sharply limited from the rest of the lung. $\times 250$.

FIG. 215.



FIG. 213.



Caseous Bronchitis and Peribronchitis.

The bronchial wall and the contained exudate are entirely caseous, and the parenchyma is infiltrated.

Tubercle in Lung Tissue.

Below to the left a tubercle with two giant cells, to the right a caseous area; the elastic fibres are separated and pushed apart. About the focus the alveolar walls are thickened. Orcein. $\times 50$.

cavity. These strands and rings are scattered through the groups of nodules or grouped by themselves. (Fig. 210.)

The process thus described is fitly termed bronchitis nodosa, the nodules are bronchopneumonic and the changes in the bronchioles constitute a caseous bronchitis.

Even in the early stages the pneumonic patches vary in character, being of different sizes, and either slightly prominent over the surface, or sunken, sharply limited, or fading into the surrounding tissue. The margins may have a fibrous character, and the caseous bronchi may be surrounded with similar tissue, and converted into a fibrous cord. The condition is partly a fibrous peribronchitis and partly a fibrous bronchitis, and the latter may occlude the lumen of the tube.

In other cases, especially with rapid and malignant forms, the caseous foci spread laterally, and about them pneumonic consolidation ensues which itself becomes caseous later. The process follows the wall of the bronchus as a caseous peribronchitis, and also infects the lymphatics, which then present a series of tubercles in their course which gradually fuse.

In these larger and larger sections of the diseased lung, softening and degeneration occur which lead to the formation of cavities, and these subsequently may reach a very large size. But in general the relation of the process to the small bronchi throughout the entire region of their distribution stamps the process as an extended bronchial tuberculosis. Sputum carries the bacilli to the larger bronchi, and in their walls tubercles develop, not so much as a caseous bronchitis as in the form of scattered tubercles of mucous membrane. Section of such bronchi displays the scattered tubercles and ulcers, and from these lesions the bacilli are carried in both directions, outward and by aspiration deeper into new bronchi, and thus the disease spreads.

In some cases the lesions begin in the walls of large bronchi and extend distally to the smaller.

Microscopically the areas of bronchopneumonia are found at the beginning of the alveolar passages, in the alveoli or the ends of bronchioles. The lumen is filled with cells, fibrin, and caseous exudate, and in the later stages the capillaries, the bronchial walls, and other tissue elements have been converted into structureless detritus. Only the elastic fibres remain for a time, as can be demonstrated by clearing the section with potassium hydrate solution. Pigment may also remain in the focus and give it a dark color.

In many places about the tubercular nodule there is a wall of

granulation tissue with giant cells, and the proliferation may follow the wall of the bronchus and cause marked thickening, so that the focus seems to have processes into the tissue about it. The granulation tissue may become caseous or fibrous.

The process of caseous bronchitis begins in the wall as a cellular infiltration, and in its lumen as a catarrhal or partly purulent inflammation, and the exudate becomes caseous. The wall of the bronchus is split into layers, and the whole is destroyed by the caseation. At the same time the adjoining parenchyma is attacked and softens, thus leading to cavities of varying size.

FIG. 214.

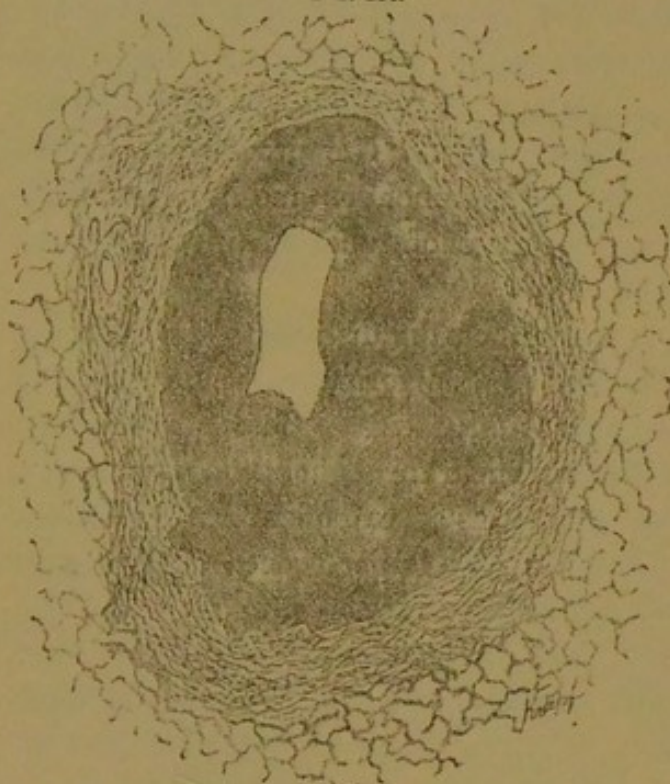


FIG. 216.



FIG. 214. Caseous bronchitis, with fibrous peribronchitis. The wall of the bronchus is wholly caseous and surrounded by a ring of fibrous tissue. $\times 25$.

FIG. 216. Interstitial, interlobular, and peribronchial tuberculosis, near a cavity. Natural size.

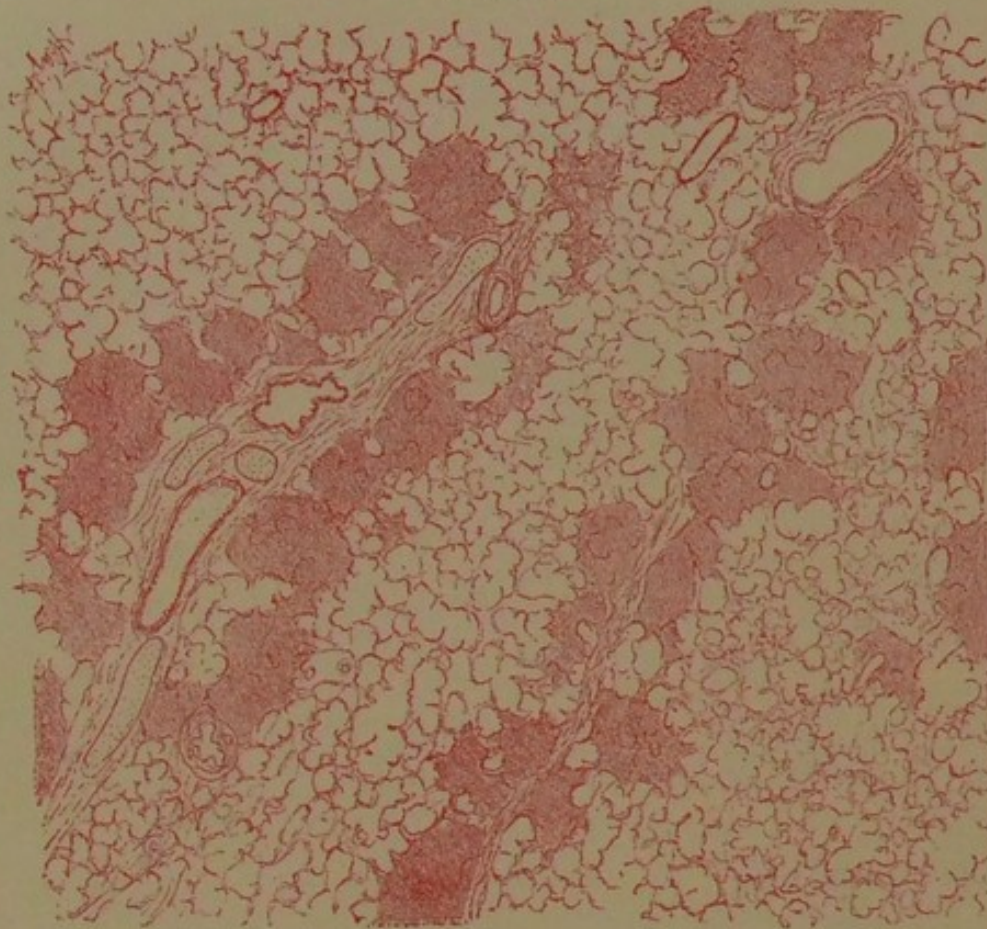
While the main process as described is going on, the lymphatics of the lung become infected and small secondary *resorption tubercles* develop in the alveolar walls and the interlobular septa, and these may become grouped so that the gross appearance resembles the original areas of bronchopneumonia.

Such resorption tubercles may be recognized with certainty only by the microscope. It is apparent that they have arisen not by exudation into a space which before contained air, but as the result of a proliferation in a septum between such spaces, into which the thickened



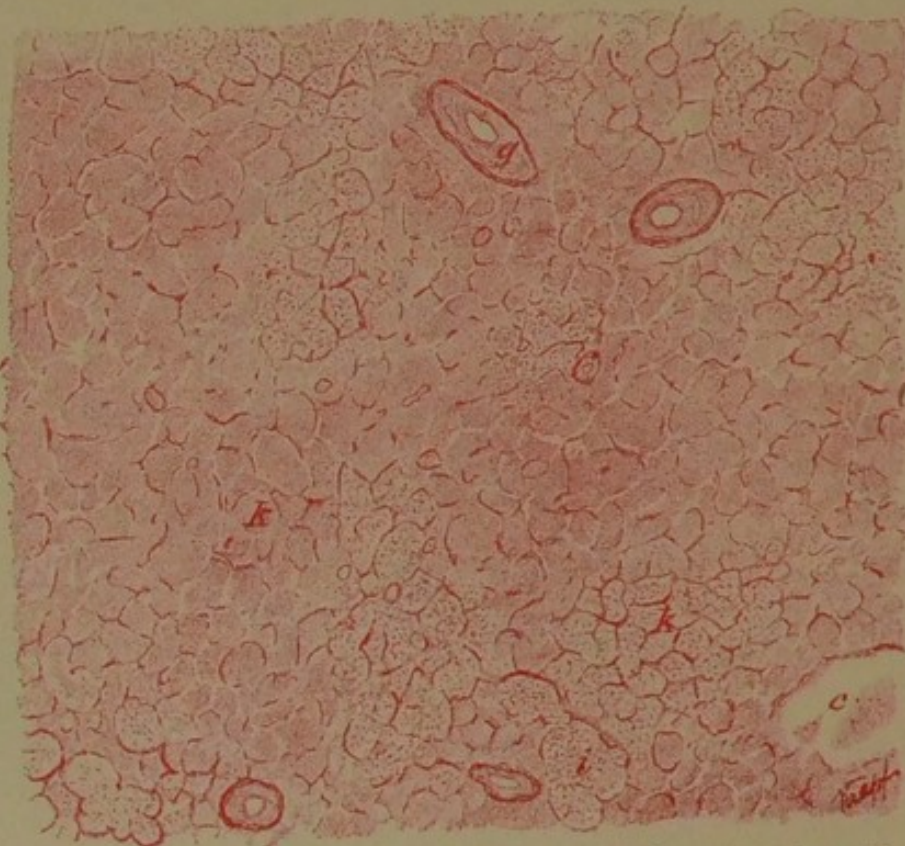
PLATE XX.

FIG. 217.



Interstitial Tuberculosis. Lines of tubercles along the course of bronchi in the fibrous tissue. Orcein. $\times 23$.

FIG. 219.



Caseous Pneumonia. Cellular exudate in alveoli.

k. Caseous exudate. g. Vessel. c. Cavity. Orcein. $\times 20$.

alveolar wall may bulge as a solid, round, or irregular nodule. Histologically these tubercles resemble similar formations in other organs, with giant cells, usually in the middle, and about them epithelioid and small round cells. They are distinguished from the pneumonic portions in not having elastic fibres disposed as about alveoli, but where the elastic fibres remain they are pushed aside by the process. Caseous and fibrous changes occur in these foci as in the other.

Such tubercles are developed when an infection remains for a long time confined to one spot or progresses very slowly. Many adjacent tubercles may fuse to a large conglomerate form, while the tissue about may become atelectatic and indurated or encapsuled by a fibrous inflammatory reaction.

II. Interstitial Tuberculosis. The eruption of tubercles in the interlobular, peribronchial, and perivascular connective tissue.

The development of tubercles in the course of lymphatics, as discussed above, suggests another manner of distribution through the lung, namely, that in certain cases the beginnings of the process do not manifest themselves in the bronchial mucous membranes, nor in the walls of the bronchioles, but are found in the fibrous septa between the lobules and in the fibrous tissue about the vessels and the bronchi, and hence this variety is called interstitial tuberculosis of the lung. The lymphatics begin in the alveoli, and from here, along their course, there may develop a series of tubercles with caseous centres which are connected by fibrous strands. This is called interstitial tuberculous lymphangitis, or lymphangitis nodosa peribronchialis. In other cases the lines of lymphatic tubercles are arranged in a network through the lung and are specially marked on the surface, where they map out the limits of the lobules.

Less frequently a bloodvessel is involved by the tubercular process, as when a caseous focus empties into it. If an artery is entered its entire distribution presents disseminated tubercles. If a vein is involved the bacilli may enter the systemic circulation and cause general miliary tuberculosis. These results are unusual, because of the proliferation of the intima in vessels lying within tuberculous lesions.

III. Lobular Tuberculous Pneumonia. The parenchyma of the lung from the first is involved in a rapidly spreading pneumonic process without the formation of nodules—caseous pneumonia.

The forms of tuberculosis so far described occur as nodules, in groups and series, and may present a distinct relation to the bronchial

system. Caseous pneumonia and colloid caseation are marked by diffuse, superficial extension through the actual parenchyma of the lung.

Caseous pneumonia begins as a catarrhal process, or there is a fibrinous element, also, by the development of multiple sublobular or lobular foci of inflammation, which are at first of a peculiar grayish-red color and firm hepatization. Then they become dry, slightly granular, of a yellower color, and at last distinctly caseous, but the caseous portion may not be uniformly softened, certain small points taking on the change, and then fusing.

The distribution in the lung may be lobular, which is uncommon, or lobar.

Microscopically the alveoli in the first stages are filled with cellular and fibrinous exudate, with which many proliferating and desquamating

FIG. 218.



FIG. 220.

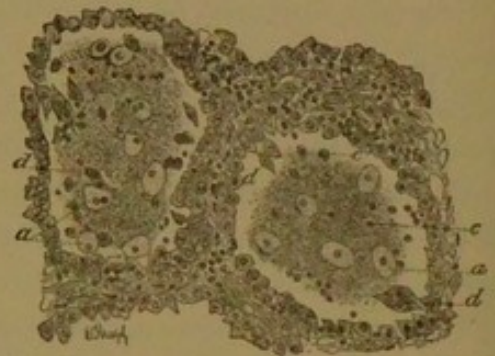


FIG. 218.—Lobular caseous pneumonia. Septa as light lines separating inflamed parenchyma (above to the right) from caseous (above to the left).

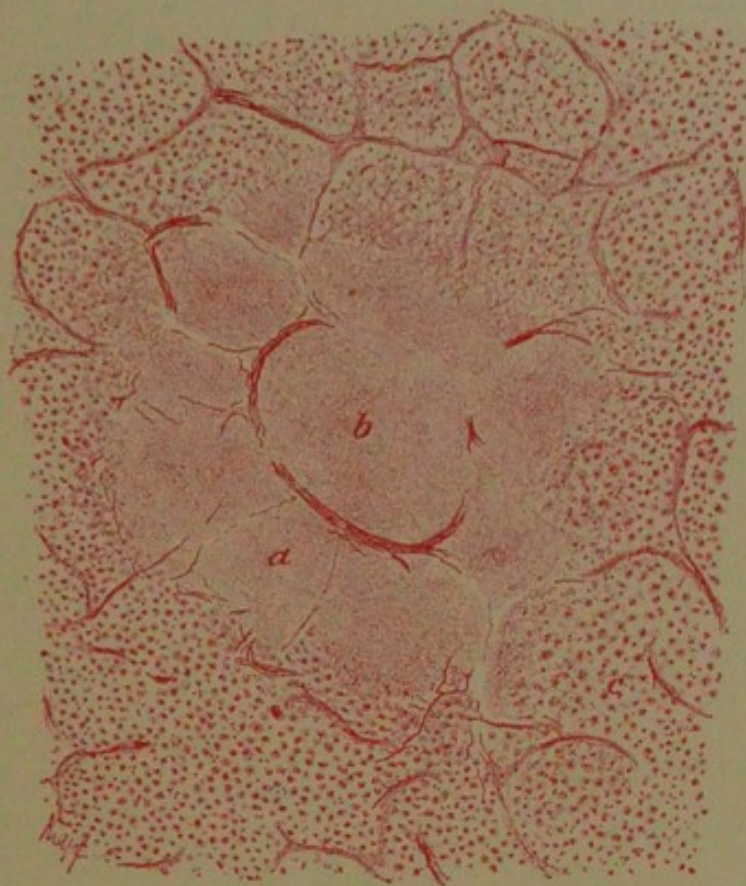
FIG. 220.—Tuberculous pneumonia. Two alveoli in which the epithelia, rich in plasma, are proliferating and form a thick layer on the wall, *d.* *a.* Desquamated epithelia in the lumen. *c.* Exudate, with round cells. $\times 230$.

epithelial cells are mixed. The proliferation is clearly followed, for the wall of the alveolus presents a thick layer of young cells, rich in plasma. When the alveolus and its contents are entirely caseous only the elastic fibres may remain to be recognized.

Where caseous pneumonia occurs in large sections of the lung we have the most rapid form of tuberculosis (florid phthisis), and in it softening of the necrotic mass may produce large and small cavities. In other cases, together with a scanty bronchopneumonic or caseous form, the lung takes on a peculiar soft, gelatinous, grayish-red or dirty gray appearance, with a smooth surface and complete absence of air. This lesion is more marked in the lower lobes and depends upon a saturation of the tissues with a colloid-serous fluid, and hence it is called colloid hepatization.

PLATE XXI.

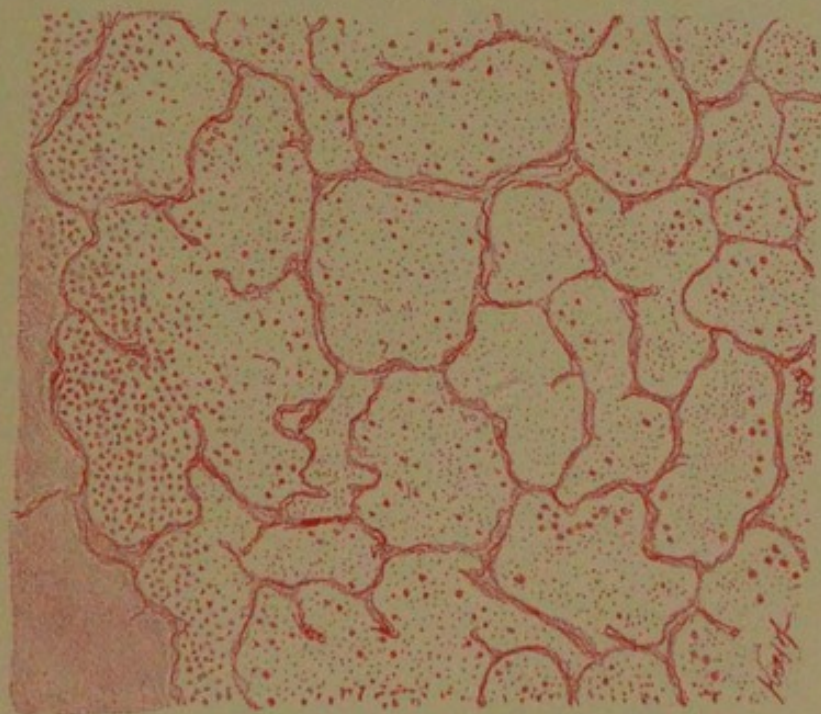
FIG. 221.



Caseous Pneumonia.

b. Respiratory bronchiole, and *a*, alveoli, both containing caseous matter; other alveoli contain fibro-cellular exudate not yet caseous. Orcein. $\times 200$.

FIG. 222.



Colloid Hepatization.

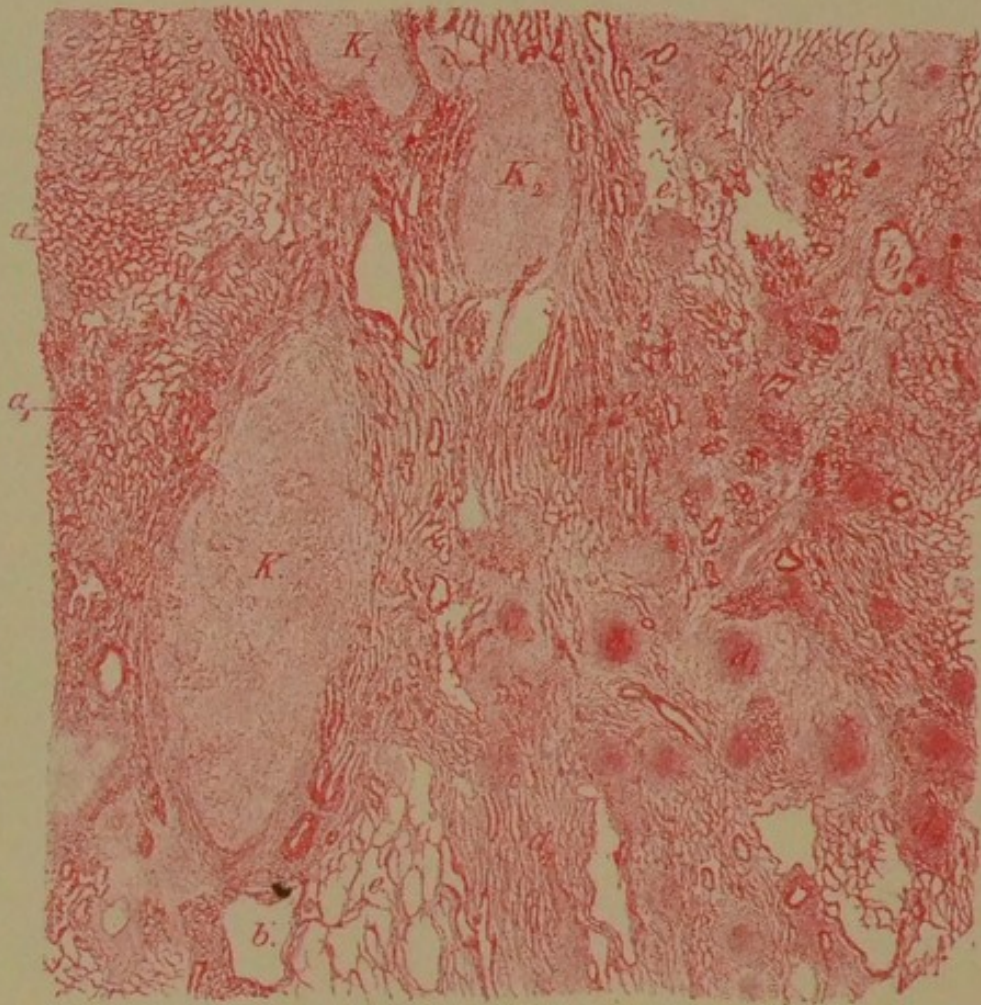
Exudate in alveoli mainly serous, containing a granular precipitate due to hardening. Orcein. $\times 50$.





PLATE XXII.

FIG. 224.



Collapse and Induration about Small Nodular Tubercles.

K_1 - K_2 . Large calcified mass. d - d_2 . Small caseous mass. b , b_1 . Vessels. e . Emphysematous alveoli. a - a_2 . Atelectatic portions. Orcein. $\times 20$.

Clinically the process causes a diffuse dulness on percussion, but this may disappear. The peculiar hepatization is probably due less to the bacilli than to their toxins.

Microscopically the alveoli are filled with a serous or slightly fibrinous exudate, with relatively but little admixture of cells or desquamation of the epithelia.

Secondary Changes—Indurative and Ulcerative Processes.

Certain further changes remain for consideration, affecting both the diseased tissue and the lung between, either as associated or subsequent conditions. Where caseous bronchitis and fibrous changes have occluded the bronchi a section of the lung may become collapsed and present the usual appearances, and this is very common in the course of pulmonary tuberculosis. Induration may follow, and hence such

FIG. 223.



Tuberculous bronchopneumonia. Natural size. The lung between the nodules is dark, sunken, and indurated: to the left are cross-sections of two normal bronchi.

Lungs frequently present tough fibrous parts which are non-aerated, grayish, or black in color from the pigment, and contain caseous masses of varying size. These indurated areas are common in the apices of the lungs.

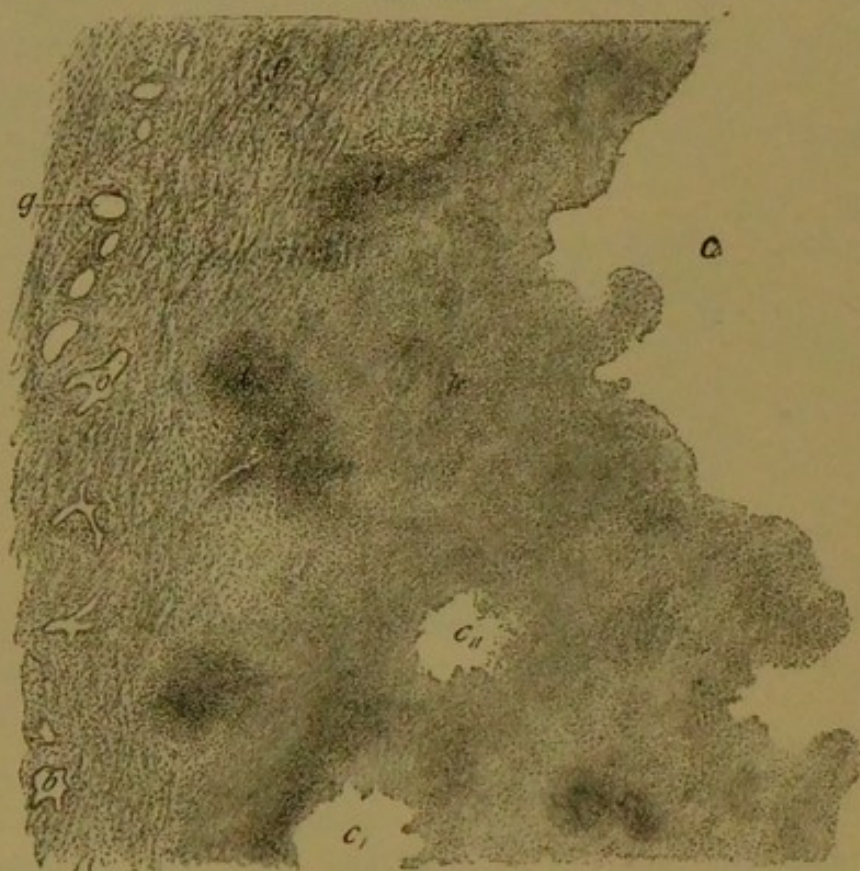
Although a portion of the lung is thus lost for functional purposes, the fibrous tissue about the mass prevents further spread, and the continuation of the fibrosis is a reparative process which converts the nodule into an innocent scar.

Caseous masses are often calcified and the contained bacilli destroyed, and thus a tubercular process may heal. Small areas of this kind are among the commonest post-mortem findings in the apex of the lung.

The worst fate which can happen to caseous masses is liquefaction, as is sometimes seen in smaller foci, but commonly in the larger. The

firm, dry mass becomes fluid by absorbing water and forms a thick yellow fluid or a more thin collection, which contains bits of caseous tissue and is held in a cavity. The smaller cavities occur in the bronchitic and bronchopneumonic nodules, the larger form in entire lobules after they become caseous. In the wall of the cavity and the tissue adjoining the process goes on until an entire lobe may be excavated. The different tissues offer varying degrees of resistance to the process, the thickened bronchi and vessels enduring it longest, and hence they are found as tough cords and projections crossing the cavity or on its side.

FIG. 225.



Wall of tuberculous cavity. *c*. Cavity. *k*. Caseous wall. *c'*, *c''*. Small fresh cavities by softening. *t*. Tubercles. *b*. Bronchi. *g*. Vessels in new fibrous tissue. $\times 100$.

The vessels are usually long since occluded by proliferation within them. If arroded before it is closed a vessel bleeds into the cavity, and if this communicates with a bronchus, hemoptysis results. The vascular stumps which project from the wall of the cavity may form small aneurisms, and the bleeding may come from these when they rupture. The wall is often covered with caseous material or shreds of necrotic tissue. After a time a bronchus is reached, as the cavity enlarges, and its contents are emptied with the sputa. The way is

then opened for further infection from outside, and thus suppurative or putrefactive changes may occur in the wall of the cavity and end in gangrene.

Cavity formation leads to the most rapid destruction of the organs, and with caseous pneumonia is most fatal in result. In less serious cases the spread of the lesion is hindered somewhat by fibrous proliferation, and when a cavity reaches a part which is collapsed and indurated it is arrested. At the same time granulation tissue forms about cavernous areas and acts as a capsule, and on the wall of cavities the necrotic tissue may be cast off, a group of red granulation tissue may take its place, and the cavity in this way may gradually heal.

The picture of chronic pulmonary tuberculosis is thus seen to be composed of many different processes, including bronchopneumonia, resorption tubercles, interstitial tuberculosis, lobular and lobar caseous pneumonia, with the sequels of collapse, induration, and suppuration.

Complications.

Chronic catarrhal bronchitis and catarrhal pneumonia are apt to occur in the course of tuberculous pulmonary disease, and the latter may take part in the production of collapse and induration. One of the most dangerous complications is purulent bronchitis, which begins in the smaller bronchi and extends to larger ones and to the lung parenchyma, with resulting purulent inflammation and abscesses. All these complications may be referred, in part at least, to the action of the tubercle bacilli, for we know that they may produce exudative and suppurative inflammation. But in the main there is a mixed infection, and these conditions are the work of the accompanying organism.

Bronchiectasis is the natural result of the fibrous contractions throughout the lung and to supplement the loss of function in other parts. Vicarious emphysema is also common in those sections of the organ which are not directly involved in tubercular processes.

All degrees of serous and serofibrinous pleurisy, synechia, tuberculosis of the diaphragm and the pleura, may be encountered with pulmonary tuberculosis. Empyema, pneumothorax, and pyopneumothorax are also observed at times.

The clinical course of the disease is as various as the anatomical changes. In general it begins in the apex with miliary and larger caseating nodules and bronchitis, and gradually extends downward throughout the lung by way of the bronchi and the lymph passages,

and partly also through the bloodvessels. Each new lesion is a source of further infection. As a rule the fibrous indurations belong to the more chronic forms, and the lobular and miliary foci in the parenchyma and the caseous bronchitis and peribronchitis to both the acute and the chronic forms. At any stage of a chronic process an acute exacerbation may be added, and, on the other hand, a process which began as a rapid phthisis may be brought to a slower course or complete cessation. In most cases both lungs are involved, though to different degrees; only the cirrhotic form is at times one sided.

Syphilis. Congenital gummata and pneumonic conditions occur, the latter forming the so-called white pneumonia. Lobular or, by confluence, lobar hepatization of white color and firm consistence develops, with complete non-aeration. Microscopically there is a catarrhal exudation in the alveoli and bronchi, and also a fatty degeneration of their contents, with a marked hyperplasia in the septa and thickening of the intima of the vessels. Acquired syphilis seldom causes pulmonary lesions, and they may be indistinguishable from ulcerative and cicatricial lesions.

Tumors. Primary neoplasms in the lung are unusual. Carcinoma may begin in the epithelium of alveoli, bronchi, and mucous glands; endothelioma may develop from the lymph vessels. Sarcoma has been found. Both sarcoma and carcinoma are usually metastatic. With endothelioma of the pleura a lymphangitis carcinomatodes may result which resembles peribronchial lymphangitis in the gross.

Parasites. Animal parasites in the lungs are infrequent; they may be cysticerci and echinococci.

Among vegetable forms actinomycosis may be mentioned, which enters the lung from the mouth and causes abscesses.

DISEASES OF THE PLEURA.

Congestive hyperemia precedes and accompanies inflammation of the pleura, and follows the relief of long-continued pressure, as when a collection of fluid is removed.

Passive hyperemia is part of a general stasis or the same condition in the pulmonary circulation. Stasis in the lungs and pleura leads to the transudation of serum into the cavity of the thorax (hydrothorax), and this may be copious enough to compress the lower lobes or a large part of the lung, producing atelectasis.

Hemorrhages of small size under the pleura occur with death from asphyxia. Large amounts in the cavity result from injuries to the chest wall. The condition is called *hematothorax*.

Inflammation of the pleura may be serous, fibrinous, purulent, and mixed; when blood occurs in the exudate it is called *hemorrhagic*, and a productive form is also recognized.

With the beginning of serofibrinous pleuritis the membrane loses its smooth and glistening look, because of degeneration of the endothelia, infiltration with cells, and slight exudation. Fibrin is deposited upon it as a dull satiny layer, which may increase in amount and become yellow; it is friable and easily lifted off. Irregular thickenings make the surface villous at times. In the cavity serous fluid collects, at times to several litres, which contains flocculi of fibrin, and is thus distinguished from a simple transudate. If copious it pushes the lung and the heart to the opposite side, and may cause *atelectasis* of the former.

A purely fibrinous inflammation is known as *dry pleurisy*.

Both fluid and fibrin may be completely absorbed, but it is commonly observed that granulation tissue forms and the layer of fibrin is replaced by new fibrous tissue, and when the two layers of the pleura are in contact this process leads to adhesions between them (*synechia*). These are distinguished from fibrinous adhesions by their firmness and their gray color. Such bands of adhesion are particularly common about the apices of the lungs. If large they may contain unorganized fibrin within them, and this may organize later or become caseous. Such a process is called *fibrous* or *adhesive pleuritis*, and it may be of this character and of chronic course from the first. Movements of the lung and the chest gradually stretch the adhesions.

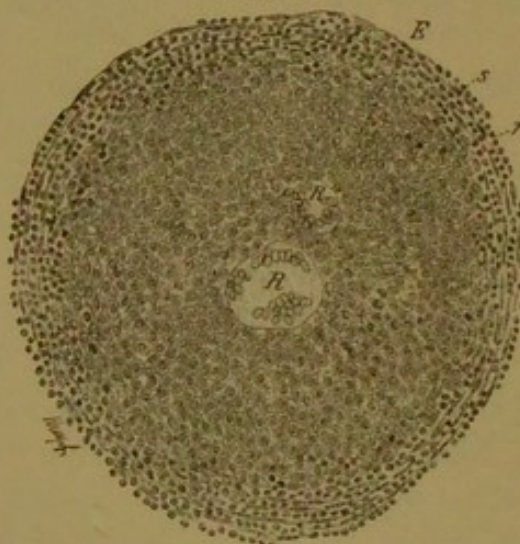
Purulent inflammation causes infiltration of the pleura, a thick covering of pus and fibrin, and the accumulation of pus in the cavity. This is called *empyema*. Its results vary from death, as the consequence of the disease, to extension to the lung and a so-called *pleurogenous pneumonia*, perforation outwardly through the chest wall, or thickening and organization of the exudate, while some of it is absorbed. An *encapsulated empyema* occurs when the production of pus takes place into a part of the pleura already shut off by adhesions, or when during the course of purulent pleuritis a portion of the exudate becomes surrounded and localized by organized fibrous tissue.

Pleurisy of various forms occurs by metastatic infection in pyemia, septicemia, articular rheumatism, typhoid fever, and other infectious

diseases. Injuries and infection of the wound may also be the source of the inflammation, or it may be carried from the mediastinum and its lymph nodes, the pericardium and the chest wall, and by far most frequently from tubercular foci in the lung. With various forms of pneumonia a certain amount of pleurisy is commonly observed, and with all these origins the result may be productive lesions and bands of new fibrous tissue. In chronic pneumonia, collapse and induration, and pneumoconioses, similar conditions in the pleura are almost constant, and along the course of its lymphatics small fibrous thickenings form which strongly resemble tubercles on gross examination.

Tuberculosis in the pleura is either a simple eruption of tubercles without accompanying inflammatory lesions, or a strictly tubercular pleuritis of exudative or productive character. The former condition

FIG. 226.



Tubercle of the pleura. *E*. Granulation cells. *R*. Giant cells. *r*. Lymphoid cells. *s*. Spindle cells at the margin. $\times 350$.

is seldom primary, but follows general miliary tuberculosis, pulmonary tuberculosis, or disease of the vertebræ, ribs, lymph nodes, or peritoneum.

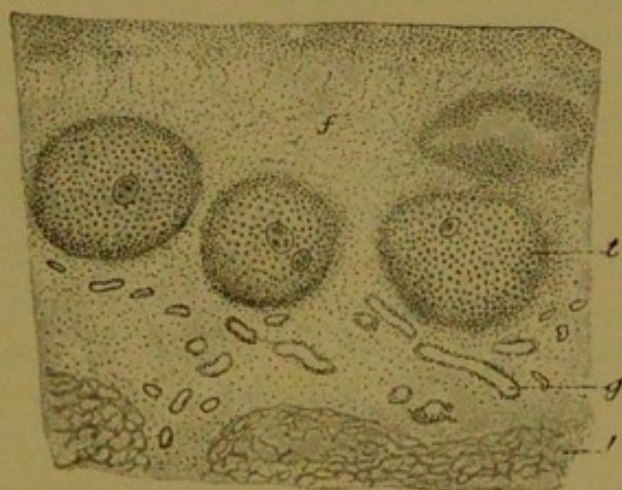
In the course of chronic tuberculosis of the lungs pleurisy is the rule. It may be fibrinous or serofibrinous without any tubercle bacilli in the lesions or the exudate, or with the form mentioned tubercles may develop, and the exudate may be hemorrhagic or purulent. The tubercles lie hidden under the fibrin or appear in the young granulation tissue which replaces it. The circumscribed pleural adhesions which occur with almost every phthisical case are localized, simple, or tubercular chronic pleuritis. As in the lesion of the lung, the pleural

tuberculosis is a varying condition, embracing acute exudation, chronic adhesive processes, encapsulation of the exudate, etc. Empyema is specially liable to follow the extension of a purulent peribronchitis or rupture of a cavity.

Tumors of the pleura are almost always secondary to other neoplasms and of their nature. Endothelioma and lymphangitis carcinomatodes may be primary and usually combined with inflammation. Fibroma and sarcoma are rare.

Pneumothorax is the collection of air in the pleural cavity. It follows perforation of the chest by traumatism, and injury to the pleura, esophagus, or stomach. The entrance of air causes the lung

FIG. 227.



Fibrous thickening of the pleura with miliary tubercles. *f.* Fibrous tissue. *l.* Lung. *g.* Vessels. *t.* Miliary tubercles with giant cells.

to collapse unless held by adhesions. If the perforation remains the pressure within the pleura is the same as that outside, and the condition is called open pneumothorax. If the perforation is closed the air is gradually absorbed. When the air enters through an injury to the pleura, most commonly by caseous perforation, it may happen that the orifice is closed by exudate or bits of tissue during expiration, and the air cannot escape, but opens again with inspiration, and more air is forced into the cavity. Thus the thoracic wall is rendered tense and the contents of the chest are pushed to the opposite side, the diaphragm downward and the intercostal spaces outward. When the chest is opened at autopsy the air rushes out with a loud hissing sound, so that a small flame held near will be blown out, or, if the thorax is opened under water, many bubbles pass out through the fluid. Even pneumothorax to the degree mentioned may disappear if the perfora-

tion is healed. In the conditions which most often lead to pneumothorax, other matters beside air gain entrance to the pleural cavity, and as pus or pyogenic organisms may enter, a suppuration follows in which gangrenous changes may occur, causing *pyopneumothorax*. Serous fluid with air is called *seropneumothorax*.

CHAPTER X.

DISEASES OF THE DIGESTIVE ORGANS.

A. MOUTH, PHARYNX, SALIVARY GLANDS, AND ESOPHAGUS.

1. Mouth, Cheek, Tongue, Teeth.

Inflammation. Simple catarrhal inflammation may affect the entire buccal cavity or certain parts of it (*glossitis, cheilitis, gingivitis*).

Aphthous stomatitis is accompanied by the formation of small grayish spots, infiltrated and slightly prominent, surrounded by a hyperemic edge and scattered over the gums and the furrows between the teeth and the cheeks. There is a fibrinous exudate under the epithelium, and when the latter is cast off small erosions are left.

Phlegmonous inflammation may involve the tongue and other parts as a sequel to erysipelas or trauma. Suppurative gingivitis (*parulis*) follows disease of the teeth. If abscess cavities discharge into the mouth or externally, fistulæ may remain. Herpetetic and pustular vesicles may be found on the lips and tongue after mechanical and chemical irritation and as a symptom with various general diseases.

Stomatitis ulcerosa is an inflammation of the gums which leads to extensive ulceration, involving the tongue and the cheeks, and necrosis and gangrene may be combined with the inflammation, yielding an extremely offensive discharge. The disease most commonly develops in young, cachectic, and scrofulous children in unsanitary conditions. In the adult it may follow certain poisons, as mercury, phosphorus and lead, or occur with scorbutus.

Noma is a disease which develops in conditions similar to those associated with stomatitis ulcerosa. It usually begins at the corners of the mouth as an edematous swelling which rapidly leads to gangrene of the parts and extensive destruction of the face; even bones and cartilages are necrosed.

Actinomyces causes suppuration and granulation in the gums and jaws.

A chronic affection of the mouth, due to hyperplasia of the epithelium and the mucosa, appears in variously shaped patches of a whitish

color, and follows excessive use of tobacco and infection with syphilis. It has received the names *leucoplakia buccalis et lingualis*, *psoriasis*, and *ichthyosis linguae*.

Tuberculosis is rare in the buccal cavity. It may appear as a primary ulcer on the tongue, which is at first limited to a superficial process, but later makes deep conglomerate tubercles which break in different directions after softening. Lupus may be transported from the face, and causes ulcers like those of the skin.

Syphilis in the mouth is more common, in all three stages. Papules or mucous patches occur on the lips, tongue, and cheek, and ulcers with fissured bases are common on the tongue. Gumma in the tongue is either circumscribed or a diffuse infiltration. After these soften and break superficially, specific ulcers with thickened edges form, but the infiltration may disappear before causing necrosis and ulceration. Necrosis of the bones of the roof of the mouth may be associated with nasal syphilis and establish communication between the cavities.

Tumors in the mouth include carcinoma, almost always flat-celled epithelioma, of the cheek, tongue, and lips. The form of the tumor may be superficial and papillary or a deeper nodule. Leucoplakia and chronic irritation of the tongue by carious teeth have been regarded as causes of lingual cancer. Epulis is a tumor belonging to the sarcomas, usually giant-celled, starting from the alveolar borders of the jaw. It is usually circumscribed. Among the benign tumors are angioma and lymphangioma, the latter appearing as thickenings of the lips or tongue (macrocheilia and macroglossia), which may either be congenital or appear shortly after birth. Other cases of macroglossia are due to congenital hyperplasia. Such thickenings are common in scrofulous children. In the gross they show linear thickenings of the mucous membrane and fissures (rhagades). Microscopically they are made of connective tissue and dilated lymphatics, both hyperplastic, and glands in the same condition.

Fibroma, myxoma, chondroma, and osteoma may also be found, and from the teeth an odontoma sometimes develops.

Cysts in the mouth are of various origins. Dermoid cysts occur in the floor of the mouth, retention cysts result from occlusion of the salivary ducts, and others form in connection with the primary epithelial cells of the teeth and dental sacs.

Thrush is common in children and cachectic patients, and specially affects the tongue, but may spread to other parts, as the pharynx, esophagus, and larynx. Grayish-white spots or larger areas cover the

parts, and the investment is made up of hyphæ and spores of *oidium albicans*. The mucosa below is inflamed and disposed to bleed.

The commonest lesion of the teeth is caries, beginning as an inflammation of the pulp and the periosteum of the root.

2. Salivary Glands.

Parotitis or mumps is an inflammation of the parotid gland, in which the other salivary glands may take part, and occurs either sporadically or epidemically. It may resolve or suppurate.

Angina Ludovici is a phlegmonous inflammation, often ending in abscesses, which takes origin in the neighborhood of the submaxillary gland.

Concretions may form in the ducts of the glands and lead to cystic dilatations, and similar changes follow contraction of scars which close the ducts.

Among tumors of the glands may be mentioned carcinoma, sarcoma, mixed tumors, cylindroma, and angiosarcoma.

3. Pharynx, Isthmus Faucium and Tonsils.

Inflammation. Catarrh of these parts appears as pharyngitis, angina, and amygdalitis, and may involve all at one time. Acute catarrh causes redness, swelling, increased secretion, and in the tonsils an acute hyperplasia and increase in size. The causes are like those for laryngitis (p. 309). In the inflamed tonsillar lacunæ yellow plugs of thick secretion may form which resemble abscesses.

Chronic catarrh of the pharynx has the same etiology as similar laryngeal inflammation. The mucosa is partly hypertrophic, with thickening and swelling, and many small granular hyperplasias of follicles and glands (*pharyngitis granulosa*). Later it becomes atrophic, smooth, and thin, and the granules appear the more prominently. The tonsils may be enlarged by chronic hyperplasia of the lymphadenoid tissue, and plugs are common in the lacunæ.

Tonsillar hyperplasia is common in scrofulous children who suffer from repeated inflammations of the parts as well as of the pharyngeal tonsil. The hypertrophy may be lymphadenoid or fibrous. The action of putrefactive organisms may cause gangrenous tonsillitis, especially in scarlatina and diphtheria.

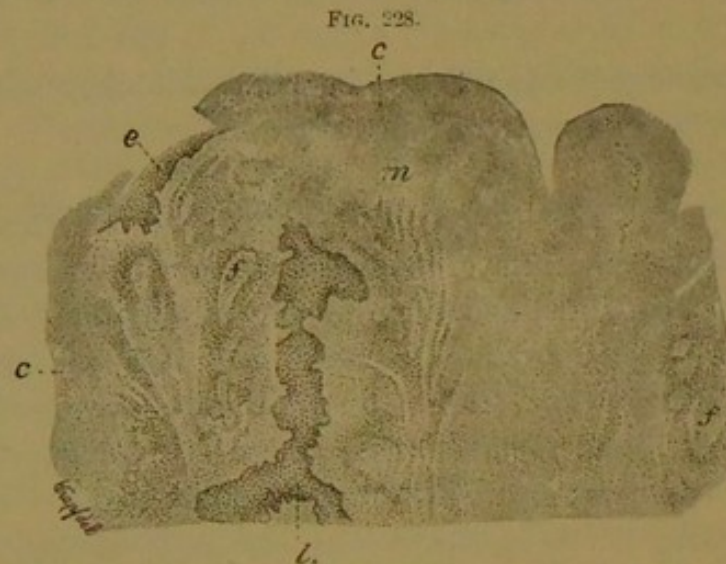
Phlegmonous inflammations produce redness and swelling of the mucous membrane with purulent infiltration, and this may go on to cause abscesses. Several kinds are recognized:

1. *Phlegmonous angina*, involving the palate and especially the uvula, as the consequence of thermic and chemical irritants.

2. *Phlegmonous tonsillitis*, which causes many small or one large abscess, which usually breaks into the mouth, but may open the carotid.

3. *Phlegmonous pharyngitis*, or retropharyngeal abscess, which is usually a secondary suppuration of the posterior pharyngeal wall and the lymph nodes of the part after infection from scarlet fever and diphtheria, injuries of the region, and caries of the cervical vertebræ. The abscess may open into the pharynx, but the danger is always present that the pus may follow the anterior surface of the spine into the mediastinum.

The most important inflammations about the pharynx are the pseudo-membranous, which are characterized by the formation of a false



Diphtheritic tonsillitis. *c, c.* Necrotic masses on the surface. *e.* Epithelium still present. *L.* Lacuna with epithelium. At *m* and on the right side the epithelium is lacking and the mucosa is necrotic. *f.* Follicle. $\times 25$.

membrane upon the mucosa and at times by involvement of the deeper tissues of the mucosa. These inflammations are grouped as diphtheria, but they may be due to various causes, as corrosive poisons, hot fluids, and any other influence which leads to necrosis of the mucosa or its epithelium.

Diphtheria. At present the name diphtheria in relation to the pharynx refers to a general infection, with its anatomical site in this region, and for which childhood is a disposing factor. The disease may be sporadic, epidemic, and in the large cities endemic, and is the cause of a large percentage of sickness and death in childhood. The most important anatomical feature is the formation of a false mem-

brane, but there are forms which present only a simple angina and are allied to the usual diphtheria only by their malignant and contagious nature and transitions to the membranous form. In most cases the disease begins on the tonsils or palate, less often in the larynx, with the appearance of grayish-white spots, which spread rapidly, become confluent, and may invest the larger portion of the mucous membrane. It is specially found on the swollen tonsils, the uvula, soft palate, and pharyngeal wall. Microscopically the membrane consists of fibrinous exudate on the surface of the mucosa, but the upper layers of the mucosa or its entire thickness may be necrotic. The membrane is loosely attached except over the tonsils. Deeper necrosis, suppuration, and gangrene may be associated lesions.

In a large number of cases the lesion travels to the larynx and produces the familiar picture of laryngeal croup or diphtheria, and from here it may involve the larger or even the smaller bronchi (descending croup). As a rule, in the middle and larger bronchi the membrane is not formed, but the exudate is mucopurulent. The lung may take part in the process, but not in a specific manner. Capillary bronchitis, atelectasis, catarrhal and fibrinous pneumonia and aspiration pneumonia, with serous or serofibrinous pleurisy, are the commonest lesions found in these organs. From the larynx the cervical lymph nodes are affected, and either simply swollen or necrotic and purulent.

Parenchymatous degeneration of the heart, liver, and kidneys, either as cloudy swelling or a fatty change, will usually be found, and at times there is distinct parenchymatous or hemorrhagic nephritis. The follicles of the spleen are swollen while the pulp is less affected. The conjunctiva and the nasal mucosa may be involved in the diphtheritic inflammation.

The cause of the disease is admitted to be the Löffler bacillus, which occurs in the membrane but not in the organs. The general effect must, therefore, be due to toxins, probably toxalbumins. With the Löffler bacillus streptococci, staphylococci, and pneumococci are associated, but their share in the disease is not clearly established.

Other pseudomembranous inflammations occur in measles and frequently in scarlatina, which may be accompanied by a catarrhal angina or a scarlatinal diphtheria. This latter complication is a genuine diphtheria in many cases, the result of mixed infection. In other cases the exudative process is less evident than deep necrotic lesions, with purulent and gangrenous destruction of the parts and extreme swelling of the tonsils. More commonly than in true diphtheria the

cervical lymph nodes become necrotic, purulent, or gangrenous, but there is less tendency to invade the larynx. The cause of this scarlatinal diphtheria is probably different from that of the true form.

Infectious Granulomata. Syphilis may be both secondary and tertiary in the pharynx. Mucous patches are the usual expression of the former. Diffuse and gummatous infiltration with ulcers is common in the latter, and the lesion may involve the deeper tissues to the bones. Perforation of the soft palate, destruction of the tonsils, and various distortion of the parts may result, partly from the ulcers, partly from contracting scars.

Tuberculosis produces lesions similar to those in the larynx.

Lupus causes thickening and infiltration of the mucous membrane, excrescences, and slow ulceration, with imperfect scar formation and a resemblance to syphilitic lesions.

Tumors. Papilloma occurs with chronic pharyngitis; carcinoma may start in the palate, tonsils, or pharyngeal wall; and from the basis cranii polypoid fibrosarcoma sometimes develops.

4. Esophagus.

Cadaveric softening of the lower end of the esophagus is due to regurgitation of stomach contents. Slight degrees of this appear as longitudinal narrow defects of the epithelium and softening of the mucosa. These changes are quite similar to those in the stomach after death.

Softening of the esophagus like that occurring post-mortem may take place during the death agony, and another form, extremely rare, is a peptic ulcer like the *ulcus rotundum* of the stomach.

Inflammation of the esophagus may follow injuries, as by fragments of bone and the action of corrosives. Phlegmonous infiltration with abscess formation and perforation of the wall may be the consequences, and the abscess may open into the trachea or large bronchi, the pleura, or pericardium, or infrequently into the great vessels.

Stenosis may be caused by external pressure, as of tumors, aneurisms, and enlarged nodes, or by neoplasms in its wall, or scars after phlegmonous inflammation.

Dilatation of the esophagus may be partial, resulting in a diverticulum, and of this lesion two varieties occur, the *pulsion* and the *traction diverticula*. A pulsion diverticulum usually develops from the posterior wall of the canal and at the junction between it and the pharynx. It consists of a sacculated protrusion of the mucosa and submucosa,

surrounded by a connective-tissue capsule, and in its wall muscle fibres are usually found only about its neck. There is a hernia-like protrusion of the layers mentioned between the fibres of the inferior constrictor of the pharynx. Such a pharyngocele is produced by the lodgement of a foreign body or other traumatic influences acting on the esophageal wall, and the muscular effort of swallowing, and consequent pressure on the part, tend to increase the protrusion. Another view is that the entire wall of the esophagus is dilated, but that the muscle fibres atrophy and leave the sac made up only of the elements stated.

Traction diverticula are caused by retraction of cicatricial adhesions upon the outside of the tube. Commonly they follow such contraction in and about lymph nodes which have become pigmented and indurated or softened by tuberculous processes and then cicatrized. The form of the pouch is conical, and at the apex is the contracting scar. Its usual seat is on the anterior wall of the esophagus near the tracheal bifurcation. Food may collect and putrefy in such a pouch, with resulting suppuration and perforation. Other diverticula, laterally placed, may result from dilatation of portions of the branchial clefts.

Simple softening of the entire esophagus may follow stenosis in its course, especially at the cardiac orifice, and occurs with carcinoma, phlegmonous inflammation, and sloughing after ingestion of corrosive fluids.

The *neoplasms* of the esophagus are practically limited to carcinoma, which occurs rather frequently in men who are hard drinkers. Esophageal carcinoma has three usual sites: behind the larynx, opposite the bifurcation of the trachea, and at the cardiac opening, and is usually a squamous-celled epithelioma. It does not spread fast along the esophagus, but soon surrounds it as a thick ring, and thus early causes stenosis. In the softer forms an ulcerative process follows on the mucosa, and the site is marked by a circular ulcer with nodular edges. This surface may suppurate or become necrotic. Carcinoma in the upper portion of the tube quickly invades the larynx; in the region of the cardiac end it spreads to the stomach. Perforation into the trachea, bronchi, and lungs is common, and pneumonia follows by aspiration of foreign material. Perforation of the pleura causes empyema. At times the large vessels adjoining may also be invaded. Metastasis is common to the cervical nodes.

In children and cachectic persons thrush may involve the esophagus in whole or in part.

B. THE STOMACH.

The mucous membrane of the stomach is characterized by furrows which lie between the prominent reticular rugæ. Between the latter the mouths of the glands lie, and in the fundus these glands are simple and tubular. They contain two varieties of cells. One of these is a large round prominent cell, the investing cell of the gland (*delomorphous*) which is supposed to furnish the hydrochloric acid of the gastric juice. The other is more cylindrical (*adelomorphous*) and furnishes the pepsin. About the pylorus the depressions are deeper and farther apart, and between them are flat and low prominences in the mucosa, the plicæ villosæ. Here the glands are branching and contain but one kind of cells, like the peptic of the fundus, and close to the pylorus Brunner's glands are found, similar to those in the duodenum. The surface of the stomach generally is covered with cylindrical cells in which many beaker cells occur which supply mucin.

Malformations of the stomach are infrequent. Stenosis and atresia of the pylorus are at times noted, and constrictions between the fundus and the pylorus which make the hour-glass contraction. The vertical position of the organ during fetal life may persist, and in *situs inversus* the stomach's position is reversed.

Regressive Changes.

Post-mortem changes are important in the stomach, because they complicate the conditions so frequently. They are the result of the following factors:

1. *Hypostasis*. In the fundus especially there is often an appearance of a dark branching network in the mucous surface which at first sight may be confused with hemorrhages. The latter lie more deeply, are not disposed in a network, and consist of sharply defined collections of blood.

2. *Diffusion of the blood pigment* occurs about the large veins, as brownish-red or black spots and lines.

3. *Softening, gastromalacia*, is due to the action of the acid gastric juice. The epithelium at first becomes opaque, and then the entire mucosa is grayish, soft, and easily stripped up. This is most marked in the spot where the fluid collected post-mortem, and its limits may be sharply circumscribed. The muscularis may be laid bare or the whole wall perforated. It is supposed that such a softening may occur during the agony, but this view has been denied.

4. *Decomposition* causes a dirty green color which in the presence of sulphuretted gases becomes black.

The ante-mortem condition of the stomach as regards digestion may resemble pathological conditions. Arterial hyperemia is normal during digestion. Microscopically cloudy swelling involves the cells in the middle and deeper parts of the glands, while post-mortem opacity is seen in the superficial epithelium also.

Cloudy swelling or parenchymatous degeneration of the stomach is accompanied by the deposit of albuminous granules in the enlarged epithelia, and it may end in fatty degeneration. The mucosa is thickened, anemic, gray, or yellow gray. Infectious diseases, pernicious anemia, and poisoning by arsenic, phosphorus, lead, and carbon monoxide may cause this lesion.

Amyloid degeneration of the gastric vessels may be part of general amyloid changes.

In diseases of the bones with free resorption of the calcium salts these may be deposited here and there in the stomach wall.

Atrophy of the stomach and decrease in its capacity and thinning of its wall, both muscularis and mucosa, may be found in chronic diseases which lead to inanition and cachexia, with stenosis of the cardiac opening, and in the course of chronic gastritis and gastro-enteritis.

Disorders of Circulation.

Anemia occurs with general anemia. Active hyperemia is normal during digestion, and follows stimulation by food, poison, etc. In the latter case the hyperemia is specially marked along the edges of the folds.

Passive congestion is the result of general stasis, and also of obstruction to the portal system. In active and passive hyperemia and with violent efforts at vomiting hemorrhages may occur. The action of the gastric juice on the blood makes it dark brown or black.

Melæna neonatorum is the term employed for hemorrhages from the stomach and the duodenum of the newly born, and during the first weeks of life. The origin of the bleeding is not entirely clear. In many cases there is ulceration in the mucosa of either organ, in other cases there is venous stasis because of imperfect respiration and consequent distention of the right ventricle, in others there is some cerebral lesion or a septic infection of the umbilical stump.

Inflammation.

Acute Gastritis. Acute catarrh of the stomach is due to many causes. Errors in diet, especially use of chemically irritating materials or those which are decayed or infected, excess of food, thermic influences, and others, may be mentioned. The disposition to the lesion is common to the anemic and cachectic, those who are suffering from tuberculosis, syphilis, or carcinoma, diseases of the liver and the heart, and those who are convalescent. Lastly, in the course of general infections, as typhoid, influenza, and erysipelas, it often complicates the disease.

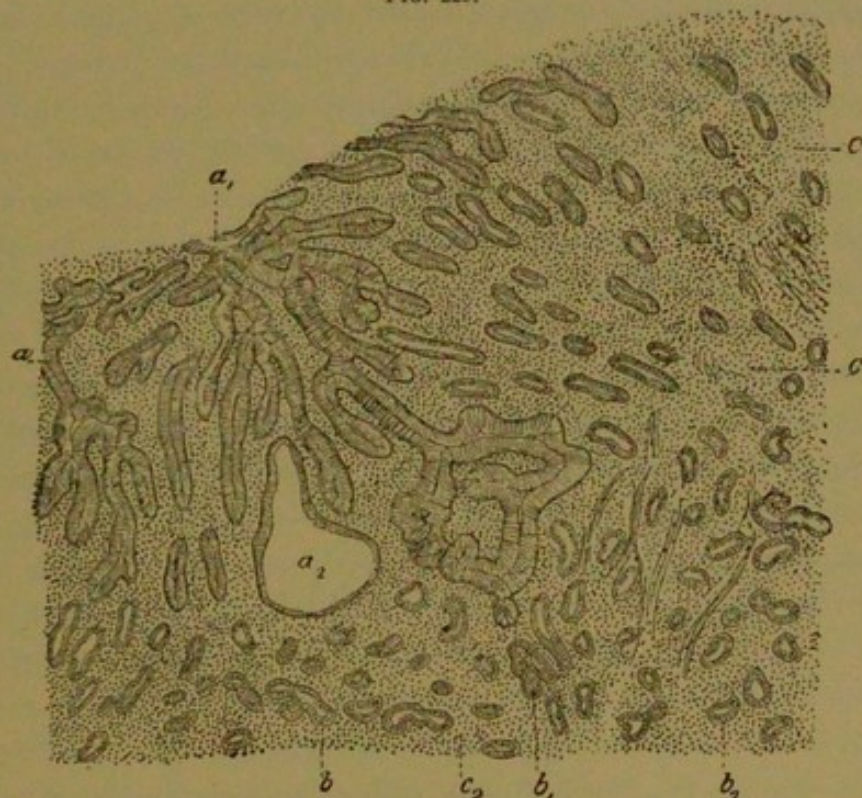
The anatomical changes due to acute gastric catarrh are seldom seen uncomplicated by post-mortem alterations. There is an excess of mucus, and the cylindrical epithelium of the surface is in a condition of cloudy and mucoid degeneration. The epithelial elements of the glands may be affected and produce a glassy, tough, lightly blood-stained and abundant secretion which covers the mucosa in a thick layer. With the epithelial degeneration there is a marked swelling and inflammatory infiltration of the mucosa which differs from the physiological hyperemia in being most evident on the summits of the rugæ, especially in the region of the pylorus. The mucosa is looser and more strongly wrinkled than normal. Many small hemorrhages may be found, and minute ulcerations about them, due to the death of a section of the mucosa following the extravasation of blood.

Chronic gastritis may be due to causes which produce the acute form, especially when they act repeatedly and for a long time. Unsuitable food, chemically irritating matters, and alcohol are very common causes. The disease may also follow the acute inflammation or accompany other diseases, as carcinoma and round ulcer, which produce chronic inflammatory lesions for a wide distance about them. Venous stasis due to diseases of the liver and the heart may be a disposing factor, and, with nephritis, a stasis may be caused by beginning weakness of the left ventricle. Chlorosis, anemia, and diseases leading to cachexia, are accompanied by chronic gastritis, and dilatation of the organ may precede or follow it.

The lesions vary according to the form and the duration of the disease. In cases which have not lasted long the mucosa is swollen, wrinkled, loose, and more or less reddened, but the latter is marked chiefly when there has been stasis. The veins may appear very full and dilated. Hemorrhages and erosions or larger ulcers may occur. The slaty color of the mucosa is striking, and is due to the original

hyperemia. There is an excess of dull-gray mucus in which, by the microscope, epithelia and pus cells are found. With the degeneration of the superficial epithelium and glands there is an infiltration of the wall by lymphoid cells and an increase of the fibrous tissue between the glands, upon which fact depends the thickness of the mucosa. The glands may be widened, lengthened, spirally twisted, freely branching, or cystic from accumulated secretion. The lymph follicles in the submucosa may be swollen, and in certain cases this leads to a diffuse hyperplasia of the entire mucous membrane.

FIG. 229.



Chronic catarrh of the stomach; gastritis granulosa. Section through stomach mucosa. The epithelium softened superficially post-mortem. *a*, *a*₂. Enlarged branching glands; many glands cut diagonally. *c*, *c*₂. Increased interstitial tissue pressing glands together. *b*, *b*₂. Glands not dilated. $\times 40$.

In many cases the infiltration and proliferation occur in discrete areas, and hence on the inner surface of the stomach there are many flat, prominent, and granular portions, which have given it the name of gastritis granulosa. These projecting parts may be as large as nipples, and then the condition is called the *état mamelonné*. Small circumscribed growths of polypoid form, made up of mucoid or glandular tissue, are described as a *gastritis polyposa*.

After long duration of the catarrhal condition the hyperemia disappears, except when there is stasis, and the mucosa is pale, gray, and

pigmented, both firmer and thinner than normal, because of atrophy of the membrane. Both the glands and the stroma are involved in the cicatricial shrinking, and the lesion is usually most marked about the pylorus.

In severe cases the submucosa and the muscularis may also be the seat of infiltration, with consequent shrinking and decrease of the stomach's capacity. In most cases of the so-called cirrhosis of the stomach, however, the lesion is carcinomatous or the result of corrosive action on the organ. Muscular hypertrophy of the pylorus may lead to stenosis of its lumen.

Phlegmonous gastritis may be caused by various poisons, intestinal mycosis, and suppurations. Infection with anthrax produces hemorrhagic infiltration of the mucous membranes, especially of the submucosa, which leads to ulceration. There are circumscribed lenticular ulcers with superficial and central necrosis, and in the gross it resembles carbuncle. A suppurative inflammation appears to be spontaneous, occasionally, in the alcoholic. Small embolic abscesses are found in the stomach with pyemia and similar infections.

Gastric Ulcer. Circumscribed self-digestion of the stomach may occur during life. Normally the mucosa is protected against the gastric juice so long as its circulation is physiological. When an area has its circulation interfered with its nutrition suffers, and the gastric juice may attack it. Thus with hemorrhages small, round, or oval erosions may occur, and these may extend laterally to large ulcers.

Ulcus rotundum is a peculiar form of ulcer which occurs in the stomach, the duodenum, and very rarely in the lower part of the esophagus. In most cases its appearance is typical. It is circular or oval, apparently punched out smoothly, and the edges are not infiltrated or but slightly swollen and changed. It is cone-shaped, the defect in the submucosa being smaller than that on the surface, and the excavation tapering toward the serosa as by a series of terraces. There is usually no exudate on any part of the ulcer, but there may be mucus and blood. The axis of the cone is not perpendicular to the wall but inclined so that the different layers are eccentric. The defect corresponds in most cases to the conical distribution of a small artery, and its axis to the main line of the vessel. In the bottom of the cone an obliterated stump of the artery may be found.

The diameter of the round ulcer varies from two to six or more cm. The smallest ones may not be seen until the stomach has been thoroughly washed free from mucus. The largest ulcers may be more

irregular in outline than described, owing to the uneven extension of the process at different places and to the fusion of two or more ulcers. The ulcer may be disposed as a ring about the circumference of the stomach, but this is rare.

The anatomical characters of the lesion show that it depends upon local disorders of the blood supply, and experimentally it may be reproduced by such means. Because of the action of the gastric juice in removing the tissue deprived of its nutrition the ulcer has been called peptic ulcer, or *ulcus e digestionē*. Diseases of the walls of the vessels, as fatty degeneration and aneurism, and any cause of thrombosis and embolism, may lead to such ulceration. After severe burns the destruction of the red cells or blood plates may lead to embolism of small arteries, and the peptic ulcers with hemoglobinemia, erysipelas, and septic infections, may be thus explained. In the course of malaria the vessel may be plugged by masses of pigment and parasites. Venous stasis and local circumscribed disorders may also lead to it. In some cases the diseased vessel may rupture and thus become the starting point of the lesion. As the gastric vessels are end arteries, emboli may cause infarction, and the part invaded may end as an ulcer. The theory of a spastic condition of the arteries and local anemia has also been advanced for some cases.

Hot fluids, injuries by fish bones and other matters in the food may explain some cases. In certain trades, as turning and sharpening metals, swallowing sharp metal particles may have a similar effect. Corrosive chemicals are also a possible cause.

The general condition of the health is important in the production of gastric ulcer, partly because the vessels suffer with imperfect nutrition. All chronic diseases which lead to cachexia, and, among these, diseases of the blood, as anemia, chlorosis, etc., may be accompanied by ulcer of the stomach. The same is true of syphilis, tuberculosis, and amyloid degeneration. It is more common in women than in men, and especially in the years immediately after puberty.

In most cases there is but one ulcer in the stomach, but several may occur together. The commonest seat of the lesion is on the posterior wall, then the lesser curvature, then near the pylorus, and lastly the anterior wall and the cardiac end.

The usual course of the disease is healing by scar formation, from the bottom and the edges of the defect, in white, radiating lines of connective tissue. When small this may easily be overlooked. The large radiate scars may contract the stomach and produce hour-glass

constriction. Scars at the two openings of the stomach may cause stenosis and dilatation, with new attacks of catarrhal inflammation and its results.

Before the ulcer heals there is danger of hemorrhage and of perforation. The former, caused by erosion of a vessel, may be immediately fatal, or when less in quantity but often repeated, severe anemia may follow. The eroded vessel or merely some altered blood and pigment may be found in the ulcer. Perforation follows the piercing of the serosa by the ulcerative process, and if this occurs into the peritoneum diffuse inflammation may result. Commonly adhesions form between the site of the ulcer, externally, before it bursts through, and adjacent viscera as the liver, the pancreas, and the colon.

The process may then advance to the destruction of the organ which is adherent, and in time large vessels may be opened, as the splenic artery, or thrombosed, as branches of the portal vein, or abscesses may form. When the ulcer opens into a hollow organ a fistulous communication may be made between the stomach and the gall-bladder, colon, mediastinum, pericardium, or pleura. Perforation externally leaves an external gastric fistula opening on the skin.

Ulcer of the anterior wall of the stomach and the cardiac portion are most dangerous, because adhesions are less often formed, and hence perforation into the peritoneum is most probable. A further danger is that a carcinoma may develop on the edge of the defect because of the atypical proliferation of epithelium and glands during healing.

Poisons. The action of poisons upon the wall of the stomach is varied, but in general they produce inflammation and necrosis. Some, however, pass into the general circulation without local effect, and others affect the stomach only as part of a general condition.

The most important local action of poisons is that due to *corrosive substances*, especially the mineral acids, certain organic acids, and concentrated alkalies. Wherever in the alimentary tract these corrosive matters come in contact with the mucous membrane they produce an *eschar*, which may be tough or friable, or loose in texture, and after a time the eschar becomes cast off. In color these eschars differ with the kind of poison, many are stained by the bleeding which they cause; from the destroyed blood they may become brown or black. The contents of the organ may also be black from this cause. The wall of the stomach may be perforated during life, and frequently is so after death, for the poison continues to act and may corrode the wall of the stomach and attack neighboring organs post-mortem.

The factors which modify the corrosion are the degree of concentration, the amount, and the duration of the action. When the poison is taken by accident the greater portion may be voided from the mouth, and only the upper part of the alimentary tract may present evidences of its action. The amount of material already in the stomach is of great importance, for the acid or the alkali may be partly neutralized thereby and so diluted as to weaken the action. Metallic salts may form harmless compounds with proteid matters, and rapid use of antidotes and vomiting may prevent or diminish the action of the poison. The effect is most intense when the stomach is empty. The corrosion varies with position, being on the posterior wall of the fundus when the patient lies on the back, and on the fundus and greater curvature in the upright position. When the organ is contracted and the amount of poison small, the edges of the rugæ are the parts to show the action especially. The wall of the duodenum and part of the small intestine may be similarly affected. About the corners of the mouth corrosive action follows the escape of some fluid during ingestion or passage of vomit, and the same is true of the lips, the buccal cavity, and the esophagus. The epiglottis and the aditus laryngis may be corroded, and edema of the glottis may result.

If death is not immediate the stomach suffers severe inflammatory changes, usually of hemorrhagic character. The stomach is strongly contracted, its mucosa or the entire wall is thickened and edematous, and suppuration may follow. The eschars leave deep ulcers when they are cast off, and these may end in perforation. Peptic ulcers may follow later.

Severe functional disturbances, contraction by scars, stenosis of the cardiac or the pyloric end, hour-glass contraction, and general cicatricial contraction may be some of the later consequences.

Diluted corrosive fluids have less escharotic action, but the inflammatory effect may be pronounced, and hemorrhagic or phlegmonous and ulcerative in character. The least degree of such a toxic gastritis resembles simple acute catarrh.

Keeping in mind the general features so far discussed, and assuming that the poisons are concentrated and active, the chief instances will now be reviewed:

Sulphuric Acid. This is frequently used as a poison. It causes black eschars in the stomach, and the contents of the organ are black, tar-like, or more fluid. The wall is hemorrhagic. The eschars are at first brittle, like leather, and then strip off in layers. Phlegmonous

and hemorrhagic inflammation and secondary ulceration are common, perforation usually post-mortem.

Leathery lines of corrosion from the mouth to the chin, corrosion in pharynx, larynx, and esophagus, and also in the intestine.

The blood is thick or clotted, parenchymatous degenerations are common in the heart, liver, and kidney. Death is due partly to local lesions, but more to the loss of alkali from the blood, so that dilute acid may be fatal.

Nitric and **hydrochloric** acids have about the same effect, but the former causes an orange-yellow color (xanthoprotein) where concentrated, and a violet to grayish white where more dilute, and the latter produces a grayish-yellow or black color.

Oxalic acid and its potassium salt produce white or grayish eschars which may be yellow from imbibition of hematin, or brown or yellow from bile. The gastric mucosa is not corroded, but transparent, edematous, hyperemic or bleeding; its contents are brownish. White opaque deposits on the mucosa of stomach and intestines are due to amorphous or crystalline oxalate of lime, and this is found also in the renal tubules. Post-mortem perforation may occur. The vessels contain black thrombi.

Carbolic acid causes white or gray eschars in the mouth which may be brownish from blood. In the stomach the eschars are not deep. The skin where affected is smooth and glistening. The odor is characteristic in the stomach, intestine, and other organs. Hemoglobinuria occurs, and pigment infarcts are found in the kidneys, and hyaline casts in the urine. The acid is excreted as alkaline salts of phenol-ether-sulphuric and phenol-glycuronic acids. The urine decomposes in the air and turns blackish.

The corrosive alkalies include potassium and sodium hydrate (lye), ordinary potash mixed with the hydrate, and sometimes ammonia. No fatal case is known due to sodium carbonate.

The alkalies produce firm eschars of white or gray color, which may be colored brown by blood, but they are not so brittle as those due to acids, and are not so often followed by ulceration. When large quantities remain in the stomach until death and after, the eschars and the intact parts between swell, and the stomach appears very soft and semitransparent. The affected portions gradually become a greasy mass of a brown or black color. The stomach may be perforated, similar conditions may be found in the intestine, and adjacent viscera are cloudy at first and then transparent.

Ammonia irritates the respiratory organs and may cause edema of the glottis. Croupous exudation may be found in the air passages and on the esophagus; in other respects it causes lesions like other alkalies.

Mercury is usually taken in the form of the bichloride, and unless absorbed without leaving traces, as sometimes happens, it causes grayish-white or brownish eschars like those from carbolic acid. The intestine is not often corroded, but it frequently suffers a severe diphtheritic inflammation, either localized in the colon or throughout, resembling the lesions of dysentery. The necrosis then is not due to the primary corrosive action but to its effect during excretion, for the results follow any mode of administration. It then causes some direct effect, but also stasis and thrombosis of the vessels, and doubtless bacteria complete the diphtheritic process. In the kidneys there are cloudy swelling, necrosis of epithelia, and, very often, deposits of lime salts, especially in the convoluted canals. Similar calcification of dead renal cells to a less degree occurs from other causes also. Copper (sulphate) causes blue or green eschars, antimony (tartar emetic) produces pustules like those on the skin, zinc causes eschars, and nitrate of silver with the action of light makes black corrosions along the alimentary canal.

Among the poisons which produce general lesions as well as localized effects in the stomach are *phosphorus* and *arsenic*. **Phosphorus** causes moderate hyperemia and ecchymoses, seldom much hemorrhage, in the stomach, but like other organs it undergoes severe fatty degeneration, and has a cloudy, at times almost milky appearance (gastritis glandularis).

Icterus and ecchymosis on the skin and mucous membranes and also in the internal organs follow, as of the heart, lungs, uterus, and serous membranes. Cloudy swelling and fatty degeneration are, perhaps, the most important lesions, and these occur in the heart, liver, kidneys, and voluntary muscles. These effects are all most evident when death follows after the lapse of several days.

Arsenic (arsenious acid) makes more intense lesions of the stomach and intestine, and these are apt to be hemorrhagic. As after phosphorus, secondary peptic ulcers may be observed. In the bloody mucus on the stomach wall and in the ulcers, white crystalline (octahedral) deposits of arsenic occur, and on ignition the odor of garlic is evolved. The gastric effects of the poison are very variable. The general effects are the same as for phosphorus, and after the poison has wholly disappeared from the alimentary tract it may be

recovered chemically from the liver, kidneys, and bones. The cadaver resists putrefaction, and long after burial may be found mummified. In many cases the anatomical condition after poisoning by arsenic resembles that of Asiatic cholera, with rice-water discharge, marked enteritis, and swelling of the follicles, so that during an epidemic the two are liable to be confused.

Hydrocyanic acid may cause gastric congestion with ecchymoses or no discoverable lesions. In general there is an odor of bitter almonds, the post-mortem lividity is markedly bright red, and the blood is not much coagulated, but the reports as to its color vary. The liver, spleen, kidneys, and brain, are congested, and the lungs both congested and edematous. Cyanide of potassium has a corrosive action on the stomach but the eschars may swell and not be found in the cadaver. The mucosa is usually swollen, bright red, covered with much mucus which may be bloody, and the contents strongly alkaline and soapy to the touch. The corrosion is due to the presence of potassium carbonate and ammonia.

Nitrobenzol (artificial oil of bitter almonds) produces effects similar to those from hydrocyanic acid.

Tumors. The commonest and practically the most important neoplasm of the stomach is carcinoma, which among males is the most frequent cancer of internal organs, though less frequent in females than uterine cancer. The percentage of gastric cancers varies in different regions. In Switzerland it occurs as 51.8 per cent. of all carcinomas in males; 31.9 per cent. in women—1.85 per cent. of deaths from all causes.

Like all tumors of this kind, gastric carcinoma is a disease of adult life. In many cases it starts in a healed ulcer rotundum, but the frequency of this origin is variously estimated.

As in other organs, it has favorite sites, as in the pylorus, on the smaller curvature, less often at the cardiac end, still more rarely in other parts of the organ. In most cases it occurs as a primary tumor in the stomach, invading the organ only seldom from neighboring tissues or by metastasis. In form it may be a nodular or prominent tumor growing chiefly into the lumen of the stomach or toward the serosa, or it may be diffuse and infiltrate the wall as a general thickening which may be arranged as a girdle. When a distinct tumor forms it may have smaller projections from its surface and assume a fungous appearance. At times there are many small, almost miliary nodules scattered through the organ, and such secondary masses in the mucosa

and submucosa often surround the principal tumor. If the surface of the tumor is not ulcerated it may be smooth, lobulated, or papillary. Contraction may produce dimpling of its surface.

A very common change in the new-growth is ulceration. If the vascular supply does not keep pace with the development of the tumor a partial fatty or other degeneration may lead to the death of relatively large portions of it, and the softened parts being digested out by the gastric juice, crater-like defects may result, with thick and prominent edges, which increase with the extension of the neoplasm. In many cases the tumor shows a tendency to scar formation, but it does not heal, for while it cicatrizes at one point it grows larger at another.

Gastric carcinoma begins in the epithelium of the glands or their ducts. With the exception of those tumors which spread from the esophagus, the tumor is cylindrical celled. The various kinds observed are as follows:

1. **Adenocarcinoma**, with many transitions to carcinoma simplex. It begins especially in the cylindrical epithelium of the glands at the pylorus. It may be large and fungous, or at times papillary, nodular, or ring-shaped, and from the surface a white juice may be scraped. In the gross it commonly appears as a large ulcer with high nodular edges. Metastasis may be limited to nodes in the vicinity or be lacking. Cystic dilatation of the glandular tubules and collection of mucoserous fluid result in the form known as carcinoma cysticum.

2. **Medullary carcinoma** is chiefly made up of epithelial cells, the proportion of stroma being slight. It may be a soft and polypoid nodule or a large ulcer with thick walls. Its consistence is soft, and much juice may be scraped from the section. All parts of the stomach may be the site of the tumor, but most often the pylorus, smaller curvature, and posterior wall. In growth and extension, both in the stomach and to neighboring organs, it is rapid; metastasis occurs early and the tumor ulcerates rapidly.

3. **Scirrhus carcinoma** occurs in about 75 per cent. of the cases. It is made up chiefly of fibrous tissue. The common form is extensive, firm, flat infiltration of the wall, less often nodules, converting the stomach into a rigid tube. At the pylorus extreme stenosis may occur. The tumor is hard, yellowish, or white, and dry on section. The stroma may contract and lessen the stomach's capacity, and the distortion may be irregular or uniform. The tendency to ulceration is slight, and the course of the disease is slow, while metastasis and direct invasion of other parts are both delayed.

4. **Gelatinous carcinoma**, colloid cancer, is an unusual form in the stomach, characterized by the tendency to mucoid degeneration of its epithelium as well as secretion of mucus in its glands. In the gross the tumor is gelatinous, semi-transparent, soft, and usually brownish. It occurs as a nodule or as an ulcer, and shows less tendency to invade other organs than the medullary form.

Many forms of gastric carcinoma contain large capillaries, and thus have a telangiectatic appearance.

Carcinoma of the stomach is complicated with many other lesions. Chronic proliferation of fibrous tissue about the tumor may lead to adhesions between the stomach and other organs. Hence the stomach and other parts are liable to be pulled out of place. As the tumor grows it extends by way of these adhesions to the vicinity, and especially to the pancreas, the liver, the esophagus, or some part of the intestine. The omentum and the peritoneum are similarly involved. Extension to the vertebral column, the pleura, pericardium, lung, and mediastinum, is not uncommon.

Continued ulceration leads to the formation of abnormal diverticula from the stomach, and also to fistulous communication with the intestine, esophagus, or gall-bladder, with abnormal flow of bile into the stomach and other parts. Less often the perforation opens into a cavity of the body, as the peritoneum, the pleura, the pericardium, or externally; against this result the fibrous adhesions protect for a time.

Metastasis occurs in part through the lymphatics. The nodes about the tumor and later the retroperitoneal and thoracic nodes are apt to be involved. Carcinomatous thrombi in the gastric veins and direct invasion of the portal lead to secondary embolism in the liver, pleura, lung, spleen, pancreas, and omentum.

The ulceration may lead to abscesses and putrefactive and gangrenous changes in adjacent organs, or sometimes in the stomach itself, but here the action of the gastric juice prevents such results for a time. Sacculated peritoneal abscess, subphrenic abscess, pyopneumothorax, and pyopericardium, may be the consequences of such ulceration. Embolic abscesses in the organs and general pyemia are later consequences.

Among further complication of gastric cancer may be mentioned hemorrhage in large quantities, which is rather unusual, or many small bleedings in and about the ulcer, which may give it a melanotic appearance.

Chronic catarrhal gastritis is a regular sequel of the lesion, and is most marked immediately about the tumor. Functional disorders are added and increase the gastritis. Pyloric stenosis may result in great dilatation of the stomach, and ulceration about the pylorus may lead to early insufficiency. Change in the position of the stomach is common if adhesions do not form, and functional disturbances follow this; the pylorus may reach the cavity of the pelvis and become adherent there.

Carcinoma at the cardiac end produces stenosis and dilatation of the esophagus and diverticula. Later on the stomach may atrophy and become very small.

Secondary gastric cancer is rather infrequent. Flat-celled epithelioma of the esophagus may extend to the stomach, and primary foci in the pancreas and liver may extend to it also. Metastases from other organs are rare.

Other tumors found in the stomach are mucous polyps in the course of chronic catarrh, fibroma and myoma in the walls, adenoma with transitions to carcinoma, and rarely sarcoma and endothelioma.

Changes in the Lumen and Location of the Stomach. Gastric dilatation results from stenosis of the pylorus after carcinoma or benign fibrous hyperplasia, and is called mechanical gastrectasia. Functionally hypertrophy of the muscular coats is apt to follow, and the same condition is found with congenital stenosis. In other cases there is well-marked atrophy of the gastric tissues, as with some carcinomas, the non-involved portion hanging as a thin-walled sac. Chronic gastritis is common with dilatation, partly because of slow digestion and consequent overfilling of the organ, partly because of irritation from decomposing material and consequent inflammation. Organisms of fermentation and putrefaction occur in the contents of the organ. These conditions are not uncommon in chronic alcoholism. Some of the inflammation may be due to stasis.

Dilatation of the stomach which does not depend upon mechanical conditions is termed dynamic ectasia, and is illustrated by the atony which occurs with nervous diseases.

Dilatation may affect only the greater curvature, which may reach the pelvic brim, or the entire organ may dilate.

Gastric stenosis is most common at the orifices, from scars and other sources of contraction. Decrease in the size of the organ may be due to hour-glass contraction from scars, to which a twisting about its main axis may be added, or to diffuse carcinoma (*atrophicans*) or general induration (cirrhosis) in its walls. Stenosis of the cardiac

opening and general inanition are other cases in which the organ is small.

The position of the stomach may be lower than normal, from enter-optosis, simple falling of the part, or dilatation, or traction of adhesions, and various internal hernias may contain a part of it.

Infectious Granulomata. Tuberculosis of the stomach is rare and causes ulcers like those in the intestine, or with general infection, miliary nodules throughout the organ. Invasion from the serosa may cause gastric tuberculosis.

Syphilis is extremely uncommon. It may produce gummata which take origin in the submucosa.

The Contents of the Stomach. In the newborn the esophagus and the rectum may be tied and the entire tract allowed to lie in water. If the child has not breathed the canal does not contain air and will sink. After the child has breathed, air is swallowed and the organs will float, and a positive result may be taken as proof that the child was born alive.

In the adult the stomach contains much gas with general tympanites. Blood is found with all ulcerations, but the vessel may not be discovered unless large. Parenchymatous bleeding may occur with inflammations, following portal stasis, as in hepatic cirrhosis, with severe icterus and some other diseases. With carcinoma, especially, the admixture of altered blood gives to the stomach contents the peculiar appearance of coffee-grounds. With occlusion of the intestine the stomach may contain feces. Bile is frequently found in the stomach.

Among parasites, *ascaris* and, with very recent infection, *trichinae* may occur in the stomach. Thrush, yeasts, and other vegetable forms are common with dilatation, and *sarcina ventriculi* is very frequently found.

C. THE INTESTINE.

In the small intestine are the *valvulae conniventes*, decreasing in number from above downward, and the villi, which may be seen after washing the surface. The entire intestine is covered with cylindrical epithelium, and in this there are many beaker cells. Brunner's glands are found in the duodenum, the crypts of Lieberkühn throughout. Two forms of lymphoid tissue occur, the solitary and the agminated, or Peyer's plaques, the former strewn over the inner surface as small

nodules, the latter arranged in groups, especially in the lower part of the ileum, with the long axis parallel with that of the intestine.

The colon presents three external bands running longitudinally, and three ridges internally corresponding, and the semilunar folds, disposed across the lumen, divide the length of the colon into a series of communicating sections. Solitary follicles and crypts of Lieberkühn occur.

Malformation. Among the congenital anomalies are *atresia ani*, relatively common, with which the rectum may be lacking, so that the lower part of the colon ends blindly; *atresia recti*, the rectum being a solid fibrous band and the anus marked by a shallow depression. These conditions are due to imperfect developments of the allantois and related structures. In the fifth week there is a cloaca in which the gut, ureters, and sexual ducts open. The anal opening is formed later by invagination from the skin. In the third to fourth month the perineal body forms and the rectum is separated from the anterior portion, now termed the urogenital sinus. When the rectum is not formed, or the external invagination does not occur, atresia of the parts results; when communication remains with the sinus the forms result which are called atresia ani, vesicalis, urethralis, and vaginalis.

Enterocystoma is a congenital condition due to the snaring off of a portion of the intestine, as Meckel's diverticulum, or a part of the intestine of a twin. Its wall has the structure of the intestine.

Disorders of Circulation. These are of great importance in connection with changes in the lumen and the position of the intestine, and will be treated with them.

In the dead body the intestine is usually anemic, even when there has been inflammatory hyperemia during life. Hyperemia is also connected with stasis of all kinds.

Infarcts occur by embolic or thrombotic closure of a large mesenteric branch, aneurisms, and atheroma in the arteries and venous thrombi. The gut is then strongly hyperemic and edematous for a certain section, and blood is found within it. Stoppage of the circulation is soon followed by gangrene and inflammation. Small purulent infarcts may come from abscesses and embolism.

Ecchymoses accompany all forms of congestion, ulcers, superficial burns, and hemorrhagic conditions. Older foci of hemorrhage are usually pigmented in retiform lines about the mouths of glands and in the follicles.

Regressive Changes. Amyloid degeneration is usually secondary, and converts the mucous surface into a dull, glistening, pale, and firm

surface. The amyloid matter lies chiefly in the vessels of the mucosa and the muscularis mucosæ. Ulceration of the affected part is common.

Pigmentation may occur in the intestinal muscles as fine brownish granules like those in the heart (brown atrophy); it is seen with cachexia and senile marasmus. A reddish-brown discoloration occurs in the intestine of chronic drunkards.

Catarrhal Inflammation. Catarrhal enteritis may be acute or chronic, confined to a small portion of the tract, or general. The causes are the same as for gastritis, and sometimes both diseases occur together as gastro-enteritis. Long retention of intestinal contents within the canal and putrefactive changes, the use of food which has been spoiled, chemical substances, as arsenic, and organic poisons (ptomains) from decaying meat, sausage, cheese, and fish, produce severe attacks of acute enteritis. Among the bacteria which assist in the effect the bacillus coli communis especially deserves mention. It constantly occurs in the intestine and without apparent injury to the host, but when there is a wound of the mucosa it may penetrate the wall and set up severe suppurative inflammation. Diffuse catarrhal lesions are the earliest stage of specific enteritis, as diphtheritic or dysenteric inflammation, and accompany it.

The intestinal mucosa is edematous, red, and swollen, and the character of the increased secretion is seromucous or mucopurulent. Microscopically there is infiltration of the mucosa, excessive formation of beaker cells, and desquamation of both superficial and glandular epithelium. The follicles are prominent and take part in the inflammation, the solitary appearing as roundish projections, the agminate as flat swellings of grayish-red color. In Peyer's patches when the lymphoid elements are the more swollen the surface is granular, when the stroma is specially involved they are smooth and reticular. Superficial erosions of the mucosa are common, and may ulcerate.

The intestinal contents vary with the seat of the inflammation. With colitis the feces are usually thin, mixed with mucus, at times in little masses, and of a green color because of imperfect decomposition of the bile pigments. With the microscope fragments of undigested food are found. Not every diarrheal stool is produced by inflammation of the intestine, for simple increase of peristalsis may be followed by thin dejections. In duodenitis a frequent symptom is icterus, due to partial or complete occlusion of the common bile duct by edema and thickened mucus.

Enteritis follicularis is an inflammation specially involving the follicles, causing infiltration and continued swelling of these structures and hyperemia about them. Escape of blood in them may leave pigmented spots. The swollen follicles may burst and leave small ulcers.

Chronic Catarrhal Enteritis. The etiology of the disease is not different from that given for the acute forms, which it may also follow. It occurs with other diseases and remains after a specific inflammation has disappeared, and many cases are to be referred to chronic stasis with diseases of the liver and the heart. When confined to special parts of the intestine it may be due to foreign bodies or stagnation of feces, and, in the rectum, to stasis with hemorrhoids. With all catarrhal inflammations due to stasis, the part is of a peculiar dark-red color with many small hemorrhages, and in time extensive pigmentation may occur and erosions of the surface. Hyperplasia of the tissue between the glands may be observed, with increase of the glands themselves and cystic dilatations. Such hyperplastic changes are apt to be localized in parts of the colon. Chronic catarrhal inflammation is more apt to end in atrophy of the glands, and the fibrous stroma may be increased. The membrane is then pale, thin, tough and smooth. The villi of the small intestine may be small and pigmented so that the satiny look of the part is lost. In children the atrophy of the muscular tissues may be so complete that the intestinal wall is thin as paper, and transparent, and the follicles are lost or to be recognized only as spots of pigment.

The intestinal contents in chronic catarrh may be thin or so thick as to be hard, and blood may be mixed with them. Certain cases, especially in women, are characterized by the production of large quantities of mucus, which collects in masses or makes casts of the bowel (enteritis membranacea or colitis mucinosa). In other cases there is a retention of mucus in the glands (enteritis cystica).

A special form of chronic inflammation is that occurring in young children, caused by unsuitable artificial food and retention of ingesta. On opening the intestine it is found filled with a thick greenish matter, of disgusting odor, composed of undigested food and mucus, whereas the normal stool of the unweaned child is thinner, of an ochre-yellow color, and faint sour smell. The entire tract may be thinned or only the ileum, and the mesenteric nodes are usually enlarged. The general condition is characterized by dry, pale, and harsh skin, a peculiar old expression, atrophy of all organs, and especially of the muscles, complete loss of fat, and an abdomen either sunken in or puffed up by gas

in the intestine. Catarrhal pneumonia and atelectasis are common, and slight degrees of these lesions are apt to be fatal with the enteritis.

Cholera Asiatica. This disease is endemic in India, elsewhere occasionally epidemic, and is essentially a severe acute enteritis with the excretion of enormous amounts of diarrheal fluid.

The post-mortem appearances vary with the stage of the disease. In the early stage (the algid) the intestine is filled with a whitish fluid, the "rice water" discharge, which is odorless and made up of serum and flocculi of mucus, and in it comma bacilli are to be found in countless numbers. The mucosa of the ileum is very red and swollen, at first covered with a layer of thick mucus. Few or many small foci of hemorrhage may be present, and the follicles are swollen and gray or reddish. Rupture of these may make small ulcers. The colon is less affected or not involved. Microscopically there are the lesions of severe catarrh and profuse infiltration.

After the algid stage a period of general infection may follow, called the cholera typhoid, and if death occurs now the intestinal condition may be negative. The hyperemia has disappeared, the mucosa is pale or marked by blood pigment, its contents are bile-stained and not so fluid, and in the colon masses of firm feces may be found. In many cases a diphtheritic sloughing of the mucosa may take place, with large, deep ulcers and hemorrhages.

In general the blood is thickened, because of the great loss of fluid by the intestine, dark and imperfectly clotted, the right ventricle and large veins filled with blood, and the left empty. The serous membranes feel slimy and are covered by a thick albuminous sticky layer. The spleen is not enlarged. The kidneys present cloudy swelling, fatty degeneration, or acute nephritis, and, in some cases of cholera-typhoid, nephritis and uremia are the chief factors. The liver is in parenchymatous degeneration. The cadaver is cyanotic, the muscles, especially of the calf, are rigid, rigor mortis occurs early and persists, and the abdomen may be much retracted.

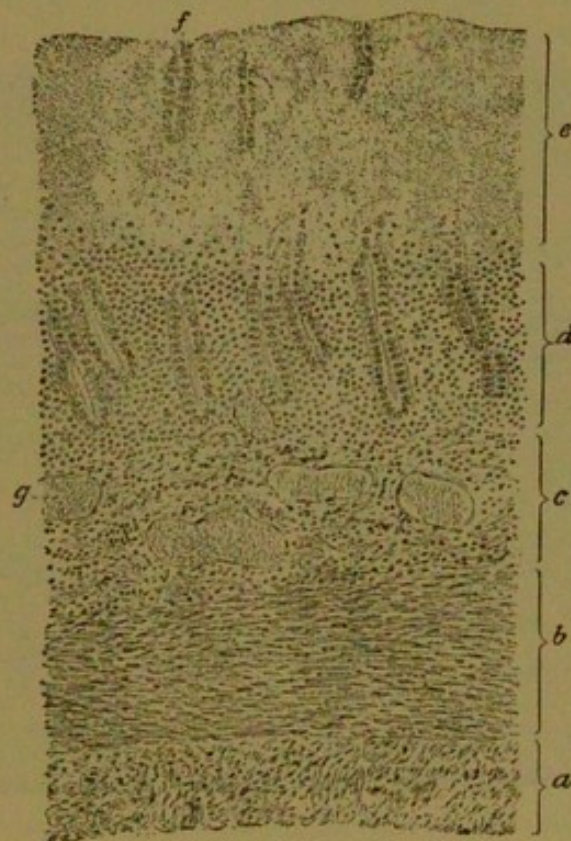
The accepted cause of cholera is the comma bacillus. In doubtful cases its discovery may be the only satisfactory proof of the diagnosis, for the severer cases of cholera nostras are so nearly identical in symptoms with the Asiatic type that only the presence of the vibrio can determine the disease. Both microscopic examination of the stools and cultivation must be employed. The cause of cholera nostras is unknown.

Diphtheritic Enteritis. **Dysentery** is a disease which is endemic in the tropics, but in this climate occurs in epidemics or sporadically.

In tropical cases the presence of amebæ is characteristic, and it is questionable whether our dysentery of hot weather is identical with the tropical type. [Both are probably referable to a specific bacillus—*Bac. of Shiga*.—Ed.]

The disease begins acutely, as a rule, but may be chronic from the first. In mild cases there is a catarrhal inflammation of the intestine of pronounced severity, and in the severe cases deep ulcerations and necrosis follow in the intestinal wall. Inflammatory hyperemia is the first step in all forms, with small submucous hemorrhages and marked

FIG. 230.



Diphtheritic enteritis after bichloride poisoning. *e*, Upper necrotic portions of mucosa. *f*, Glands: all nuclei here are lost. *d*, Portion not yet necrotic, infiltrated with cells. *c*, Submucosa. *g*, Vessels. *a*, *b*, Muscular tissue. $\times 40$.

edema of the mucosa. The other layers of the wall may be similarly changed. A profuse exudation of mucous or mucofibrinous material occurs on the surface, and in severe cases the epithelium becomes necrotic in many places, forming with the fibrinous exudate peculiar white layers here and there. At first these lie on the folds in the mucous membrane, and may be easily stripped up. Together with these conditions the necrosis leads to rapidly spreading ulcers which pour out a purulent secretion. In the worst cases, so-called diphthe-

ritic dysentery, large sections of the mucous membrane may die and form whitish sloughs which are specially marked on the summits of prominent parts. The feces and bile stain these sloughs grayish yellow or brown, and now it is not possible to strip them from the tissue beneath, for their under layers are the dead mucous membrane itself, a true diphtheritic lesion.

The upper layers of the mucosa have lost their nuclei, are invaded by leucocytes, and form a granular mass in which the glandular structure may still be recognized. The deeper layers in the case presented (Fig. 230) are not yet necrotic, but much inflamed, and the layers

FIG. 231.



Acute dysentery. Natural size. Sloughs on the summits of the mucous folds.

are infiltrated and hyperemic. Microscopically all the layers are thick and swollen, of a dark color, and the serosa may be covered by fibrin and pus.

The sloughing tissues break down into a granular mass or are cast off in large pieces, after which extensive ulcers remain. The ulcers follow the longitudinal and transverse folds and, by fusing, make map-like lines on the surface. Their edges are uneven and sharply distinguished by their bloody exudate from the surrounding swollen mucosa, which gives them a characteristic appearance. In time the furrows between the ridges are involved, and the entire membrane may

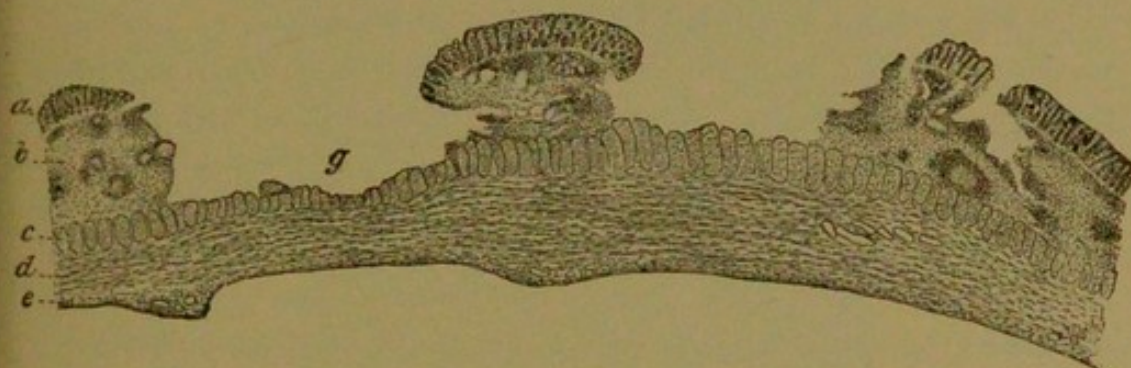
be destroyed. The worst cases are accompanied by suppurative and gangrenous changes.

The contents of the intestine may be thin, mucoserous, or purulent, light-colored or mixed with blood; bits of fibrin and sloughs or large portions of dead mucosa may be mixed with it. The mucus may form sago-like masses. In gangrenous cases the contents are dark and of unpleasant odor.

Deep ulceration may lead to tearing and perforation of the wall, with consequent peritonitis or periproctitis and fistulæ. As a rule, in chronic cases the wall becomes so thick as to prevent this complication.

Healing is complete when the ulcers have been superficial and only small pigmented scars remain. With deeper destruction the scars may at last produce stenosis, and in all cases the membrane is apt to be somewhat atrophic.

FIG. 232.



Dysenteric ulcers, with polypoid swelling of remaining portions. *a.* Projecting remnant with retained epithelium. *b.* Submucosa swollen and infiltrated. *g.* Ulcer which lays bare the muscularis. *c.* *d.* Longitudinal muscle. *e.* Serous coat. $\times 12$.

In chronic dysentery hyperplasia of the mucous membrane produces great thickening of that layer, the glands atrophy, the surface may present polypoid projections, and at last an atrophic stage leads to a smooth and firm intestinal wall which is without elasticity. The muscular coat may be much hypertrophied.

Dysentery is usually confined to the colon, and the rectum is the part which suffers most, while in the small intestine slight catarrh or some little production of fibrin may be noticed.

Follicular dysentery is usually chronic, occurs in the colon, and affects its lymphoid follicles. These swell and suppurate, and when the pus breaks a small "lenticular" ulcer is left, with thin, sharp, undermined edges which become elevated when water is poured upon them. While the pus is evacuated through a small opening on the summit of the follicle the ulcerative process extends in various direc-

tions through the submucosa, and a large section of the mucosa is thus undermined; hence these ulcers are called sinuous. When two or more of these lesions fuse the mucosa forms loose bridges over them and can be lifted up. The process is seldom diphtheritic.

Chronic thickening of the tissues and atrophy follow, and more or less scar formation and retraction are common.

Other pseudomembranous forms of enteritis occur as follows:

1. After mechanical irritations, as from fecal stasis and concretions. The pressure of the contained material causes necrosis of the intestinal wall, and fecal ulcers result, due to the action of the bacteria present or diphtheritic exudates, and the ulcers may perforate the wall. These are called *stercoral* ulcers and diphtheria. The lesion is commonest where the large intestine bends, as the hepatic and splenic flexures and the appendix. In strangulation of the intestine it is the fecal stasis, as much as anything, which leads to necrosis of the wall.

2. Many chemical substances, especially the corrosive poisons, may produce the lesion, both when they pass through the intestine and when they are excreted by it. Arsenic and mercury are the best examples of this kind, but ptomains from decayed meat have the same effect.

3. Catarrhal inflammation of various degrees in many cases appears to prepare the ground for a diphtheritic process, as occurs in typhoid fever at times, intestinal tuberculosis, cholera, and general septic conditions, puerperal fever, scarlet fever, and pharyngeal diphtheria.

4. A form of the lesion is associated with retention of urine, and is known as *uremic* dysentery or enteritis. It is supposed that carbonate of ammonia is formed in the intestine from excreted urea, and acts locally as an irritant, but probably the bacteria of the parts cause a diphtheritic exacerbation of the catarrhal inflammation always present with intestinal stasis.

5. Wound infection and various operative procedures about the abdomen may be followed by diphtheritic enteritis, and its localization is then irregular.

Beside the follicular inflammation mentioned, suppurative lesions in the intestine may follow septic embolism as in mycotic endocarditis, the small abscess corresponding to a twig of an artery and surrounded by a hyperemic margin. On examination by transmitted light the occluded vessel may be visible. Small mycotic aneurisms may also occur in such conditions. Primary phlegmonous enteritis is very rare.

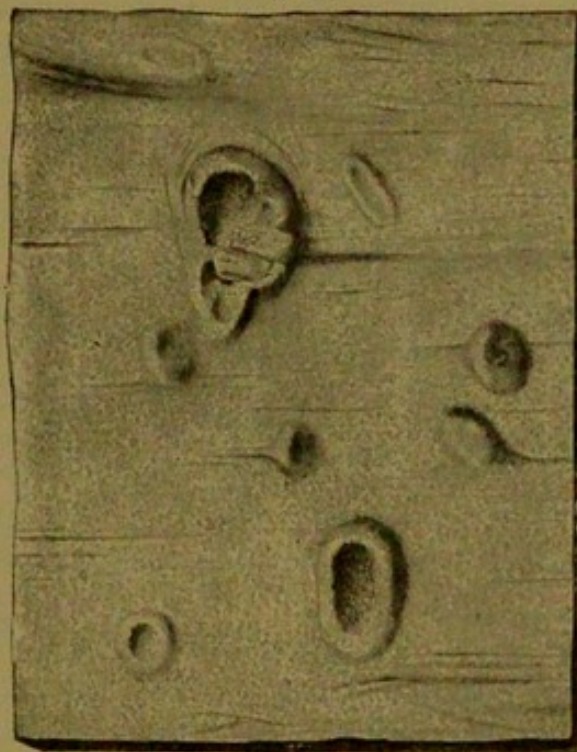
Specific Inflammations and Infectious Granulomata. Typhoid Fever. This is an infectious disease which is due to a specific bacillus,

causing lesions specially localized in the intestine, but including other organs also, and marked general symptoms, especially of the nervous system.

After an incubation which usually lasts two to three weeks the intestinal disease begins as a catarrhal inflammation with particular involvement of the lymphoid structures, both solitary and agminate. The clinical course of the disease is divided into stages, and to these the pathological infiltration, sloughing, ulceration, and cleansing of the ulcer correspond.

In the first stage, which usually lasts to the beginning of the second week, there is well-marked redness of the mucosa in the lower ileum

FIG. 233.



Intestinal lesion of typhoid fever. Natural size. Third week. Above, the large ulcer contains necrotic sloughs, the smaller ones are clean.

and upper colon, with edema and often small hemorrhages. The follicles swell to the size of a pea, and the Peyer's patches become as much as 3 to 4 mm. higher than the rest of the mucosa. On the valve of Bauhin there may be such an agminate follicle arranged transversely, the rest have their long axis in the direction of the intestine. The surface of the patches is swollen, smooth, or marked by lines of special prominence, on which there may be a fibrinous exudate. The lymphoid areas then become paler, gray, or reddish yellow, and at last white and soft. The infiltration may involve the adjacent mucosa and

the wall to the muscular layer. It depends upon cellular infiltration, inflammatory hyperplasia of the lymphoid cells, and proliferation of endothelial cells. Under the microscope the follicle, at first sharply defined, fades into the surrounding tissue.

The chief site of the lesion is about the lower end of the ileum, near the ileocecal valve, and the vermiform appendix, which is full of lymphoid tissue, is often involved. Proceeding in either direction from this point the intensity of the inflammation becomes less. Rarely the solitary follicles of the colon are the chief point of attack.

In mild cases the infiltration resolves and the disease ends. In severe cases necrosis follows the stage of infiltration. The central part of the follicle dies and becomes a mass of structureless granular matter, perhaps holding leucocytes, called the typhoid slough. The mucosa alone or the whole thickness of the wall to the serosa may be

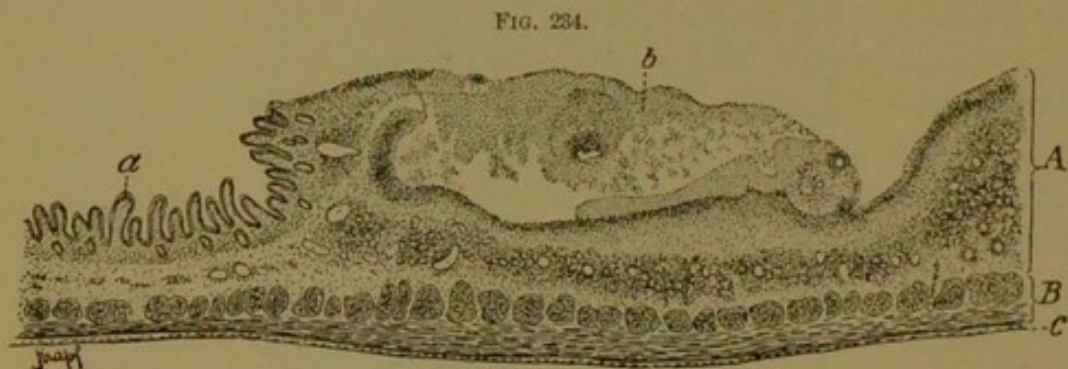


FIG. 234.
Intestine in the second week of typhoid. A. Mucosa and submucosa. B. Muscularis. C. Serosa. a. Villi. b. Slough with broad infiltrated edges on each side. $\times 12$.

involved in the necrotic mass. This is white and lies in the middle of the plaque, with thickened margins about it, but in time it becomes yellow or brown from bile pigment. This stage lasts to the end of the second week.

Demarcation and removal of the slough occur in the third stage, by gradual loosening about its edges and breaking down or expulsion as a mass. In the cadaver it may be lifted off its base. The resulting ulcer is round in the solitary follicle, oval in the agminate, its long axis parallel with the intestine, with a broad, high wall, which is undermined, and, as a rule, the ulcer does not extend beyond the lymphoid area. The base of the ulcer may be necrotic in fine points or larger masses, and is formed by any layer of the wall in proportion to the depth of the necrosis. At times the ulcer spreads secondarily. The removal of the slough occurs in the third to the beginning of the

fourth week. When the ulcer is clean the edges lose their infiltration, the undermined margin helps to lessen the size of the defect, and granulation from the bottom leads to formation of a flat scar. Pigment may remain at the place for a long time. Cicatricial contraction does not occur. The healing process is completed in about two to three weeks, and the follicles may be partially regenerated.

Intestinal hemorrhage and perforation may complicate the disease, the former due to arrosion of a vessel in the ulcer at the end of the second or the first of the third week. It may be fatal. Perforation may be due to destruction of the serous surface or tears in the weakened part from active peristalsis. It occurs most often in the third or fourth week and causes general peritonitis.

To estimate the duration of the disease from the gross appearances we must remember that the lesions do not develop all at one time, but those near the ileocecal valve are usually the oldest, and in passing upward newer foci are found. The lower portion may contain cleansed ulcers and the upper forming sloughs. When there is a relapse, usually during the fourth week when the ulcers are being cleansed, new foci may be found by the side of those nearly healed.

Infection probably occurs through the alimentary tract, where the bacilli are to be found in numbers, and from here both bacilli and their products enter the blood and lymph.

The mesenteric nodes are early involved by an infiltration like that in the follicles, so that they reach a large size and often show necrotic changes. Suppuration and rupture may cause fatal peritonitis. From these nodes the infectious material reaches the blood and causes marked swelling of the spleen. This depends upon both intense congestion and hyperplasia of the pulp, and may last to the fourth week and be of large size. From circulatory disorders and the action of bacteria the spleen may contain infarcts, and if these suppurate and break they cause peritonitis. The marrow of the bones suffers a similar hyperplasia, and osteomyelitis may follow.

The respiratory organs take such an active part in the disease that they have been regarded as the port of entry of the infection. The larynx may present catarrhal inflammation, superficial erosions, or deeper ulceration. The bronchi are the seat of catarrhal inflammation, and the lungs of lobular or lobar pneumonia, but it is not clear how much of the complicating lesion is due to the organism of typhoid and how much to some other form.

Typhoid bacilli have been recovered from the spleen, the blood of

the rose spots, the liver, gall-bladder, serous exudates, the blood, and the central nervous system.

In the skin there is a rosy eruption in the beginning of the second week. Pleurisy and peritonitis may be due to metastatic infection. The joints and periosteum may be inflamed, parenchymatous degeneration in the heart, liver, and kidneys, and waxy changes in the muscles, especially the recti abdominis, are associated lesions. Other suppurative inflammations may follow the disease, affecting the middle ear, the parotid, the brain, etc.

Tuberculosis of the intestine resembles the same lesion in other mucous membranes. It begins with the formation of scattered nodules

FIG. 235.



Tuberculous intestinal ulcer. Natural size.

surrounded by cellular infiltration, and both in time caseate, open through the epithelium and make ulcers which spread in all directions as new portions become caseous and break down. A recent tuberculous ulcer has thick edges which are beset with nodules or in places caseous. The lesion is usually disposed with its long axis transverse to that of the intestine, and many of the girdling ulcers may blend and make large map-like defects in which little islands of unchanged mucosa may persist.

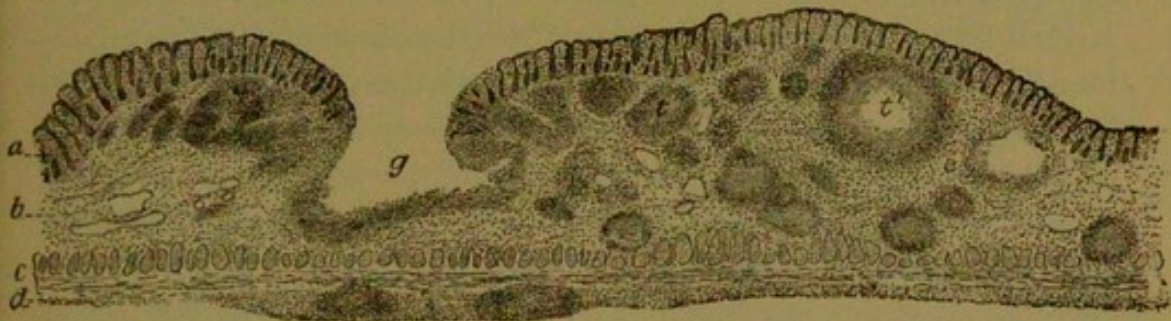
Older ulcers have a very irregular form, partly due to the uneven extension of the process and partly to merging of ulcer with ulcer. The edges are sinuous, more or less undermined and overhanging, and along them there are foci of new and caseous tubercles, as also on the

floor of the ulcer. The ulcer seldom cleanses itself and still more seldom heals.

When a tuberculous ulcer extends into the wall for any distance the serous surface is usually beset with small tubercles, and about them there is a productive inflammation which covers the tubercles with fibrous tissue. Adhesions form between loops of intestine, the organs of the abdomen, and the wall. Perforation may thus open one loop of intestine into another (*fistula bimucosa*). Tuberculous peritonitis may develop in several forms. Perforation into the peritoneum is rare, and when it occurs the opening is already surrounded by fibrous tissue and the resulting inflammation is localized.

The ileum is the common seat of the lesion, especially about the ileocecal valve, but it may occur elsewhere in the tract. The ulcers may be few or multiple, and the follicles are usually swollen.

FIG. 235.



Tuberculous intestinal ulcer. *a*. Mucosa. *b*. Submucosa. *c*. Muscularis. *g*. Vessel. *t*. Tubercle in the mucous membrane. *t'*. Focus which is caseous in the centre. $\times 12$.

In most cases the disease arises from swallowing tuberculous sputa, and it regularly complicates pulmonary tuberculosis with cavities. But it may occur primarily in the intestine, and some of these cases are to be ascribed to the use of milk contaminated with bacilli. Tuberculous lesions in the mesenteric nodes are a frequent complication.

Syphilis is not common in the alimentary canal. It may occur as gummata and ulcers. (See Rectum, p. 382.)

Special Diseases of Certain Sections of the Intestine.

(*a*) **Duodenum.** The chief lesions are *ulcus rotundum*, like that of the stomach, and catarrhal inflammation with icterus. Carcinoma may develop from the papilla.

(*b*) **Cecum and Appendix.** Inflammation is caused by fecal accumulations, and may be of any kind. The appendix is surrounded by peritoneum and has a mesentery of its own. The cecum has a

serous covering only on its anterior, lateral, and lower aspects, and behind it there is much areolar tissue. The entire cecum may have no serous investment. When inflammatory perforation occurs in this region the pus may invade the retroperitoneal tissue (*paratyphlitis*), or ascend to the kidney, or descend into the pelvis or the inguinal and crural rings. It may also perforate into the peritoneum and set up general or localized inflammation.

Perityphlitis is a circumscribed peritonitis over the cecum and appendix, localized in favorable cases or ending with perforation and general inflammation. Healing of these lesions is accompanied by fibrous adhesions between the cecum and any neighboring parts. Sacculated collections of pus may thus be formed and persist for a long time, or gradually seek an outlet through some dependent part. Dropsy of the appendix is caused by the accumulation of thin mucus in it, and obliteration may be the result of senile involution or fibrous hyperplasia.

(c) **Rectum.** The most important disorder of circulation is varicose dilatation of the hemorrhoidal veins, making piles or *hemorrhoids*. Thrombosis is common and also inflammation of the rectal mucosa.

Catarrhal and gonorrheal inflammation of the rectum are observed. Ulcerative and diphtheritic lesions occur here, and from such processes the tissue about the rectum may be inflamed (*periproctitis*) and cause abscesses or chronic induration. Abscesses opening into the rectum alone leave fistulæ which are called incomplete internal; opening on the skin they are incomplete external; joining both mucous and outer surfaces they are fistulæ ani completæ. The bladder, vagina, and other organs may be perforated also.

A form of *proctitis* which occurs only in women converts the entire mucosa just above the anus into tough, fibrous tissue, with hypertrophy of the muscular tissue and stenosis of the part. It may be due to gonorrhea, syphilis, fecal stasis, and other causes.

Tumors. Fibroma, myoma, and lipoma are fairly common in the intestinal walls. Polyps result from chronic inflammations. Adenoma may be polypoid or flat, the latter leading to great thickening of the wall, and showing transition to carcinoma.

The malignant intestinal tumors are especially carcinomas, which most often invade the rectum, sigmoid flexure, cecum, and appendix, and papilla of the duodenum. The disease is more frequent in men than in women. In form the tumors resemble those of the stomach, and rapid ulceration is common. The usual point of origin is the

glands of Lieberkühn. Adenocarcinoma and carcinoma simplex, carcinoma gelatinosum, and epithelioma at the anus are the commonest varieties.

The results are stenosis of the lumen, which may appear to improve when ulceration sets in, fecal impaction, dilatation of the upper part, adhesions, and hemorrhages. Diffuse carcinoma and suppurative inflammation of the peritoneum may occur. Purulent periproctitis complicates rectal cancer. Sarcoma of the intestine is rare.

Changes in Location and Lumen. **Hernia** is the passage of an organ or part of an organ from a body cavity to the outside or into another cavity, and the protruding organ is covered by the serous lining of the original cavity. The dislocation occurs in all the serous cavities of the body, but is usually understood as applied to the abdomen and its contents. The routes by which the hernia leaves the cavity are usually the course of vessels, nerves, and ducts or weak places which give way to pressure. The disposition may be congenital or acquired. Common sites for hernias are the inguinal ring (passage of the seminal cord or round ligament), crural ring (vessels), the umbilicus, the inguinal canal, parts which have been distended and weakened as by pregnancy, and scars of wounds (laparotomy, etc.).

The peritoneum investing the hernia is called the sac. Where the serous covering is lacking the protrusion is called a prolapse. The narrow portion of the sac which occupies the place of exit is the neck. The hernial sac may be congenital, as in hernia at the umbilicus and into the scrotum. The other coverings of the hernia consist of various layers of muscle, fascia, and skin.

The contents of the sac may be a portion of the intestine or of omentum. Hernia of intestine alone is called *enterocele*, containing omentum it is called *epiplocele*, and with both *enteroepiplocele*. In the larger herniæ the stomach, liver, spleen, uterus, and other organs may be found, or practically the entire abdominal contents (*eversion*). A special form of hernia (Littre's) contains only a part of the intestinal wall. The sac may be occupied by a serous fluid in addition, at times in large amount.

In time the sac forms adhesions with its surroundings as the result of inflammation, but the contents may still be reducible. When the adhesions occur between the sac and its contents they can no longer be returned to the abdomen, and the hernia is said to be *irreducible*. The tendency of any hernia is to become larger as the neck of the sac widens and more of the organ descends into it, and hence, from simple

volume or from narrowing at the neck, the tumor cannot be reduced, and with a wide neck the contents of the sac return as soon as replaced. With the largest hernias the abdominal cavity may become smaller and incapable of containing all the protruded viscera. When the neck of the sac is tight the intestine suffers from compression, which lessens its lumen, and the disordered circulation in the part leads to inflammatory adhesions. The portion of intestine above the hernia may dilate and its muscular fibres hypertrophy. Fecal stasis may result from the compression.

Among the most serious consequences of hernia is *strangulation* of the contents of the sac. When a small portion of the intestine has been pressed through a narrow opening it is emptied by the pressure of passing through. Constriction of the neck by adhesions, scars in the fascia and peritoneum, false membranes, and other causes reduce its lumen and cause elastic strangulation. When the contents of the intestine aid in producing strangulation it is called fecal strangulation. This usually follows some sudden increase of the intra-abdominal pressure, as on lifting heavy weights, coughing, expulsion of feces, which produce a marked distention of the protruded portion of the intestine. Passage of a portion of the omentum into the sac by the side of the previous intestinal hernia may have the same effect. The immediate result is distention and complete occlusion of both parts of the loop, the descending and the ascending.

The veins are compressed, while the thicker arteries for a time are not so much affected. This causes passive congestion and stasis, serous transudation, increase of fluid in the sac, and its discoloration by red cells. Bacteria pass through the wall of the gut and multiply in the fluid. In time the hernia becomes necrotic and inflamed. The serum is more purulent, fibrinopurulent deposit occurs on the walls of the sac, the wall of the intestine softens with suppurative and necrotic changes, and may tear or rupture. The process may pass to the general peritoneum and set up purulent peritonitis. After perforation of the intestine a fecal abscess is formed, and when this opens through the integument a fecal fistula, or *anus preternaturalis*, results. In rare cases the arteries also suffer compression, but the result does not differ.

The Single Forms of Herniæ.

1. **Inguinal.** (a) *External.* The hernia passes into the internal abdominal ring to the outer side of the epigastric artery, and emerges

PLATE XXIII.

FIG. 237.

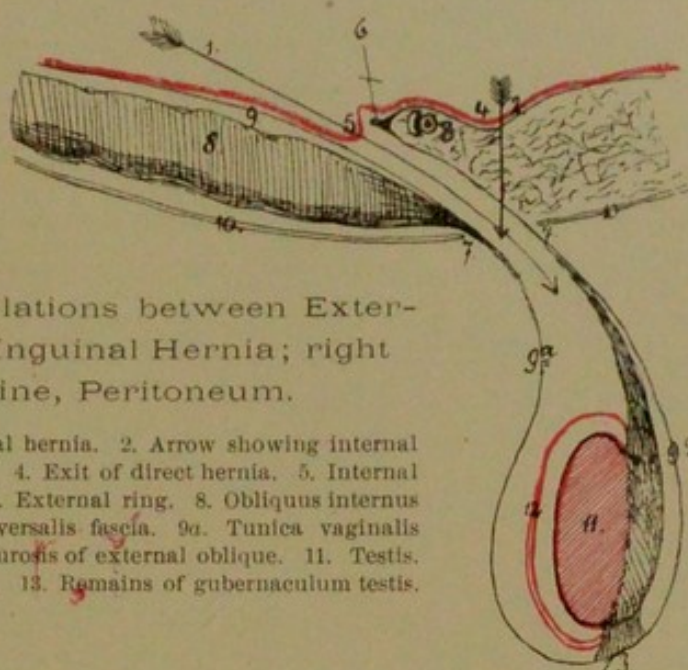
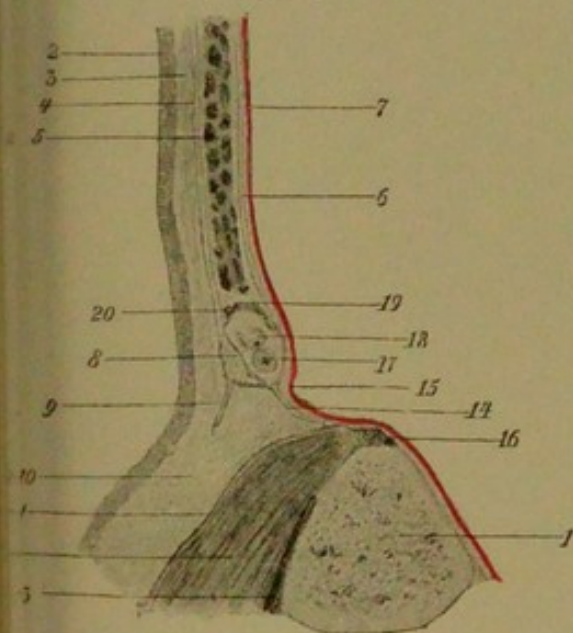


Diagram of the Relations between External and Internal Inguinal Hernia; right side. Red line, Peritoneum.

1. Arrow showing external hernia. 2. Arrow showing internal hernia. 3. Epigastric vessels. 4. Exit of direct hernia. 5. Internal ring. 6. Its upper margin. 7. External ring. 8. Obliquus internus and transversalis. 9. Transversalis fascia. 9a. Tunica vaginalis of cord and testis. 10. Aponeurosis of external oblique. 11. Testis. 12. Tunica vaginalis propria. 13. Remains of gubernaculum testis. (After GRASER).

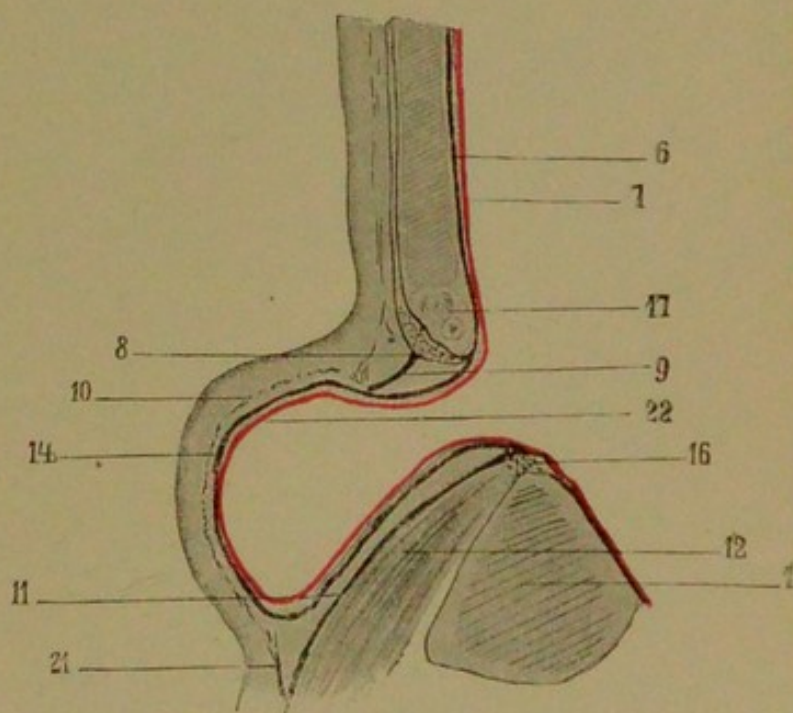
FIG. 239.



Diagrammatic Sagittal section through the Inguinal Canal.

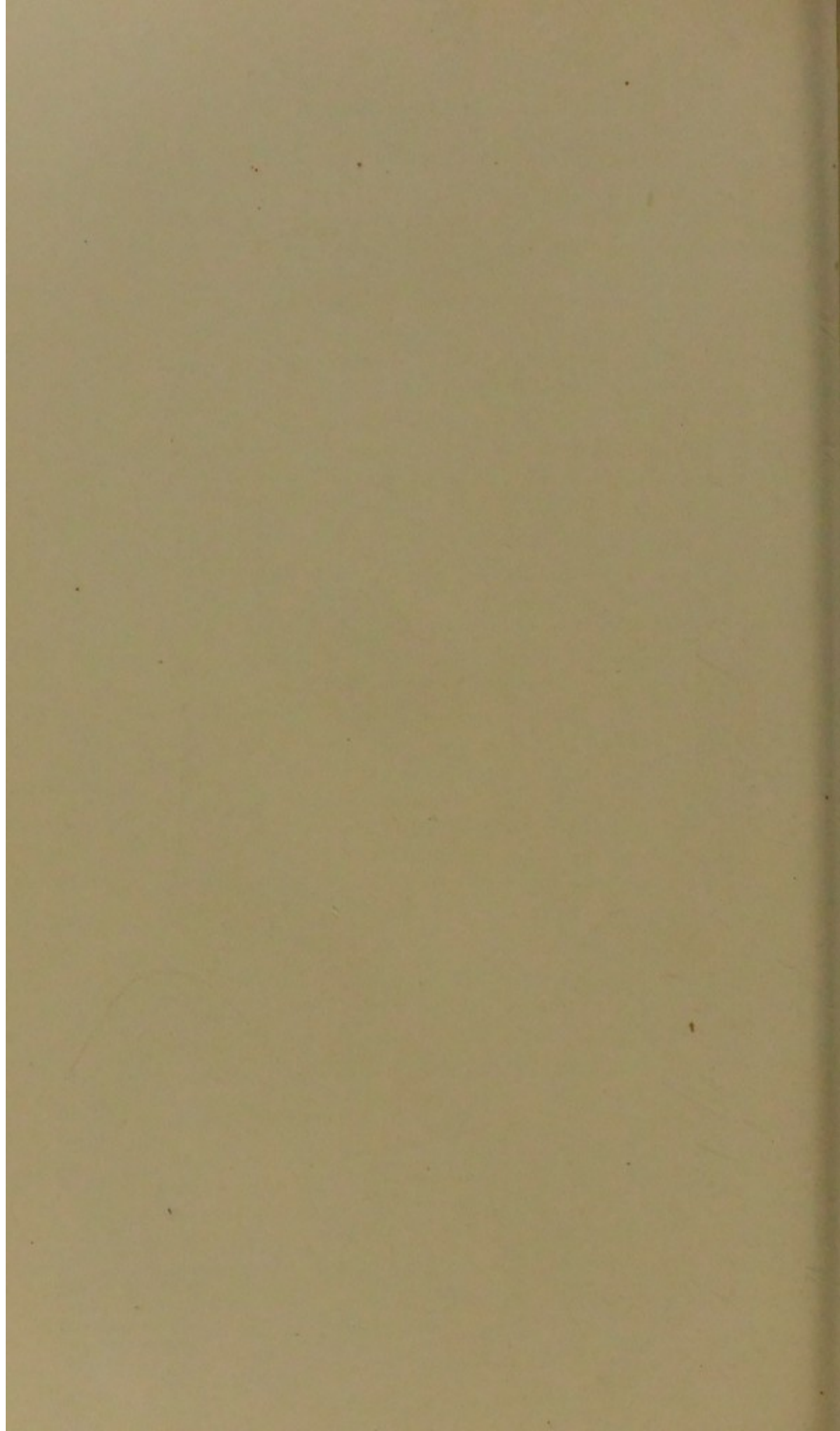
1. Horizontal ramus of pubes. 2. Skin. 3. Subcutaneous fat and fascia. 4. Aponeurosis of external oblique. 5. Internal oblique and transversalis united. 6. Transversalis fascia. 7. Peritoneum. 8. Poupart's ligament. 9. Upper portion of falciiform process. 10. Fossa ovalis. 11. Pectineal fascia. 12. Pectineus. 13. Bursa. 14. Septum crurale. 15. Site of femoral hernia, exit. 16. Cooper's ligament. 17. Vas deferens. 18. Internal spermatic vessels. 19. Cremaster. 20. Internal spermatic nerve. (After GRASER).

FIG. 240.



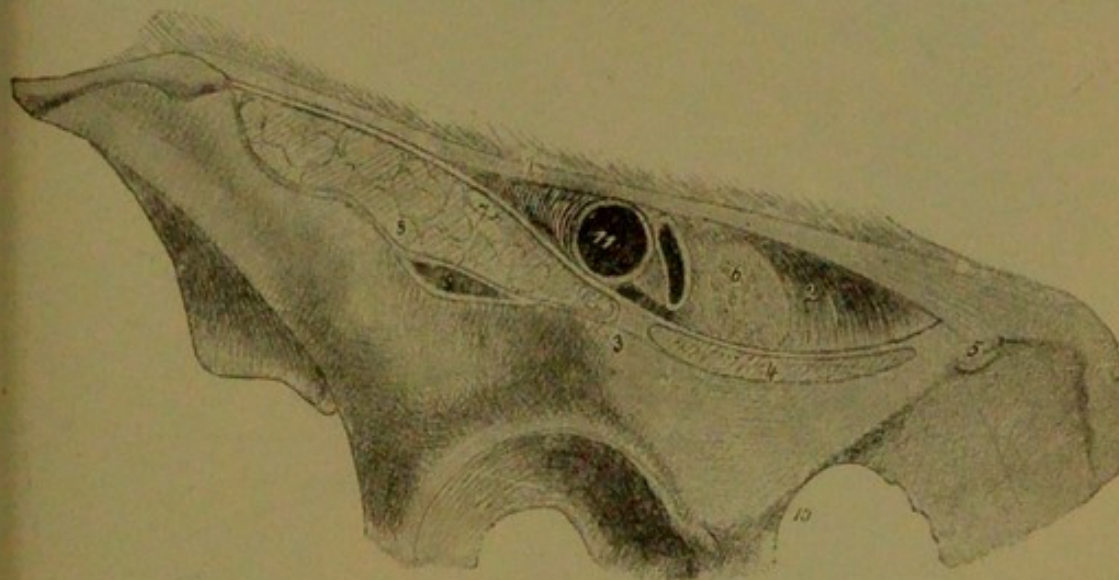
Diagrammatic section through a Femoral Hernia.

1. Horizontal ramus of pubes. 6 and 14. Transversalis fascia. 7 and 22. Peritoneum. 8. Poupart's ligament. 9 and 21. Parts of falciiform process. 10. Lamina cribrosa. 11. Pectineal fascia. 12. Pectineus. 16. Cooper's ligament. 17. Spermatic cord. 20. Internal spermatic nerve. (After GRASER).



from the external ring. This is possible when the processus vaginalis from the peritoneum, which is carried down with the descent of the testis, is not obliterated at the ring, though it may be shut off just above the testis, or when, although obliterated, it is pushed ahead of the protruding intestine. If it does not emerge from the outer ring an interstitial hernia results, if it reaches the bottom of the scrotum it is called scrotal hernia, and if it remains between these limits alongside of the spermatic cord it forms a funicular hernia. In the female it passes out with the round ligament and enters the labium majus, making hernia inguinalis labialis. As the direction of the inguinal canal is from without inward, and from above downward, hernia passing through it is called also oblique or indirect.

FIG. 238.



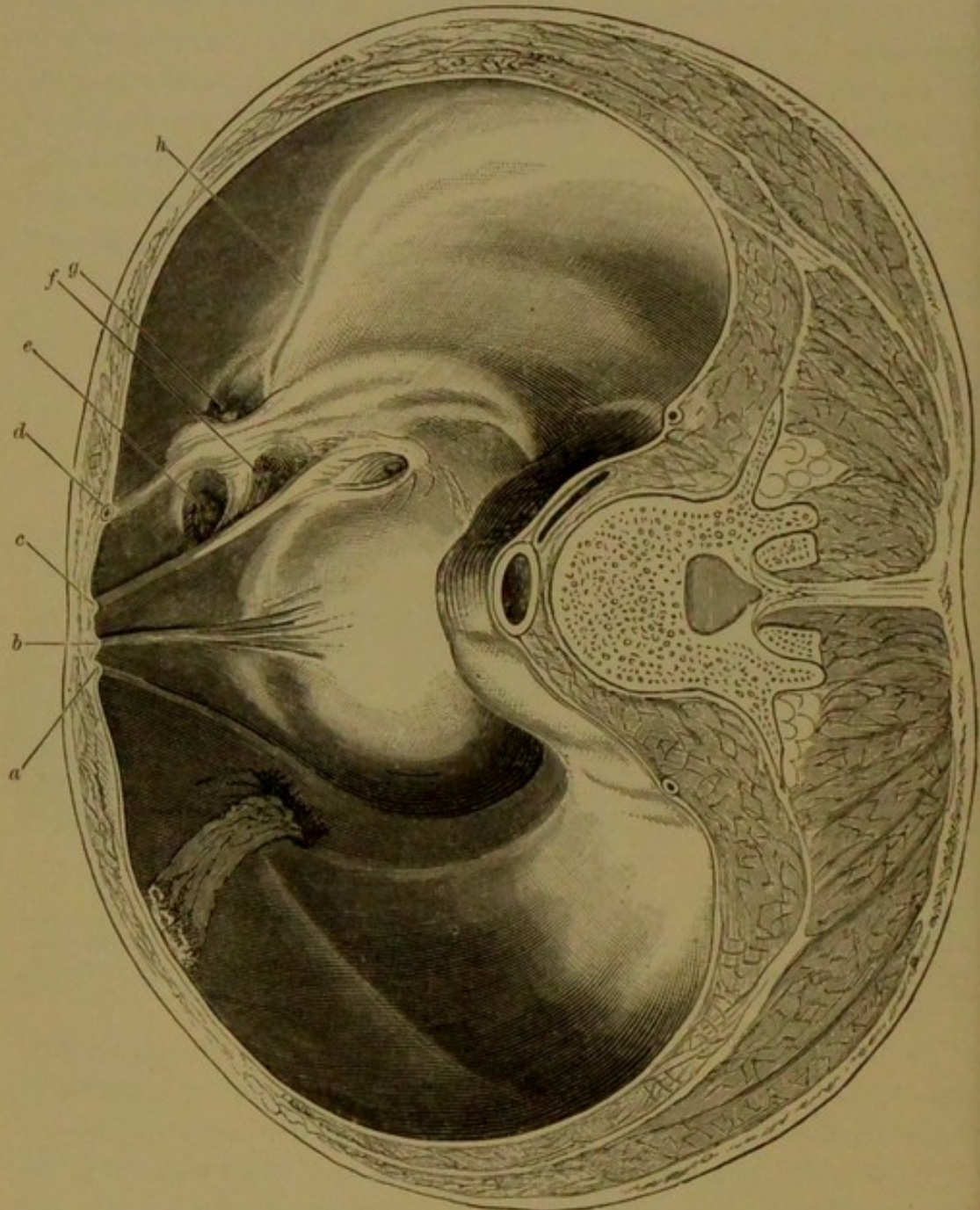
Section at the crural ring. 1. Poupart's ligament. 2. Gimbernath's ligament. 3. Iliopectineal eminence. 4. Pectineus muscle. 5. Pubic spine. 6. Crural ring with septum. 7. Anterior crural nerve. 8. Psoas iliacus muscle. 9. Mucous bursa. 10. Obturator foramen. 11. Femoral vessels.

(b) *Internal.* A triangular area bounded below by Poupart's ligament, above by the internal oblique and transversalis, and internally by the rectus, is the point of exit for this form of hernia. In front of it is the external ring, and protrusion through this weak area out of the ring is called direct inguinal hernia. It seldom reaches the scrotum, and usually has the epigastric artery and the spermatic cord to its outer side.

2. **Crural hernia** passes out through the crural ring, below Poupart's ligament, external to the pubic spine and Gimbernath's ligament, internal to the femoral vessels. It may be strangulated by the falci-form process of the fascia lata, or at the crural ring. It does not

occur congenitally, but usually late in life, and more often in women than in men. The contents are usually small intestine, at times also omentum. Littre's hernia is common.

FIG. 241.

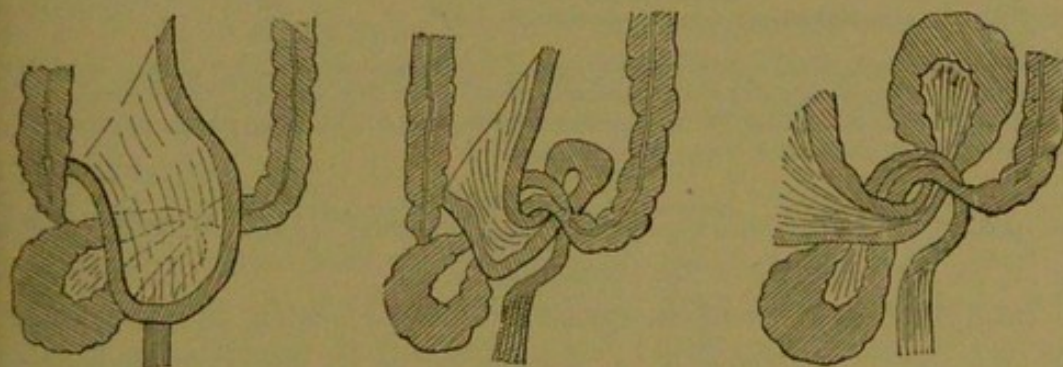


Transverse section through the abdomen, the intestine removed. Above, the bladder and the anterior abdominal wall. Above the vertebra lie the aorta and vena cava, to either side the ureters. On the right side between the bladder and the lateral ligament is a pocket through which obturator hernia passes. Just above it is the exit of femoral hernia which is separated from the two inguinal hernias by Poupart's ligament. Between the external and the internal inguinal lie the epigastric vessels. To the left a femoral hernia with contained omentum. *a*. Lateral vesical ligament. *b*. Median vesical ligament. *c*. Lateral vesical ligament. *d*. Epigastric artery. *e*. Internal inguinal hernia. *f*. Femoral hernia. *g*. External inguinal hernia. *h*. Poupart's ligament. (After HILDEBRAND.)

3. **Umbilical.** The congenital form is strictly not a hernia. It is due to imperfect closure in the anterior middle line and varies in size from a small protrusion with a portion of the intestine inside it to large defects and eventration of all the viscera, covered only by the amnion. Such children are born dead or succumb to gangrene of the hernia or its contents. In children an acquired form consists of a protrusion through the upper portion of the umbilical ring, where the tissues are not reinforced by remnants of the urachus and umbilical vessels. In adults the umbilicus may be stretched open by pregnancy and permit the hernia. Occasional rare forms of hernia are the ventral, lumbar, obturator, sciatic, perineal, and diaphragmatic, which are understood from their names and the explanation of Fig. 241.

Retroperitoneal Hernia—Internal Strangulation. In various parts of the abdomen there are recesses in the peritoneum which may

FIG. 242.



Formation of a knot between the rectal flexure and a coil of small intestine. (After KÖNIG.)

receive portions of the organs and by them become dilated. As examples may be cited the duodeno-jejunal fossa, at the transition from duodenum to jejunum, the ileocecal fossa, and the foramen of Winslow. More often the strangulation is caused by fibrous adhesions between the coils of intestine and the omentum. In all these cases constriction and twisting of the included part may produce results similar to those described with strangulation.

Volvulus is usually caused by twisting of a portion of the intestine about its mesenteric axis so that the two limbs of the loop cross each other. Torsion thus narrows the lumen and compresses the veins of the part and causes strangulation. It is most easily produced where the mesentery is long and its attachment narrow, as at the sigmoid flexure. Here the disposition may be congenital, the result of peritonitis and adhesions, or simply of overfilling and consequent sinking of the upper portion.

Sudden rapid increase in the vigor of peristalsis after contusion of the abdomen, enteritis, and colic may have a similar effect. Solution of the torsion may be prevented by increase of contents, the pressure of other organs, and constriction of fibrous bands. Gangrene and perforation follow after varying periods.

The formation of knots in the intestine is at times possible when the mesentery is very long and the abdomen relatively large and its walls lax, as after many pregnancies and in old age. The knot occurs most commonly between the sigmoid flexure and a coil of small intestine. It may follow axis-torsion, and the manner of its gradual

FIG. 243.

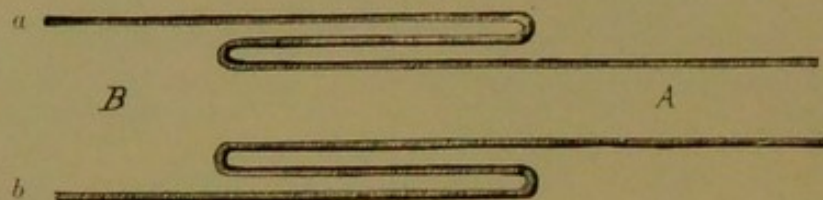


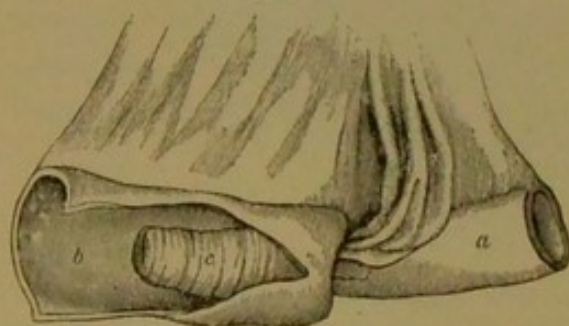
Diagram of invagination. A. Upper part received into B, the lower. a. Serous coat. b. Mucous coat shaded. At the middle of the invagination the mucosa is three times encountered; in the middle and outer layer directed inward as normally, in the remaining portion reversed; the middle and inner layers have the serosa in contact.

formation appears from the appended diagrams. Its results are strangulation and necrosis of the intestine.

Invagination—Intussusception. When a portion of the intestine is, at it were, swallowed by a portion below it, the intestinal wall at the side of the invagination is twice folded on all aspects, so that a section reveals three layers on each side, as appears from the diagram. These layers are the continuous wall of the received part, the reversed

wall of the same, and the wall of the receiving part. Invagination usually results from irregular peristalsis and occurs in the direction of the flow of its contents. When a section of the intestine is paretic and strong peristalsis occurs in the upper section, the latter is pushed by its own motion into the lower, and this goes on until a section

FIG. 244.



Invagination of the small intestine. a. Upper portion of intestine. b. Lower portion, intussusciens. c. Intussusceptum. (After ALBERT.)

still farther along, which is not paretic and dilated, is reached. The mesentery of the receiving part is also invaginated, and hence liable

to suffer compression and also to swell and plug the part. Gangrene of the received part may follow, and with adhesion of the serous layers this may result in healing, with the passage of the dead section per anum. In other cases complete gangrene and rupture may take place.

Invagination is most common in the small intestine, or this may pass into the colon, and the process may go on until the ileum presents at the anus. In children, after diarrheal diseases, invagination may occur just before death, but the displacement is wholly free from inflammatory reaction and easily reduced.

Prolapse. Protrusion of a viscus from a serous cavity without pushing the serous membrane before it is called prolapse. It may follow incised wounds or tears or fissures of the peritoneum, and diaphragmatic hernia is usually of this kind. Organs which are free from serous investment may also leave the cavity, as the bladder, vagina, and uterus. A special form occurs at the anus, and of this two varieties are recognized:

1. Prolapse of the rectum (total), from relaxed sphincter and perirectal tissues, as after chronic catarrhal inflammation. It usually follows straining at defecation, and is most common in atrophic children and in the aged.

2. Prolapse of the mucosa of the rectum (*prolapsus ani*) may accompany hemorrhoids or polypi which exert traction on the part. Invaginations which present at the anus may be distinguished by the fact that the lumen of the rectum may be entered alongside the presenting intestine.

Preternatural Anus—Fecal Fistula. These are different degrees of abnormal communication of the intestine with the body surface, the former allowing the discharge of nearly the whole contents of the intestine and the latter of only the fluid portion, usually. Strangulation of the intestine and inflammatory adhesions to the abdominal wall are the commonest preceding conditions, and not only the limit of the knuckle of gut may become adherent, but its adjacent sides may fuse, so that when the convex portion dies the fused sides make a prominent spur internally, which directs the fecal matter through the unnatural opening. Hence the lower portion is apt to narrow so much that it will no longer take any material coming from the upper, and all fecal matter is voided externally.

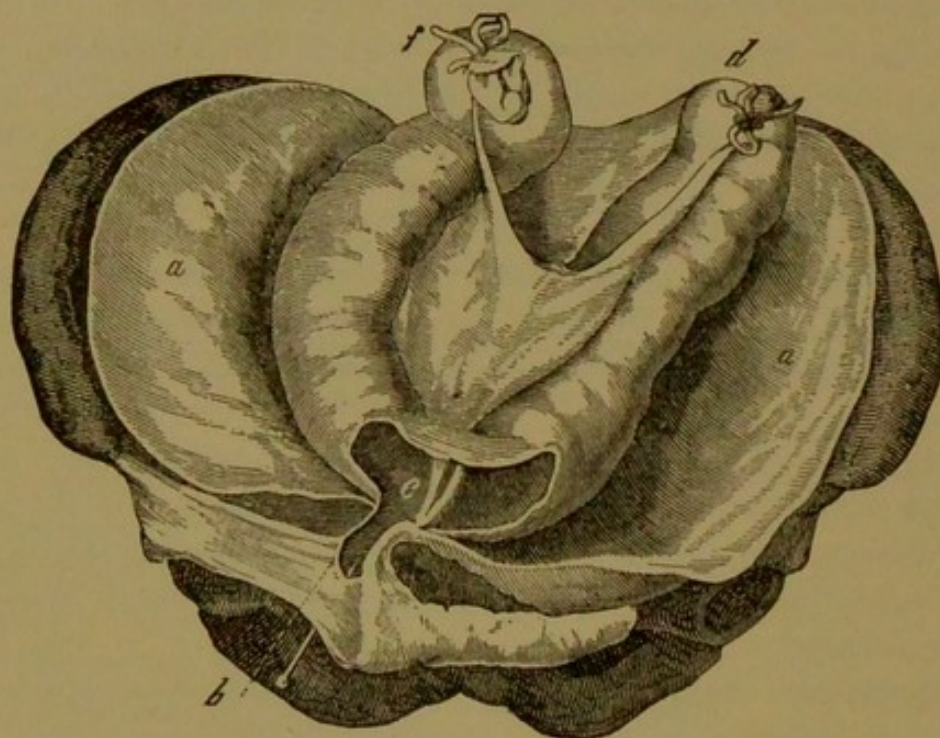
Very commonly the skin about the opening is pierced by one or more fecal fistulae. In many cases the adhesion between the skin and the intestine is such that the abnormal passage is wholly lined by

epithelium. Other cases of abnormal anal openings occur with tuberculous processes in the intestine. Fistula may heal by itself, the larger openings never do.

When the abnormal opening lies in the upper portion of the small intestine the general condition suffers, but in the lower part of the ileum or in the colon it may cause only inconvenience.

Artificially such an opening may be established after hernia, when the protruded part is too necrotic to return to the abdomen, or in carcinoma with stenosis.

FIG. 245.



Anus preternaturalis. *a.* Parietal peritoneum. *b.* Anal opening. *c.* Intestinal spur or septum. *f.* Afferent limb. *d.* Efferent limb of intestine. (After SCARPA, in König's Lehrbuch d. Chir.)

Changes in the Intestinal Lumen. Stenosis may occur with constriction or pressure from without or from lesions within the intestine. Strictures are usually the result of diphtheritic or, in the rectum, of syphilitic lesions. Invagination, torsion, and other causes have already been treated. Severe inflammation and starvation may lead to general decrease in the size of the intestinal lumen. Dilatation with hypertrophy of the muscular layers occurs above constrictions, and this is both a result and a cause of paralysis of the wall in acute dilatation. Large accumulations of gas and feces may also dilate the canal. Partial dilatation may occur in the sections of the colon, and false diverticula are found in the sigmoid and at the mesenteric attachment in the

small intestine by diastasis of muscle fibres and protrusion of the mucosa between them.

Rupture of the intestine may follow gangrenous and ulcerative processes, especially when the part is filled with feces. The serous coat ruptures first and places may be found where this alone is torn. Very small ruptures may not allow the feces to pass out, and healing is possible. Fecal peritonitis and abscess are the usual consequences.

Intestinal Contents. After every ingestion of food the small intestine contains more or less chyme, and in proportion to the advance to the colon this becomes more fecal, and gas is mixed with it. In the newborn meconium is found, composed of mucus, bile, epidermal cells, lanugo hairs, and meconium bodies, which consist of bile pigment. Crystals of hematoidin and cholesterin also are found.

Pathological contents have already been mentioned. A large accumulation of gas is known as meteorism or tympanites, and this both causes and follows paralysis of the muscular layers. Large admixture of blood gives a brownish-red or black color to the contents, and occurs in ulceration, stasis (cirrhosis), strangulation, hemophilia, icterus, and other diseases. Mucus is either fluid or in masses and false membranes.

Intestinal stones (*enteroliths*) are found in the appendix and the cecum. Some are made up of vegetable fibres felted together, with fecal matter and mineral salts and bile. Those in the appendix are usually hardened feces and mucus in alternating layers, or a foreign body, as a seed, on which such deposits have been made. Medicines, foreign bodies, gallstones, and pieces of necrotic mucous membrane are also occasionally found.

Parasites. The most important intestinal forms are the tapeworms, tenia and bothriocephalus, and ascaris lumbricoides, anchylostomum duodenale, trichocephalus dispar, oxyuris vermicularis, cercomonas, and trichina.

D. DISEASES OF THE LIVER.

Within the liver there is fibrous tissue between the lobules which is derived from the capsule of Glisson, accompanying the hepatic artery, the portal vein, and the bile-ducts. From the artery and the vein a system of capillaries enters the lobule, and, from the bile-ducts, capillary biliary vessels, and these do not communicate with the blood capillaries. Those from the vein enter the central vein of the acinus,

which occupies its axis, and empty into the sublobular veins, which then unite to form the hepatic vein. In the periphery of the acinus there is an anastomosis between the portal radicles and the capillaries from the hepatic artery. The site of the central vein is the central zone of the acinus, and the part between this and the periphery is the intermediate zone.

The division of the organ into lobules can be seen with the naked eye, and still better by a magnifying glass. Where no vessels run between acini their borders are not distinct.

The central portions are darker than the rest of the acinus, because in the cadaver the blood collects in the veins, and the periphery is lighter because of its contained fat. This contrast is especially distinct in passive congestion.

After death the action of the H_2S from the alimentary canal makes certain parts of the organ black. Decomposition is accompanied by the production of gas in the large veins, and certain bacteria may cause this condition during life.

Malformation—Dislocation.

Congenital Abnormalities of form are common in the liver. Sagittal grooves on the anterior and upper aspect may be the result of pressure from strong bands of diaphragmatic muscle, and also occur with irregular action of the diaphragm, as during long-continued dyspnea. External pressure leaves transverse grooves, and with dyspnea the impress of the ribs may be seen. In *situs inversus* the liver lies on the left side, and in congenital hernia it may be found in the sac. Abnormally long ligaments permit the organ to fall; this is called *hepar mobile* or wandering liver.

Disorders of Circulation.

Anemia of the liver is part of a general anemia, and occurs also with cloudy swelling and fatty infiltration.

Active hyperemia is physiological during digestion, pathological with inflammations. The importance of **passive congestion** depends upon impeded flow from the hepatic vein and its causes, and the organ presents characteristic gross appearances. It may follow compression of the vein by tumors, or pleural exudates, or be due to general conditions of slow circulation, as diseases of the lungs, the heart, and the kidneys. The liver is large, at least at first, and its capsule is tense. The cut surface is marked by numerous dark spots, either as points or

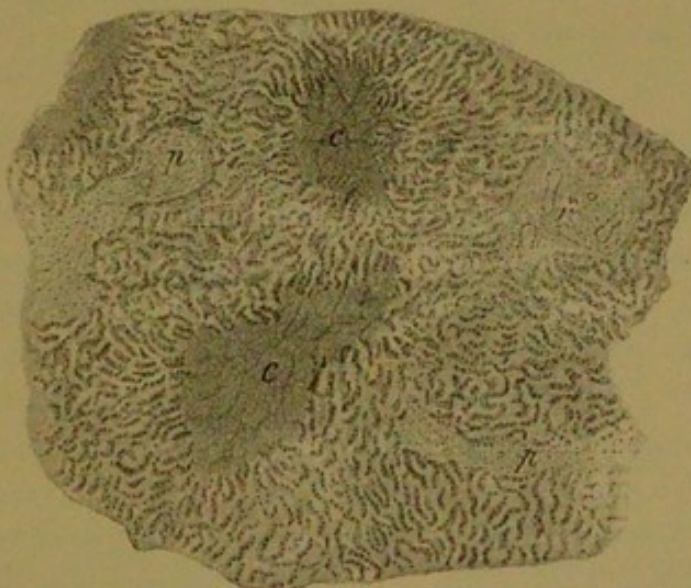
lines, which correspond to the central and sublobular veins, and the peripheries of the acini are lighter. This contrast has given rise to

FIG. 246.



Nutmeg liver magnified by a hand-glass. Dark spots and lines corresponding to the hepatic vein and its radicles. In the lighter areas the slender portal branches are visible.

FIG. 247.



Atrophic indurated nutmeg liver. *p, p.* Periportal fibrous tissue increased. *c, c.* Cells in central portions atrophic; capillaries dilated. $\times 50$.

the name "nutmeg liver." It is particularly marked when there is an unusual amount of fat in the peripheries (fatty nutmeg liver), and in time this always follows passive congestion.

A further result of stasis is atrophy of the hepatic cells about the central vein, because of the pressure from the dilated capillaries. The cells then contain pigment. The atrophic parts sink slightly below the surface and are dark (atrophic nutmeg liver, red or cyanotic atrophy).

In the course of time there is a fibrous increase in such congested livers, and the section is then marked by lines of new fibrous tissue between the acini. Severe degrees are characterized by an irregular distribution of the fibrous material, because islands of small-celled infiltration and special proliferation of this tissue are added to the general and uniform fibrosis (cardiac cirrhosis). Contraction of the new tissue may give a granular atrophic appearance to the organ.

Thrombosis of the portal vein seldom leads to infarction, for the anastomoses with the hepatic artery compensate for loss of part of the blood. The secretion of the bile is, however, lessened. Occlusion of small branches of the portal vein and the hepatic artery, in conditions of general weakness, may produce many small infarctions of irregular form throughout the liver. This occurs in puerperal eclampsia and with ulcerative endocarditis.

Hemorrhage may follow injuries, as sudden force applied to the abdominal wall without dividing it, because of a certain brittleness in the organ; the lesion is observed with some poisons also. Marked edema is unusual in the organ.

Degeneration and Parenchymatous Inflammation.

Cloudy swelling is observed in conditions which cause it in other organs. If distinct the liver is opaque, a cloudy brown in color, somewhat enlarged, yielding and friable, and anemic from compression of the capillaries.

Fatty Liver. Two forms are distinguished, the fatty infiltration and the fatty degeneration, the latter marked by granular degeneration in the hepatic tissue.

Fatty infiltration begins where the physiological deposit of fat occurs, in the peripheries of the acini. This gives them a light-yellow color, and the arrangement is reticular from the fusion of one with another. When the central parts are congested a nutmeg appearance results. When the amount of fat is large it occupies the inner zone of the acinus also. The organ is large, its borders are blunted, it is doughy and inelastic, and slight pressure dimples the surface. A dry knife

passed through it becomes coated with fat. The organ may also be jaundiced and of a green tinge. In the cells large and small drops of fat are observed, many of which push the nucleus aside or conceal it.

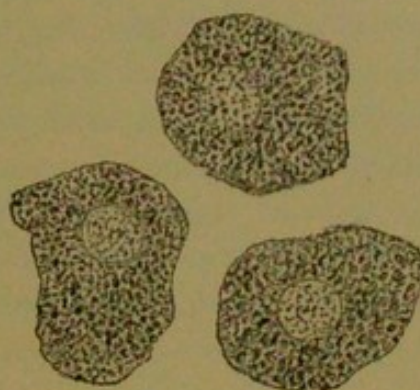
Fatty infiltration is part of a general obesity, and regularly occurs in alcoholic cases. In tuberculous patients it may result from imperfect oxidation.

The fat is partly ingested with food and partly derived from the subcutaneous tissue, especially in alimentary diseases which produce rapid disappearance of the integumentary fat.

Fatty degeneration of the liver occurs in pernicious anemia and in poisoning with arsenic, phosphorus, and some fungi.

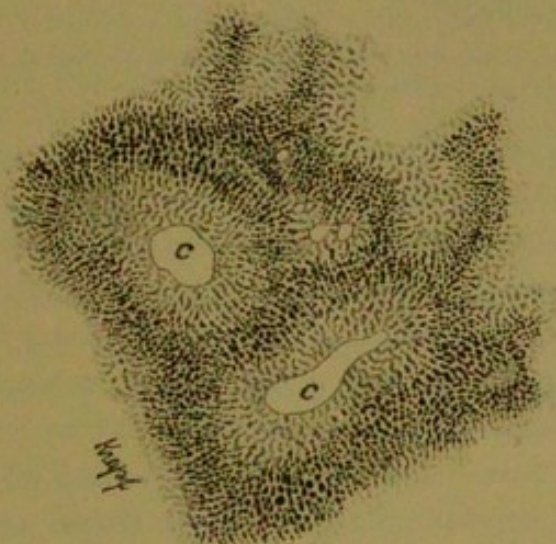
Acute yellow atrophy of the liver is an infectious disease, which is distinguished by its hepatic lesions, although it causes similar changes in other organs. As a rule, it ends fatally within a few days. In the

FIG. 248.



Liver cells in cloudy swelling.
× 350.

FIG. 249.

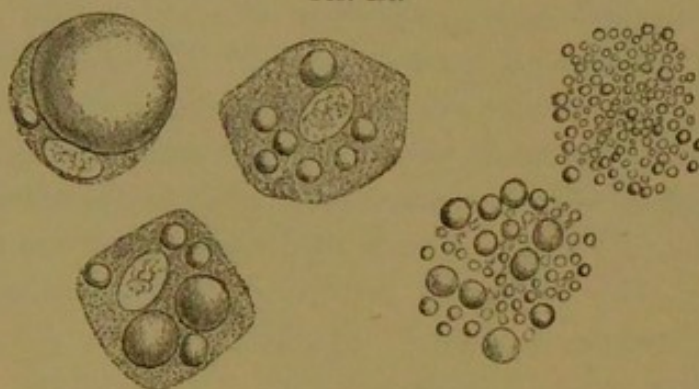


Fatty infiltration of the liver. The fat appears black from osmic acid: it lies in the peripheries of acini, which merge with each other. c. Central portion, free from fat. × 40.

liver there is a rapid parenchymatous degeneration which converts the cells into a detritus of fat and albuminous granules. Until the cells are destroyed or while their products remain in the organ, it has a diffuse yellow color, which combines with bile-staining to make a deep ochre

tint. The liver shrinks in volume, becomes very soft and yielding, and its edges are thin. The imperfectly filled capsule wrinkles. On the yellow surface there are red lines and bands which increase in extent and fuse, giving the surface a mottled red and yellow color. The red parts are slightly sunken and at first appear as red islands on a yellow base, but later they may exceed or replace the yellow. The red spots are due to the resorption of the softened material by the lymphatics, leaving only the hyperemic capillaries and the fibrous tissue. They represent the highest grade of destruction, and hence are sunken. Darker hemorrhagic areas may also be found. Small-celled infiltration and proliferation in the fibrous tissue, and multiplication of the endothelia of bile-ducts also occur.

FIG. 250.



Fatty liver cells. To the left three with fatty infiltration. To the right, fatty degeneration, destruction of the cell, and detritus remaining. $\times 350$.

Acute yellow atrophy is a rare disease which at times follows infectious and septic conditions, and may occur during pregnancy or with puerperal fever. It is more common in women than in men.

A condition similar to the above follows phosphorus and arsenic poisoning. The essential element is fatty degeneration. Since death occurs earlier than with acute yellow atrophy, often in a few seconds, and at the longest after a few days, the liver may be studied in an early stage when there is no removal of the degenerated tissues, but when excessive fatty changes are beginning the process. The liver is then large, icteric, soft, and friable. If death is delayed for a time the condition reproduces that of yellow atrophy.

In all three conditions the heart, the kidneys, and the alimentary epithelium suffer albuminous and fatty degeneration. With the poisons mentioned the striated muscles present the same changes.

Scattered areas of fatty degeneration are found in the liver after many diseases, as well as focal necroses. Among these are typhoid,

recurrent fever, variola, scarlatina, malaria, Weil's disease, and puerperal eclampsia. Some of these lesions are to be explained by closure of small vessels and anemic or hemorrhagic infarction.

Amyloid degeneration usually begins in the intermediate zone and affects the portal capillaries. Their walls become thickened masses, which give the iodine reaction and close the lumen and also compress the liver cells. The latter remain intact for a time, but then suffer pressure and loss of nutrition, which ends in atrophy. In the worst affected portions only the degenerated masses of amyloid may persist, and the entire acinus may be destroyed.

Usually amyloid degeneration develops in discrete areas which may be microscopic. If well marked, the amyloid liver is larger than normal, and has a peculiar glassy look, as well as being anemic and fatty.

Glycogenic degeneration is found in the liver with diabetes. The glycogen is contained especially in the cells of the peripheries.

Pigmentation. The liver is an organ in which deposits of pigment are very common.

1. Destruction of blood cells within the organ leaves altered blood pigment within it, as is common in stasis.

2. Hemochromatosis. Where many red cells are destroyed within the vessels, as with certain poisons, and in diseases like pernicious anemia, and when large extravasations of blood are reabsorbed, large amounts of pigment are deposited in the liver. When this pigment contains iron the condition is called hemosiderosis. It is found as granules and larger masses in the capillaries between acini and in their peripheries, and in the fibrous tissue (Kupfer's cells). In other cases the dissolved pigment is carried to the liver and there changed into granules, being deposited in the peripheral cells and the tissue between them. In all these cases it seems as if more blood pigment were carried to the organ than it could use in the manufacture of bile. The granules are yellowish brown, and may color the organ in mass, or it may be black in malaria (melanemia) and make the organ greenish black.

3. Hemofuscin is found in brown atrophy of the liver when the entire organ is atrophic, as during various cachectic conditions, and also cirrhosis. The central portions of the acini contain most of the pigment, and are visibly dark on section. Possibly in these cases there is both an increased supply of material from the blood and also a decrease in the functional activity of the liver.

4. Biliary pigment (p. 75, and icterus, *infra*).
5. Material from outside the body, as coal-dust from the lung, may be deposited in the connective-tissue elements of the liver, and also in the stellate cells in the central parts of the acini.

Suppurative Inflammation—Hepatic Abscess.

Primary purulent inflammation is very rare in the liver. Abscesses most often follow the entrance of pyogenic bacteria from distant foci, and the most important routes are the portal vein, the hepatic artery, the hepatic vein, the umbilical vein, and the bile-ducts.

1. Any suppurative process in the territory of the portal origins, as ulcers of the stomach and intestine, may permit pyogenic organisms to pass through the portal vein to the liver and there cause single or multiple, small or large and confluent abscesses. If the portal vein and its branches become inflamed a purulent thrombophlebitis may result (*pylephlebitis*), which invades the liver directly or by means of emboli.

2. Occasional infection from mycotic endocarditis is carried by the hepatic artery, and causes small, usually hemorrhagic, infarcts, or embolism by cocci, and both end in abscesses.

3. In the hepatic vein pyogenic organisms which have passed the portal radicles may set up an inflammation and thrombosis, as happens sometimes with *pylephlebitis* (*hepatophlebitis*). Possibly a retrograde infection might come from the vena cava with suppuration about the vessel.

4. In the newborn suppuration at the navel may pass to the umbilical vein, and thence to the liver.

5. Suppurative cholangitis is relatively common, from infection through the gall-ducts (cholangitis) and from ulcers of the intestine. In other cases typhoid fever, dysentery, and intestinal parasites, are the exciting causes. The suppuration passes from the bile-ducts to the parenchyma of the organ and causes abscess by dilatation of the gall-ducts and destruction of the liver tissue adjacent. Such foci of pus tend to enlarge, and may reach a great size. This form of suppurative hepatitis may follow a chronic course and spread from the gall-bladder and ducts to the smaller radicles, and then to the liver cells. Indurative processes may accompany it, which encapsules and perhaps heals the abscesses after evacuation of the contents. The stasis of bile which follows usually imparts a yellow color to the organ. Biliary cirrhosis may follow.

Apparently idiopathic abscesses of the liver occur in the tropics and are probably connected with the endemic dysentery.

Atrophic and Indurative Processes.

Atrophy of the liver accompanies all cachectic conditions. The organ is small, its edges are sharp, its consistence is firm, and its color rather dark. With pigmentation the condition is called brown atrophy.

Partial atrophy occurs in women from pressure of the corset and ribs. A shallow groove is seen on the anterior surface where the capsule is thick and the organ atrophied. If very deep the furrow divides the right lobe into two.

Induration of the liver means a uniform increase of its fibrous elements, both between acini, about the vena centralis, and elsewhere in the lobules. The separation of one acinus from another is then more distinct than usually, and the capsule is apt to be thicker. Induration occurs with stasis, both of blood and of bile, and may lead to cirrhosis.

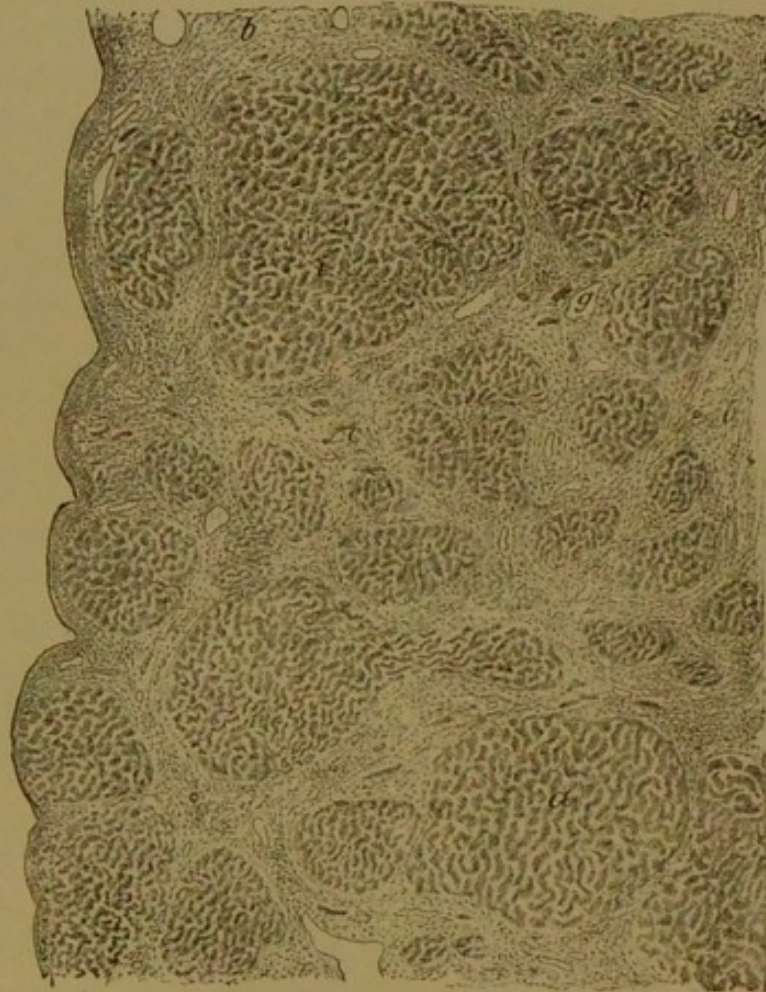
Atrophic Cirrhosis (Laennec's). The essential element is the formation of granulation tissue between the lobes and its conversion into contracting cicatricial tissue, with consequent atrophy of the hepatic cells. The process starts from the branches of the portal system and is irregularly distributed. All stages may be found from groups of young round and spindle-shaped cells to complete fibres. The portal branches and the intra-acinous bile passages are lost, and the nutrition more and more depends upon the hepatic artery.

The acini surrounded by the fibrous tissue present both fatty infiltration and imbibition of bile, from the impeded flow of the latter. Brownish pigment may be deposited in the cells. The fibrosis may cease at the margin of the acini, but usually slender processes run in between the hepatic cells from the edge, and thus peripheral parts of the acini may be snared off and encapsuled by periportal fibrous tissue. Atrophy follows, and thus a fibrous mass occupies the place of the lost cells. The remaining acini are decreased in size and separated from each other by bands of fibrous tissue.

In the fibrous bands newly formed bile-ducts are found, often very much contorted, which have grown from the older canals, and hence the excretion of the bile is but little interfered with, and icterus of marked grade seldom occurs in the atrophic form.

Early in the disease, before the liver has suffered much loss of parenchyma, the organ is large and not much firmer than normal. This is called the stage of hyperplasia, and is seldom observed post-mortem. Usually a stage is encountered in which there is marked contraction of the fibrous tissue, and the organ is small. The cut surface is then divided into small, gray, and firm nodules by bands of connective tissue which lie slightly sunken, and the acini are fatty and

FIG. 251.



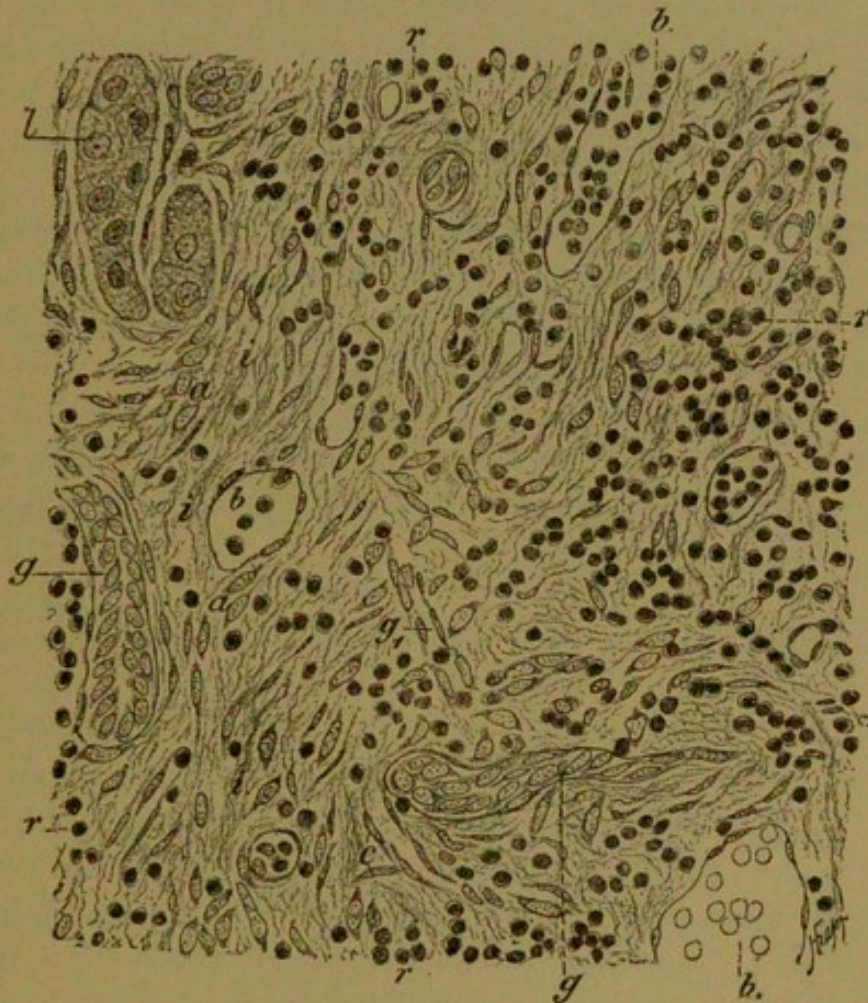
Interstitial hepatitis or atrophic cirrhosis. *a*. Acini of smaller size. *b*. Fibrous tissue between acini with newly formed bile-ducts. *c, g*. Portal vessel. To the left contraction has caused granulation of the surface of the organ.

prominent and of a greenish or yellow hue. This contrast is described as granular, and the granules of remaining tissue may include several acini or single ones. The acini may be much larger than normal, but they can not always be distinguished separately. The left lobe frequently presents the most marked lesions. Beside the granular surface and the decrease in size, a characteristic feature is the firmness of the organ and its resistance to the knife when cut.

Occlusion of many branches of the portal vein leads to passive congestion throughout its origin. A collateral circulation is imperfectly established through the veins of the esophagus, the adrenals, those of the renal capsule, and the spermatics. Catarrhal conditions prevail along the alimentary canal, and the spleen becomes larger, and ascites develops.

Hypertrophic Cirrhosis. In contrast to the ordinary form of cirrhosis, in which the fibrous hyperplasia occurs between the acini, and seldom

FIG. 252.



Interstitial hepatitis. *a*. Granulation cells. *r*. Lymphocytes. *i*. New fibrous tissue with spindle cells. *g*. Young gall-duets. *l*. Groups of liver cells surrounded by growing connective tissue. *b, c*. Young vessels. $\times 250$.

sends processes into the acinus, the hypertrophic form is marked by fibrous hyperplasia within the acinus, also between the hepatic cells, which are thus separated and compressed. Because of the great increase of fibrous tissue everywhere throughout the organ it is large, and its weight may reach 2 to 4 kilos. It is smooth on the surface or presents low prominences, not much firmer, often deeply bile stained.

In many cases the fibrosis has the character of a uniform hyperplasia rather than of a strongly cellular proliferation. Although transitions between the two varieties of cirrhosis occur, the single cases of the hypertrophic form may be regarded as distinct.

Ordinary cirrhosis may be due to excessive use of alcoholic liquors. It occurs more often in men than in women, and is common in countries where hard liquors are used. In beer drinkers early stages of hypertrophic nature may precede the atrophic type, but cirrhosis is not so common with this form of alcoholic excess. Chronic poisoning (phosphorus), biliary stasis, and unknown causes may produce the lesion. Biliary cirrhosis is especially hypertrophic and seldom causes ascites, but usually marked icterus.

Perihepatitis thickens the capsule and is known as "icing liver" (Zuckergussleber).

Hypertrophy of the liver occurs with glycogenic degeneration in diabetes. Partial hyperplasia of single acini or groups of them is common with cirrhosis and echinococcus, as a regenerative process. After as much as three-fourths of the organ have been removed from animals (rabbits) the normal size of the organ is regained in a few weeks from hypertrophy of the remainder. In healing after wounds with formation of scars, hepatic cells and ducts may be reproduced.

Infectious Granulomata.

Tuberculosis of the liver may be of two forms, disseminated miliary nodules and tuberculosis of the bile-ducts.

In the disseminated form there are many small nodules which may be microscopic or larger, and which become caseous later and confluent. They are most numerous in the tissue between the lobules, at the edge of the acini and sometimes within them. They are regularly found with tuberculosis of other organs, as of the lungs and bones.

Tuberculosis of the large bile-ducts, cholangitis tuberculosa, is more uncommon and is apt to be secondary to the same lesion in other organs. Large nodules are found, made by the fusion of many small ones. They develop in the outer wall of the duct and appear as caseous foci in which there is a lumen, corresponding to the duct, about which there are circles of miliary tubercles.

Syphilis of the liver is of three forms: (1) Interstitial inflammation with resulting fibrosis; (2) circumscribed granulomata ending in caseation and fibrous scars; (3) mixed forms, in which caseous nodules lie imbedded in fibrous hyperplasias.

1. The first of these forms occurs in either hypertrophic or atrophic cirrhotic processes. The former presents fibrous hyperplasia of the interacinous and intra-acinous tissue, and is found in children with

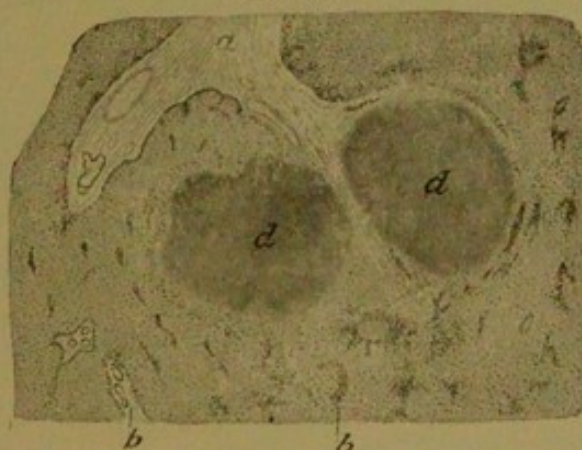
FIG. 253.



Hepatic tubercle. Section three microns thick. Giant cells with processes; between the cells a delicate network which is partly reticulum and partly fibrin. $\times 500$.

hereditary syphilis. The liver is large, firm, smooth, and mottled, usually throughout the entire organ. The atrophic form presents localized areas of fibrous scars with marked contraction and patholog-

FIG. 254.



Caseous gumma in the liver. a. Thickened periportal tissue. b. Small-cell infiltration. d. Gumma. $\times 12$.

ical lobulation (*hepar lobatum*). This is common in the adult during tertiary syphilis, but diffuse atrophic forms also occur, resembling ordinary cirrhosis.

2. Circumscribed masses of granulation tissue are found in the liver with both congenital and tertiary syphilis. In the gross they appear as grayish-red, soft, or gelatinous deposits of a size varying between miliary and a few centimetres in diameter, either singly or in numbers. The gumma has a tendency to fibrous changes, especially at the margin, where a capsule gradually forms with radiate extensions. While the smaller nodules may be wholly fibrous the larger are commonly softened in the centre. Contraction of the fibrous capsule makes

FIG. 255.



Syphilitic cirrhosis of the liver. *a.* Capsule of the liver. *b.* Thickened periportal tissue. *g.* Large fibrous focus. *e.* Depression due to contracting fibrous tissue. *l.* Parenchyma. *c.* Vessel. $\times 50$.

furrows, and the tissue between thus becomes lobulated. This is most common along the lower border and about the attachment of the suspensory ligament. Superficial gummata involve the capsule also in the fibrous hyperplasia, and adhesions form with adjacent structures (perihepatitis fibrosa).

3. Combinations of the caseous and fibrous processes are more common than pure examples of either. General cirrhosis and lobulation, biliary stasis and icterus, and amyloid degeneration frequently

accompany the lesion. These changes are less often encountered with acquired syphilis than with the congenital variety.

Leukocytoma and lymphoma of the liver occur with leukemia and pseudoleukemia as diffuse infiltrations or as small nodules of lymphoid cells in the interacinous tissue.

Tumors. Cavernous angioma is rather common in the liver. Adenoma may begin in the bile-ducts or develop from the hepatic cells, and is less frequent.

Primary malignant tumors are rare. Carcinoma may develop from the biliary epithelium, or at times from the hepatic cells, and usually forms circumscribed nodules, though diffuse forms are seen. In most cases the neoplasm invades the liver from other organs, as the stomach and the gall-bladder, or by metastasis, and the latter may occur through the portal vein. Sarcoma of the liver also occurs, usually secondary.

Parasites. The echinococcus is the most important. It occurs as *e. unilocularis* and as *e. multilocularis*. The former appears as one or more small or larger vesicles, surrounded by a fibrous capsule disposed about a chitinous capsule in regular layers, and within are brood capsules and scolices. In rare cases *distomum hepaticum* and *lanceolatum* may be found.

DISEASES OF THE GALL-BLADDER AND LARGE BILE-DUCTS.

Gallstones and their Results; Inflammation; Occlusion of Ducts.

Biliary concretions are very common in the gall-bladder and may have various results. In size they may be small as sand or large enough to fill the gall-bladder, and in number they may be countless. The larger commonly have an ovoid form, those in the ducts are cylindrical or branched. If several lie in the gall-bladder they assume angular and polygonal shapes because of growth while they are in contact, not because of mutual attrition. In color gallstones are white, green, or blackish green, and they vary much in firmness. Chemically they consist in chief of calcium salts with bilirubin and cholesterin, and of the salts, carbonates and phosphates are commonest. They have a framework of organic matter which is impregnated by the other materials.

Pure cholesterin masses are yellow, easily cut, friable, and float in water. On fracture the surface has a peculiar glistening look, and is

often laminated and marked with radii. Under the microscope tables of cholesterin are discovered. Pigment stones are often small, heavier than the former, rough on the surface, of a yellow or black color, and made up of biliverdin or bilirubin with lime.

The majority of these concretions are mixed forms, into which both cholesterin and lime salts enter, and the material may be cholesterin arranged about a nucleus of the other kind, or *vice versa*. If chiefly consisting of lime and pigment the stone is small and hard, rough, and yellow.

The formation of bilestones is not wholly understood. Probably there is first a catarrhal inflammation of the mucosa of the part, as a result of which cholesterin is formed from the degenerated epithelium and precipitated, and at the same time the albuminous bile precipitates calcium salts and pigment, and in the mixture of organic matter, which serves as a nucleus, the inorganic is deposited. Stasis of the bile and alterations in its composition, and probably bacteria also (*b. coli communis*), play a part in the process.

Small stones may occur in the gall-bladder, which, during life, have given no discomfort, and at times they pass out of the common duct with symptoms of colic. When a calculus remains lodged in a bile-duct its consequences vary with its locality. If the cystic duct is occluded the bile can no longer flow into the gall-bladder, but from its inner surface there is a catarrhal secretion, and while the bile is gradually absorbed the gall-bladder becomes distended by thin mucous fluid; this is called *hydrops vesicæ felleæ*. In other cases the walls of the gall-bladder become fibrous and contracted, its cavity disappears, and calcification may follow. What little contents remain may be thick and mortar-like.

When the hepatic and common ducts are closed the bile can no longer flow from the liver, and acute or chronic icterus results. Cystic dilatation of the duct at the site of the calculus, and a more uniform widening of all bile channels frequently follow, and about the varicose capillaries and ducts of the system fibrous hyperplasia leads to *cholangitis fibrosa* or general cirrhosis. Foci of necrosis in the liver are apt to occur. Single branches of the main ducts may be occluded, and these appearances then are found only in the corresponding parts of the organ.

The local consequences with biliary calculus are important. In the gall-bladder catarrhal inflammation increases the size of the stone, atrophic fibrosis leads to obliteration of the part. Mechanically the

pressure of the stone may cause necrosis of the wall of the gall-bladder, and the presence of the bacillus coli may lead to diphtheritic inflammation and perforation. The fistula usually communicates with the adherent duodenum or transverse colon, seldom with the stomach, ileum, or other organs. The fibrous adhesions are the result of *pericholecystitis*. Very large stones which enter the bowel by way of such a fistula may cause occlusion even here. In rare cases the adhesions form so that the stone is voided through the skin. Without adhesions about the perforation, peritonitis follows, and is usually fatal.

Phlegmonous cholecystitis is the result in other cases, either as a diffuse thickening and suppuration of the wall of the cavity or as purulent catarrh of its mucosa. When the pus cannot escape the condition is called empyema of the gall-bladder, and may reach a large size and lead to perforation.

Similar consequences follow in the large ducts, necrosis of the wall from pressure, cholangitis of several kinds, multiple hepatic abscesses, and perforation in various directions.

Diverticula sometimes form from the gall-bladder by the growth of a stone between prominent folds of its mucosa.

Beside inflammation in the bile-ducts produced by the irritation of calculi, independent inflammations may occur which are transmitted from the intestinal canal, and the bacillus coli is frequently the organism which excites the lesion. Parasites wander into the ducts at times and produce the same effects.

Gastroduodenal catarrh is apt to involve the lower section of the common bile-duct and close it by combined swelling of its mucosa and the formation of a plug of mucus in its lumen. The ordinary result of this is called catarrhal jaundice. The excreted bile is under such slight pressure in the ducts that it cannot overcome such an obstacle, and hence stasis and resorption occur.

Typhoid fever is at times accompanied by this form of icterus, and the bacilli in the gall-bladder may cause purulent cholecystitis. Certain other organisms may be brought through the blood to the gall-ducts and bladder and cause abscess. Further causes of retention icterus are compression of the ducts by scars, tumors, and echinococci, and round worms in the ducts.

Among circulatory disturbances edema of the gall-bladder may be mentioned, which is part of marked general edema, and also accompanies inflammations.

Tuberculosis of the gall-bladder is very rare. Similar lesions of the ducts have already been treated.

Carcinoma is not an unusual tumor in the gall-bladder, and it may be considered to have some relation with the chronic irritation due to calculi. Adenosarcoma, scirrhus, and gelatinous forms occur. The wall of the gall-bladder may be so infiltrated with the neoplasm that but a small lumen remains, filled with necrotic tissue, or hydrops may result. In all cases the carcinoma attacks the liver directly, and by piercing the portal veins. It may also involve the common duct, the stomach, and other organs, and cause thrombosis and occlusion of the vena cava inferior.

Cylindrical-celled carcinoma develops independently in the bile-ducts or the channels within the liver. The chief effects are closure of ducts, inflammation, and abscess formation.

E. DISEASES OF THE PERITONEUM.

Disorders of Circulation. Active hyperemia is partly an inflammatory lesion, partly due to sudden relief of pressure within the abdominal cavity, as by removal of large tumors and ascitic fluid.

Venous stasis causes a transudation of fluid into the pelvic or general cavity, according to its amount, and if in large quantity presses the diaphragm upward. General stasis causes ascites and also hydropericardium and hydrothorax; portal stasis causes simply ascites, as with hepatic cirrhosis. Hemorrhages may be small ecchymoses, as with death by asphyxia, and in the hemorrhagic diathesis, or large amounts of blood after injury to abdominal organs.

Inflammation. All forms of inflammation in serous membranes occur in the peritoneum, as well as mixed forms. If confined to various sections of the cavity the disease receives special names, as perihepatitis, perityphlitis, pelvic peritonitis, etc.

Productive peritonitis may be the sequel to an exudative inflammation or be productive from the first, as about chronically inflamed sections of the intestine. Adhesions between various organs are the result, and fibrous bands so formed may be the cause of internal strangulation. Exudates and transudates may be encapsulated, and general obliteration of the cavity by adhesions between its walls may result.

The etiology of peritonitis is manifold, but most cases are secondary. Primary idiopathic peritonitis is extremely rare.

A metastatic and commonly suppurative peritonitis complicates pyemia, typhoid fever, and other infectious diseases. Other common sources are the genital organs, as with puerperal fever, the intestine with typhlitis and perityphlitis, the liver and spleen when the seat of inflammations, infection from wounds during operations involving the walls and perforation of hollow organs, as the stomach, from ulcers and carcinoma. Trauma of the intestinal canal, hernia and strangulation, volvulus and invagination, also give rise to peritonitis. Death may follow quickly from absorption of toxin from putrefactive organisms, even before the inflammatory reaction occurs, or there is a feculent and purulent inflammation.

In regard to prognosis the most important question concerns the localization or spread of the lesion. Perforations usually cause a diffuse peritonitis unless enclosed by adhesions. Localized inflammation may extend from other organs, especially in the productive form, but also with the exudative if not of too great intensity. Fibrous adhesions may be themselves broken through, or they may confine the inflammation and its purulent exudate.

Tuberculosis. Simple tuberculosis and a tuberculous inflammation are to be distinguished. The former is seldom primary, but follows intestinal and other lesions of the same nature, and is often circumscribed. Tuberculous peritonitis is fibrinopurulent, or at times hemorrhagic, and commonly secondary. As in tuberculous pleurisy, the nodules are found in and with the exudate. Chronic forms of the lesion may be diffuse or circumscribed, and produce firm adhesions, which enclose caseous masses. Circumscribed chronic inflammation of this variety is common with chronic tuberculosis of the intestine, and leads to thickening of the serosa and adhesions of the intestine.

Tumors. Primary carcinoma, sarcoma, and endothelioma occur as diffuse multiple neoplasms with small scattered or grouped tumors, and with these there is usually serous or serofibrinous peritonitis. Productive inflammation and adhesions are common. As subserous tumors, sarcoma, lipoma, and fibroma occur, and dermoid cysts are not uncommon.

Of animal parasites echinococcus may be mentioned.

F. DISEASES OF THE PANCREAS.

The pancreas consists of many glandular lobules, visible in the gross, and between them there is fibrous tissue. The epithelia are cylindrical and polyhedral, and in the ducts cylindrical.

Atrophy of the pancreas accompanies marasmus and cachexia, especially diabetes.

Cloudy swelling and fatty degeneration occur with infectious diseases and poisonings, especially phosphorus.

Partial self-digestion may occur during the death agony or before it, and is common post-mortem.

A frequent regressive change is *lipomatosis*, with great increase of the interlobular fat and atrophy of the gland. It is met with in general obesity and also in marasmus, and may convert the gland into a simple mass of fat surrounded by a capsule. In other cases the atrophy of the gland may be primary. The cells are infiltrated with fat.

A peculiar lesion of the pancreas is known as *fat tissue necrosis*, falsely called "fat necrosis." In slight degrees there are single or multiple small points of opaque yellowish-white or gray color, which may become confluent and involve the major portion of the gland. The lesion begins by the death of the interstitial fat tissue, and adjacent lobules of the gland are then involved in necrosis. Microscopically these parts are lacking in nuclei, and in them there are fat cells, retained or suffering destruction, fat crystals and irregular masses of lime combined with fatty acids. In such foci hemorrhage is common, and about it infiltration with small round cells leads at last to demarcation. The dead tissue presents then as a grumous material, of pale or brownish hue, floating in a cavity which is partially encapsuled. When the whole gland is destroyed it also may float in the cavity. Hemorrhages may be severe and at times fatal. With the necrosis there may be perforation of the duodenum or into the peritoneum. With infection from the intestine, suppuration and gangrene may follow. Similar lesions are at times observed in the omentum, the subperitoneal fat, and the mesentery.

It is not clear how much the pancreatic condition is the cause, and how much it is the result of the changes in the fat tissue. The action of the pancreatic ferment splits the fat, and the fatty acid combines with lime, and hence may cause the lesion, as appears after traumatism of the gland. Disease of the parenchyma, pancreatic stasis with closure of the duct, hemorrhage into the tissue, and inflammatory processes, have also been considered causative, and the use of alcohol to excess, general obesity, cholelithiasis, and infections have been looked upon as disposing factors.

Septic and marantic results may follow fat necrosis, and similar necroses may be noted in the subcutaneous fat. Clinically many

of these cases resemble intestinal obstruction, perhaps connected with secondary lesions in the celiac plexus.

Among circulatory disorders *hemorrhage* deserves special mention, for it occurs at times in severe degrees and without assignable cause. Pancreatic apoplexy may be fatal apart from the amount of blood lost, probably from reflex paralysis of the heart, shock, and involvement of the celiac plexus and semilunar ganglion. The rest of the body on autopsy may be negative.

In conditions of general cyanotic induration, especially in alcoholic and cardiac patients, the pancreas may be very firm.

Inflammation. Cloudy swelling occurs as in other organs, and parenchymatous inflammation also; the latter is accompanied by hyperemia, and is thus distinguished.

Suppuration involves the gland from neighboring processes, as gastric ulcer, or is metastatic. With fat necrosis it depends upon infection from the intestine.

Indurating inflammation occurs with atrophy of the epithelium from fibrous hyperplasia and contraction of the new tissue, and this process is often seen in the course of tuberculosis and syphilis. Indurative changes and diabetes appear to have a peculiarly distinct relation. Diabetic atrophy differs from ordinary cachectic atrophy in several particulars. In diabetes the organ is relaxed and dark, the diminution affects especially the thickness of the organ while in cachexia it is uniform, the gland is adherent to other organs while in cachexia it is more distinct, and in diabetes, together with atrophy of epithelial elements, there is hyperplasia of the fibrous.

Tumors. Carcinoma is the most important pancreatic tumor. It is usually scirrhous and begins in the head of the gland. It may cause compression of the common bile-duct with icterus, compression of the duodenum with gastric dilatation and catarrh, compression and invasion of the portal vein with stasis. It attacks the structures about it and causes metastases, especially in the liver.

Dilatation of the duct of Wirsung may follow closure of its lumen by calculi or tumors, and usually the obstacle involves the opening of the duct at the papilla. The dilatation may affect the entire duct, and on its wall prominent folds of mucous membrane divide its length into a number of communicating diverticula. In other cases a cystic dilatation forms behind the obstacle. This resembles similar conditions in the salivary ducts, and is known as *pancreatic ranula*. Multiple small cysts of the ducts, from catarrh and plugging, have been

termed acne of the pancreas. Cysts filled with bloody fluid, most often in the tail of the gland, depend partly upon primary hemorrhages or those with fat necrosis, and partly upon cystic dilatation and self-digestion. In the duct pancreatic calculi form, like those in the salivary ducts, and may reach the size of a walnut. They consist of carbonate and phosphate of lime, and their formation may be due to catarrh of the part. They cause dilatation and cysts, degeneration and interstitial hyperplasia, and with infection a suppurative pancreatitis may develop.

CHAPTER XI.

DISEASES OF THE URINARY SYSTEM.

A. THE KIDNEY.

THE glandular parenchyma of the kidney consists of two main divisions, the medullary portion and the cortex. In the medulla the pyramids occur, with their apices in the calyces of the pelvis, and between them are the columns of Bertini. From the periphery of each pyramid the medullary rays run out into the cortex. The pyramids consist of straight collecting tubes and the cortex of convoluted tubes. In the cortical lobules the Malpighian bodies or glomeruli occur, which consist of a coil of arterial vessels enclosed in a capsule of Bowman, both of whose layers are covered by epithelium. From the capsular cavity the first convoluted portion begins, then bends down as Henle's loop into the medullary region, ascends to the cortex again, and forms the second convoluted tubule, and from here passes into the larger collecting tubes. Many of these last join to form a papillary duct which empties into the renal pelvis. All the tubule, except the descending limb of Henle's loop, is lined with rather high cubical or cylindrical epithelia which are large and rich in protoplasm.

The vascular system comes into close relation to the epithelium at the glomeruli. The branches of the renal artery pass between the pyramids and form arched vessels along their convexities, and from here interlobular vessels pass out to the cortex and vasa recta inward to the pyramids. At the glomerulus the afferent vessel leads into the coil, the efferent leads away and divides into capillaries about the convoluted tubes. Other vasa recta come from the first portion of the interlobular arteries and from efferent vessels, and with the accompanying veins give the peculiar alternate markings of the part which are visible in the gross. Anastomosing branches come from the vessels of the renal capsule, derived from twigs of the renal, supra-renal, lumbar, phrenic, and spermatic arteries. The veins in general correspond to the arteries as described. They begin as prominent stellate veins under the capsule.

In the normal organ there is but a small amount of fibrous tissue apart from the vessels; between the tubules the microscope discovers little beside the richly developed capillaries with their endothelial nuclei. In the papillæ the fibrous tissue is more abundant.

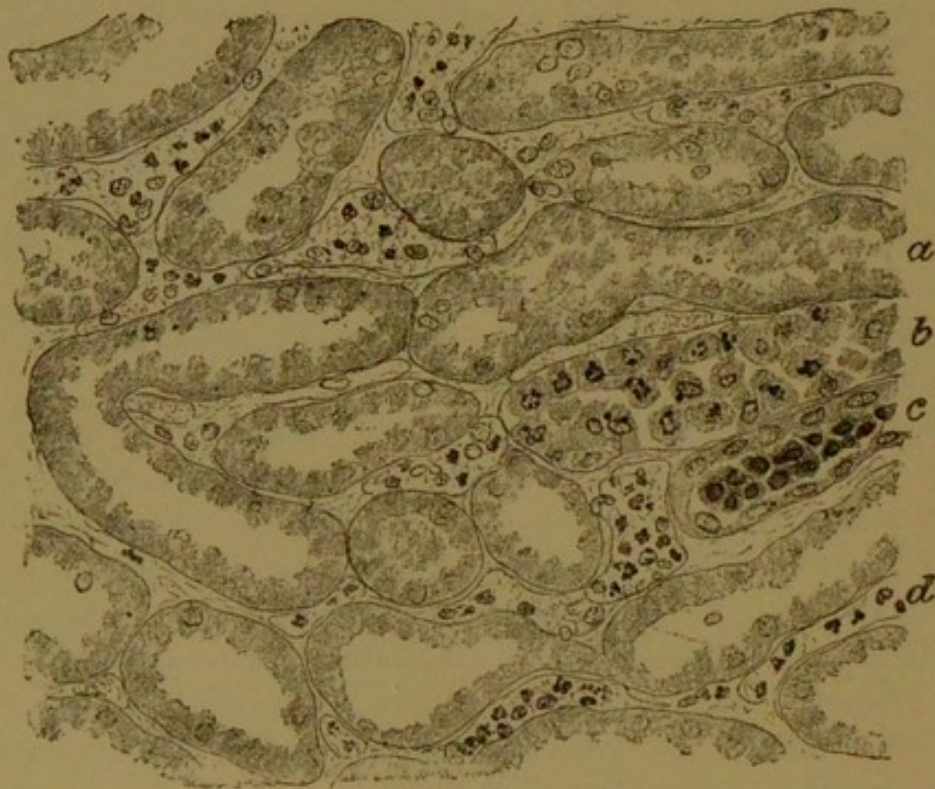
Malformation.

Congenital union of the two kidneys and doubling of the ureters are the commonest anomalies. The former is called "horseshoe" kidney. When the organ is not firmly attached the wandering kidney results. Numerous cysts may be found in the organ (congenital cystic kidney). One kidney may be lacking and then the other is vicariously hypertrophied.

Disorders of Circulation.

Albuminuria. In certain conditions the albuminous serum passes out of the vessels into the renal tubules, and histologically it can be

FIG. 256.



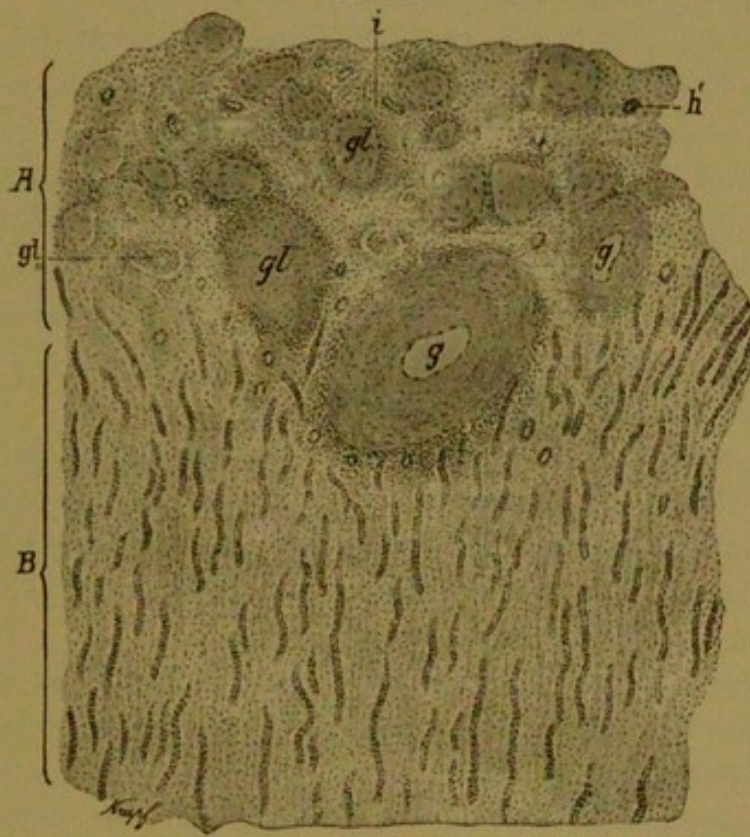
Section from a fresh anemic infarct of the kidney. Nuclei lost in most epithelia. *a*. Karyorrhexis. *b*. Leucocytes in the capillaries. *d*. Thickening (pyknosis) of desquamated epithelia and their nuclei, *c*. $\times 350$.

found here by boiling or otherwise coagulating it. Albuminuria occurs with nearly all intensive inflammations of the kidneys, and also in general diseases with no apparent renal lesion, as a transitory symptom

in fevers, after poisons, in hydremia, and other diseases of the blood, with general circulatory disorders, and with epilepsy.

Probably the albuminuria is caused by some change in the epithelia of the glomeruli and the tubules, and in the capillaries, because of impaired nutrition, or general or local disorder of the circulation, or the action of toxic substances. The albumin may form solid masses in the tubes, called hyaline casts, of glassy appearance, very tender and perhaps scarcely visible, which may reach the length of several millimetres and dissolve quickly with acetic acid and slowly with alkalis.

FIG. 257.



Embolic scar from the kidney. A. Cortex. *gl.* Glomeruli. *h.* Tubule. *i.* Scar tissue. *g.* Thickened vessels on the edge of the infarct. B. Medullary portion. $\times 250$.

Anemia may be part of a general condition, but it usually accompanies degenerative and inflammatory lesions in the cortex, especially fatty and amyloid changes.

Embolism and thrombosis of renal arteries cause infarcts which are commonly anemic, pale yellow, firm, and of the usual wedge shape with the apex inward; they are often surrounded by a broad hyperemic or hemorrhagic margin. In most cases they lie in the cortex, and may be multiple. Hemorrhagic infarcts are rare.

With *ischemia* from thrombosis and embolism the affected area within twenty-four hours presents a loss of nuclei and conversion of the epithelia into granular masses. The connective tissue, being less sensitive, remains alive longer. From the surrounding tissue a productive process leads to absorption of the necrotic elements and formation of a scar, in which the glomeruli may persist as homogeneous bodies without nuclei between fibrous bands, more or less pigmented where hemorrhage has taken place. Subsequent contraction, especially if multiple, leads to a coarse lobulation of the organ.

Congestive hyperemia is often the beginning and an accompaniment of inflammation, and is most evident in the medulla.

Venous stasis may be due to local causes, as thrombosis of the renal vein or the vena cava inferior, and renders the kidney larger and darker and more filled with blood than normal.

Disorders of the general circulation cause *cyanotic induration*, which may be recognized by the increased blood content, the slight increase in size, the broader cortex, and firmer consistence. In part this is the immediate consequence of hypertrophy of the heart and associated arterio-fibrosis, which causes lengthening and tortuosity of the capillaries and thickening of their walls.

In other cases it follows the general passive congestion from weakness of the heart. The stellate veins and those of the glomeruli and between the lobules are filled with blood and appear as dark lines in the cortex, and the pyramids are very dark with the filling of the *venae rectae*.

Microscopically this condition causes an increase of the delicate connective tissue throughout the organ as a simple hyperplasia without much cell proliferation. It is especially noticeable in the medulla. In the cortex where the stellate and the interlobular veins unite and elsewhere about the vessels, fibrosis with atrophy of the epithelia in places may be found, and in consequence of the loss of tissue there are depressions on the surface of the organ. With further atrophy the surface becomes distinctly granular, and the pyramids may also be visibly smaller. The origin of these changes is found in the increased pressure from the dilated vessels and the contraction of hyperplastic fibrous tissue.

Hyaline casts accompany the condition very soon, the result of transudation, and minute hemorrhages also may occur both in the glomeruli and the interstitial tissue. Pigment granules are then found in the epithelia.



PLATE XXIV.

FIG. 260.



Acute Parenchymatous Nephritis. Fixed in Flemming's fluid, stained with safranin and picric acid, fat stained with osmic acid.

a. Desquamated fatty cells in the tubules. *b.* Granular cast, in the centre to the right two homogeneous casts; in many tubules free fat and leucocytes. Stroma infiltrated with leucocytes in lower half of picture.

Degeneration and Parenchymatous Inflammation.

Simple parenchymatous degeneration is specially common with general diseases, either as cloudy swelling or as a fatty change. The convoluted tubules and the glomeruli are most involved, the collecting tubes less so. In cloudy swelling the cortex is anemic, broader, and more opaque than normal. In fatty degeneration it is spotted with yellow points of fat. Both kidneys are affected.

Such lesions accompany diphtheria, scarlatina, measles, and other infectious diseases, as well as poisoning by phosphorus and arsenic, pernicious anemia, and general circulatory disorders which lessen the nutrition of the kidneys.

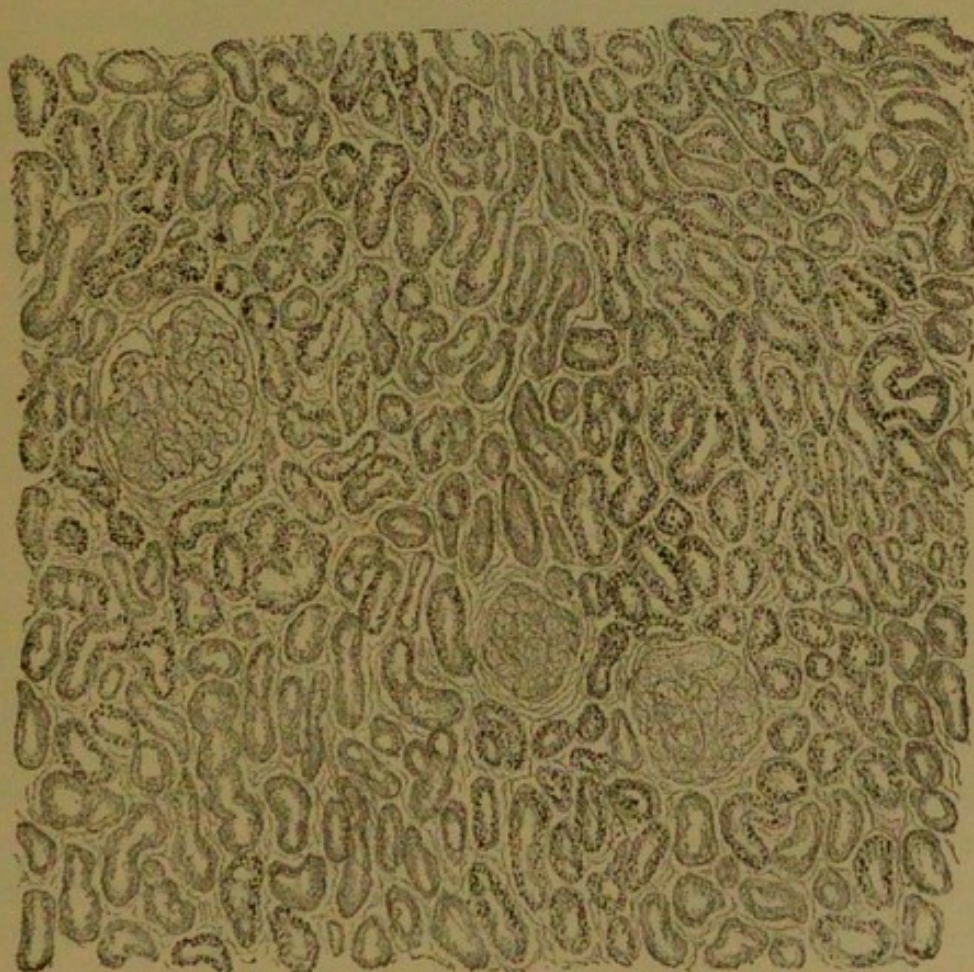
From simple parenchymatous degeneration there are many transitions to parenchymatous nephritis, that is, to processes where an added

FIG. 258.



Cloudy swelling of renal epithelia. (After FÖTTERER.)

FIG. 259.

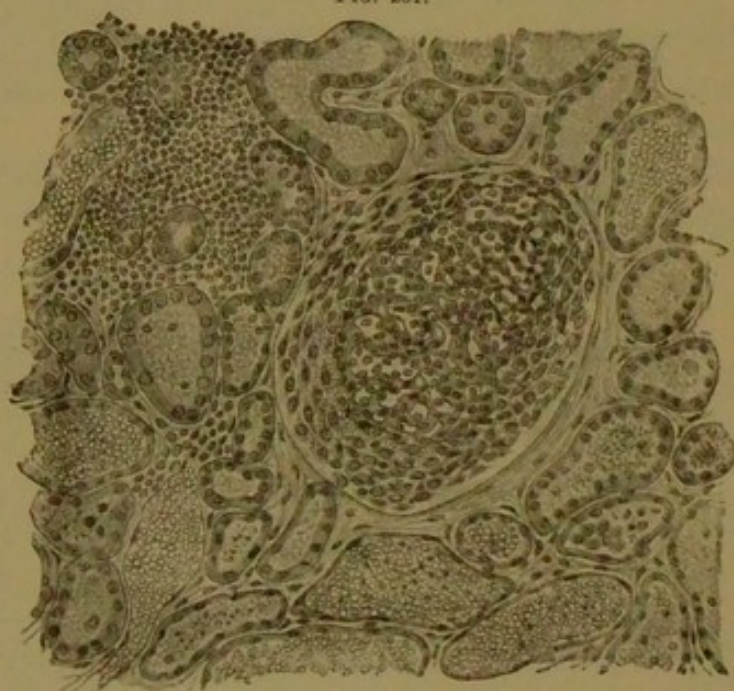


Fatty degeneration of the kidney. The fat stained black with osmic acid. $\times 50$.

element is found beside the regressive. Transudation, exudation, cellular infiltration and proliferation which involve the tubules, the glomeruli, and the interstitial substance, and more or less fatty degeneration of the interstitial tissue may be found.

According to the prominence of special features, the kidney presents various appearances. In many cases cloudy and fatty degeneration are the most pronounced lesions. Hence the cortex is opaque, of a cloudy gray, anemic, somewhat broad and swollen on section, and the medullary rays, less affected, appear as clear shining lines in the cloudy background. Albuminuria and hyaline casts are commonly observed,

FIG. 261.



Parenchymatous hemorrhagic nephritis with desquamation in the glomeruli. In the capsule of Bowman lie many desquamated epithelia. In many tubules there are masses of red cells. Above to the left a focus of round-cell infiltration in the stroma. Fibrous increase about the glomerulus. $\times 250$.

the latter especially in the straight tubes. In the epithelia of the tubules there is either granular or fatty degeneration, and, in certain poisonings, extensive necrosis; desquamation of the epithelia may lay bare a long section of the tubule. The epithelia, singly and in groups, with casts, both granular and homogeneous and blood, together with red and white blood cells, are found in the urine. The glomeruli may be distended with blood, and if it fills their capsules they may be visible in the gross as red points. Hemorrhages in the stroma give the kidney a mottled look at times. When much blood occurs in the urine the lesion is termed hemorrhagic nephritis. Edema of the whole

kidney may enlarge it. The pyramids are often very congested, in marked contrast to the anemic cortex.

In many cases there is an inflammatory proliferation of the cells in the capsule of Bowman, like that seen in inflamed mucous membranes, but the new cells rapidly undergo cloudy and fatty degeneration, desquamate, and distend the capsule. The collection of leucocytes within the vessels aids in giving the part an abnormal richness in nuclei. Altered glomeruli may be visible to the naked eye as grayish corpuscles. In some cases of nephritis the glomeruli are alone or especially involved, and the rest of the organ presents but little which is abnormal. This is called glomerular nephritis and is common with scarlet fever. Because of the functional importance of the glomeruli the consequences of the lesion are severe.

In other cases there is small-cell infiltration of the stroma and increase of the fibrous tissue about glomeruli and between urinary tubules. This is called acute interstitial nephritis. On the fresh section the markings of the cortex are lost because of the grayish infiltration.

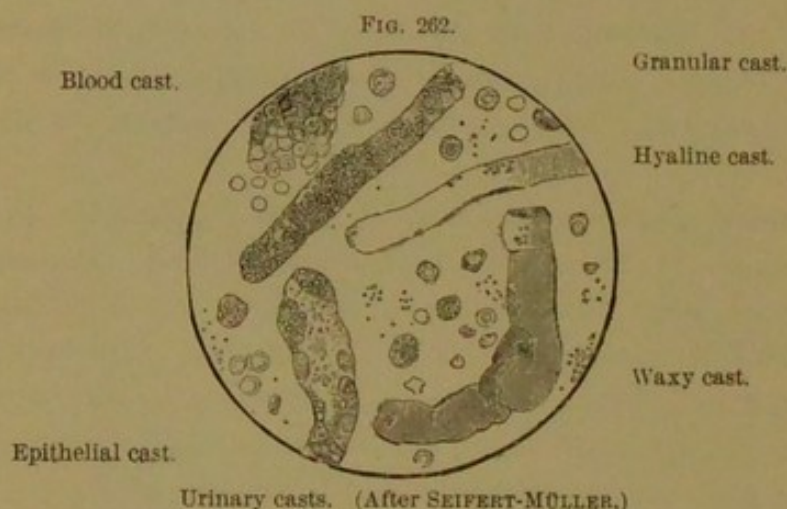
Desquamative papillary nephritis is usually secondary to pyelitis. It is accompanied by catarrhal proliferation and desquamation of epithelia in the large collecting tubes, especially at the papillæ, similar to the lesions in the capsules of the glomeruli. The pyramids are then marked by grayish-yellow lines converging to the apices, corresponding to the distended tubes. Pressure expels from the papillæ a turbid fluid made up of epithelium and leucocytes.

Acute nephritis is sometimes primary, sometimes secondary to the diseases mentioned. The lesion is bilateral, and may be referred to the excretory function of the organ for injurious and toxic substances which circulate with the blood.

The lesions so far described may characterize *chronic parenchymatous nephritis* also, either as a sequel to an acute attack or developing slowly from the start. The tubules are filled with red and white blood cells, desquamated epithelia, and casts of various kinds, and in the glomeruli desquamation and degeneration, and proliferation, occur as already noted. In the stroma cellular infiltration and proliferation, and often hemorrhages, may be observed. All these changes combine in varying proportions, and may affect certain areas of the kidney rather than the whole of it. In general they are of slighter intensity than the acute lesions, and the epithelium is usually in fatty degeneration.

Atrophic and *indurative processes* follow. Urinary tubules lose their epithelium, collapse, and become obliterated. The glomeruli become altered and functionless, and the inactive tubules connected with them atrophy. When such defects lie near the surface, especially if fibrous hyperplasia exists about them, there is a depression, and with multiple areas the whole surface is granular.

The gross appearance of the kidney varies with the prevailing lesion. The organ may be slightly enlarged, but less than in the acute form, and the cortex is swollen. Very fatty organs are yellowish white. In the cortex the section has alternate yellow, fatty lobules, and dark veins, and the pyramids are hyperemic. This form, the so-called large white kidney, is a relatively severe and rapid form of nephritis. Hemorrhages may take place in varying degrees. The large red kid-



ney, or chronic hemorrhagic nephritis, presents less evidence of fatty degeneration, but far more hemorrhage in glomeruli, tubules, and stroma, and hence it has a uniform or mottled red color. The distended vessels and glomeruli may be clearly visible. With each of these forms amyloid changes are common. With the large red kidney, because of its slow course, the localized depressions are very common, and the organ is at once enlarged and granular. This may pass finally into a true granular atrophy. In general the course of the disease may be reckoned by months.

Parenchymatous nephritis is recognized by the presence of certain elements in the urine. Albumen, red and white cells, degenerated epithelia, and casts are the important constituents. The casts may be of the following kinds: (1) Hyaline; (2) granular, made from detritus or covered with it; (3) compact yellow, waxy cylinders; (4)

made of blood cells; (5) masses of desquamated epithelia; (6) cylinders, long, delicate, irregular cylinders with longitudinal striæ and ravelled ends; (7) casts on which red, white, or epithelial cells are adherent.

At the autopsy in the chronic forms of nephritis the heart is large, there is general arterio-fibrosis; with uremia there may be catarrhal or diphtheritic enteritis and frequently edema of the brain.

FIG. 263.

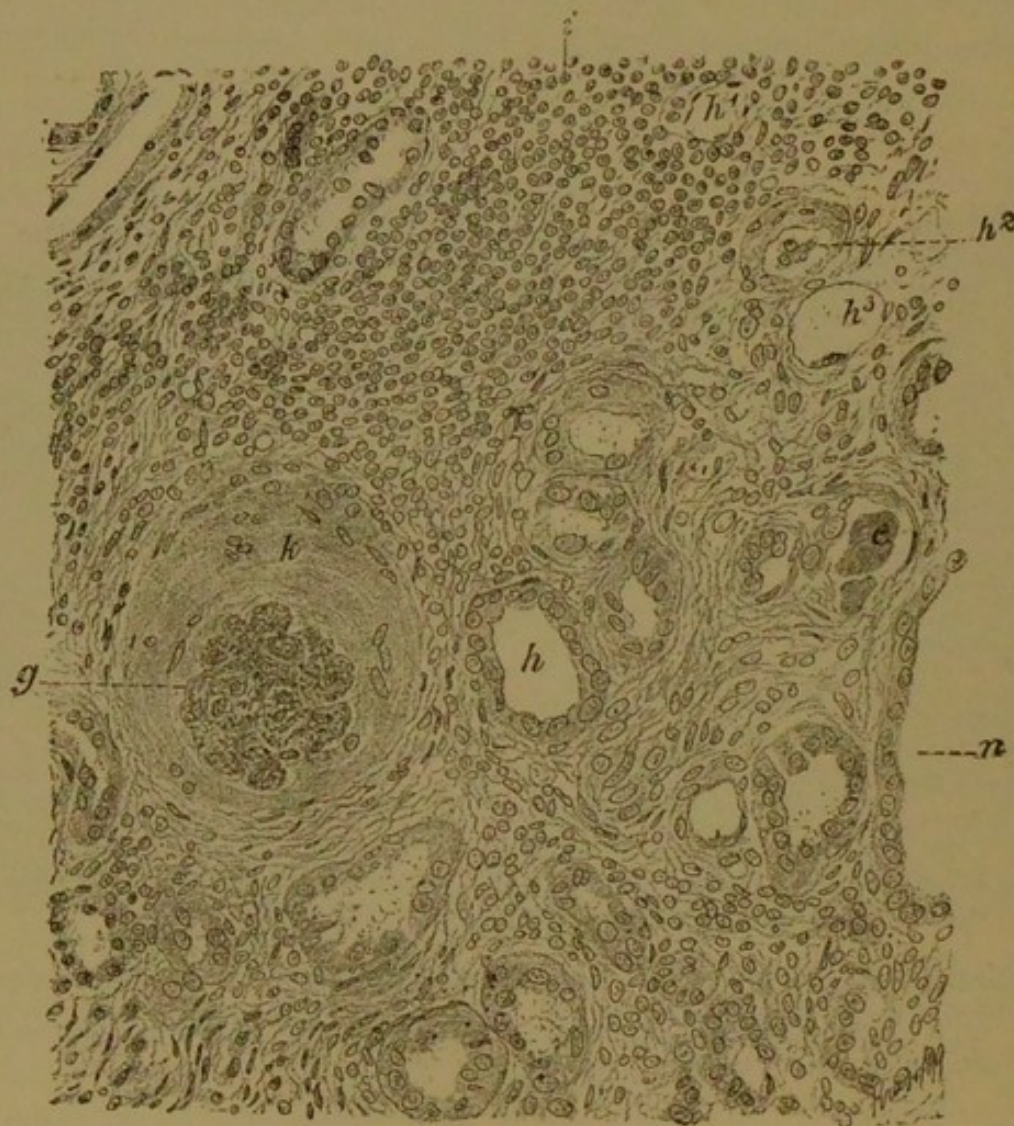


Amyloid degeneration in the kidney. *a, b.* Glomerular vessels, still permeable. *c, c₁, c₂.* Amyloid vessels; at *c₁* the lumen can still be traced. *d.* Amyloid capillaries of the stroma. *f.* Tubule. *e.* Artery. $\times 40$.

Amyloid degeneration may be part of a general change of this nature, or local in the kidney, and in the latter form it often accompanies chronic inflammatory processes. The part affected is most often the glomerulus, certain coils of its vessels and then the entire arterial tuft becoming obliterated, and the tubule connected with it, deprived of its blood and its function, suffering fatty degeneration. From the glomeruli the amyloid process involves the basement membrane of the tubules.

while the parenchyma may for a long time be spared. The tubules in the atrophic places are small with a narrower lumen and flattened epithelium, and may contain hyaline or waxy casts. Between them there is granulation tissue in various stages of proliferation and contraction, and in many places the tubules are lost and only fibrous tissue remains. The glomeruli suffer hyaline changes in a few, and then

FIG. 265.



Chronic interstitial nephritis. *h, h²*. Tubules without epithelium or with atrophic and desquamated cells. *i*. Stroma between them, infiltrated and proliferating. *g*. Degenerating glomerular tufts. *k*. Thickened hyaline capsule. *n*. Normal wide tubule. $\times 250$.

in many of their vessels, which become impermeable, fibrous hyperplasia constricts their vessels at the hilum and invades their cavities, fusing with the denuded capsule, and the end of the process is the conversion of the glomerulus into a homogeneous mass of fibrous tissue. These lesions have their main seat in the cortex, where they alternate

with islands of tissue which is little affected or in fatty degeneration. Both arteries and veins also suffer thickening of their walls in the course of time.

In the gross the kidney of chronic interstitial nephritis may be reduced one-half to two-thirds in size, it is increased in consistence, the fatty capsule may be increased, the fibrous capsule is thick and adherent. After removal of the capsule the kidney appears anemic, beset with grayish-yellow granules, rounded, and of various sizes, and the depressed portions of redder color give the surface an irregularly mottled look. Small whitish points corresponding to destroyed glomeruli may be found on the surface. Small retention cysts are very common, and may be numerous. On the cut surface the cortex may be reduced to 1 to 2 millimetres, and specially contracted parts occur. The pyramids may be short and the pelvis widened.

Both kidneys are uniformly affected as a rule. The producing cause of the lesion may be an attack of acute nephritis with an infectious disease, disturbances of metabolism as gout, and chemical action as from alcohol and lead.

The long clinical course and the relatively few clinical symptoms may be explained by the slow development of the atrophic foci and the retained function of the parts between. Hypertrophy of the heart aids by increased arterial pressure in the excretion of the urine. In many cases the daily quantity of urine is enormous, a fact not yet clearly explained. In the end the kidney becomes insufficient, and the cardiac compensation is lost, and the symptoms of edema, albuminuria, retinitis, and uremia develop.

Chronic parenchymatous nephritis may pass over into chronic interstitial nephritis, and this is called the secondary contracted kidney, as distinguished from the primary form, which begins as already described.

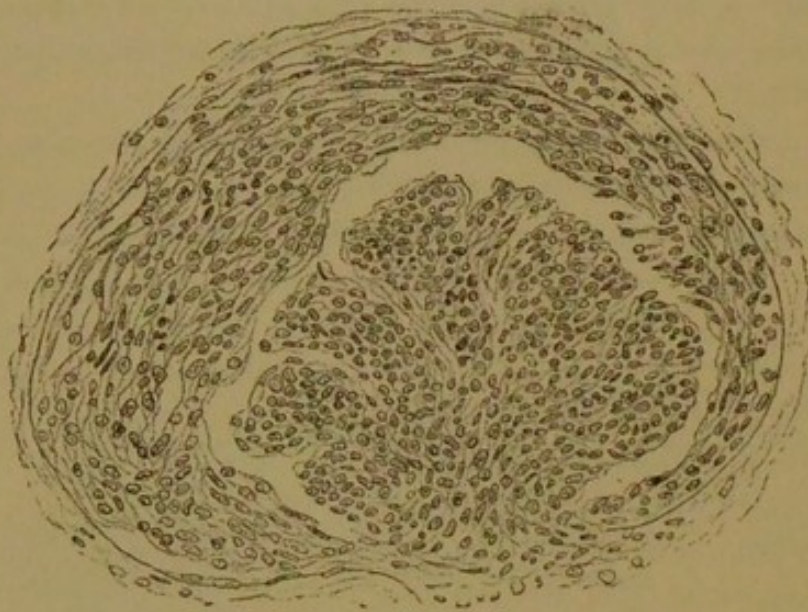
Other combinations may occur. Amyloid granular atrophy may accompany marked degeneration of this variety, but usually amyloid lesions accompany the inflammatory lesions.

FIG. 266.



Glomerulus in degeneration. Thick hyaline capsule tightly applied to the tuft, its cavity lost, some vascular coils hyaline (darker); externally loose connective tissue. $\times 350$.

FIG. 267.



Growth of connective tissue into the capsule of Bowman from the hilum, the original limits as a darker line. $\times 350$.

Renal Cysts.

Colloid cysts result from the production of such material by the epithelium of diseased tubules. Their contents may be gelatinous or dried, yellow or brownish matter. They are common in chronic inflammation, especially in the arterio-sclerotic atrophy.

Retention cysts are common with chronic interstitial nephritis, contain a thinner fluid, and are due to cicatricial occlusion of renal tubules. If confluent they may attain a large size.

Other cysts appear to be small papillary adenomas, and these, like simple retention cysts, may occur in apparently normal kidneys. Other cases present large cysts which may leave but little parenchyma between them, and may affect one or both kidneys. They are usually a congenital anomaly.

Urinary Stasis—Hydronephrosis. Various obstacles may interfere with the outflow of the urine from the kidney. Urinary calculi in the pelvis, the ureter, or at its entrance into the bladder, dislocation of the kidney, and folds or twists in the ureter, hypertrophy of the prostate, scars and tumors which press upon various portions of the canal, carcinoma of the uterus invading the ureters, pregnancy with compression of these tubes, and congenital conditions, all may lead to hydronephrosis. The result is dilatation of the renal pelvis and perhaps of the whole ureter also. The pressure flattens the papillæ, dilates the calyces, and causes atrophy of even the cortex at last.

The glomeruli show all stages of atrophic degeneration, and the epithelia of the tubules are flattened; indurative processes make a granular surface, and still further reduce the size of the organ. At last the kidney may be nothing but a thin-walled sac, and continued secretion of mucous fluid may enlarge it many times beyond the normal size. The fluid, at first urinous, becomes more and more simply hydropic or contains fatty and colloid material.

Concretions.

Deposits of various materials from the circulating blood are bound up with the function of the kidney. Such precipitates are common in the straight collecting tubes and less often in the stroma, and are sometimes called infarcts.

1. **Uric acid infarcts** form in the newborn after the second day, often in connection with slight icterus, and appear on the surface of the pyramid as converging lines of yellowish color, which consist of urate of ammonia. Microscopically there are granular and spiculate masses in the tubes which dissolve with hydrochloric and acetic acid and leave uric acid crystals after evaporation of the solution.

2. **Calcium salts** make such deposits in the aged, frequently associated with calculi in the renal pelvis. Addition of hydrochloric acid dissolves these precipitates with formation of gas. Slight degrees of the condition are common. It is fairly constant in poisoning with bichloride of mercury and other chemicals, and with metastasis of bony material in osseous destruction of various kinds.

3. **Precipitates of urate of soda** make whitish points and stripes in both cortex and medulla in gouty subjects.

4. **Bilirubin** infarcts in the medulla are common with uric acid precipitates of the newborn. The pigment occurs as needles or tables. Granular biliary pigment is found in the adult kidney with chronic icterus and acute yellow atrophy; it is usually crystalline.

5. **Hemoglobin** infarcts are composed of masses and granules of brownish amorphous or crystalline nature, arranged in spots and lines throughout the kidney, especially in the medulla. This is observed in poisoning by potassium chlorate and in hemoglobinuria.

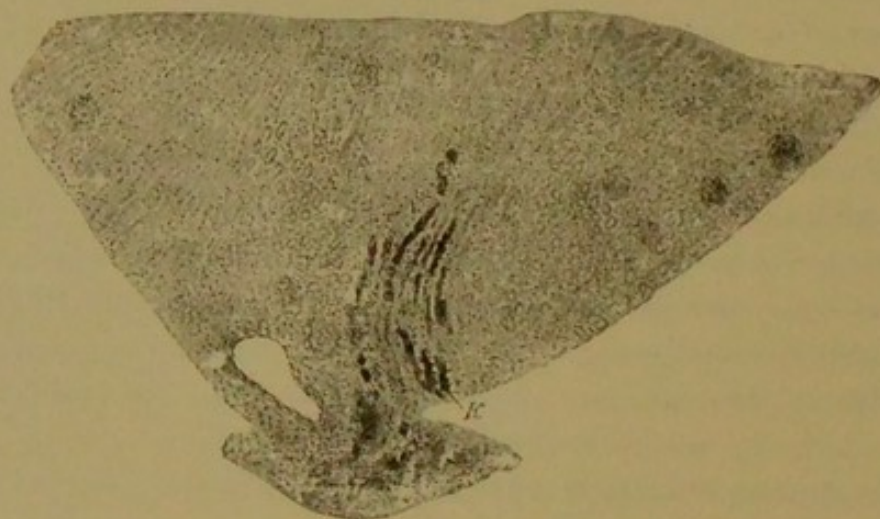
Suppurative Nephritis.

Pyogenic organisms may reach the kidney through the blood, from the urinary passages, and from the vicinity of the organ (paranephritis).

Arriving by the blood the organisms usually lodge in the glomeruli and capillaries of the cortex, and produce small abscesses of the size of a pin's head, numerous and surrounded by a ring of hyperemia. Parenchymatous degeneration of the organ is commonly present, simple or inflammatory. These abscesses are found with pyemia, ulcerative endocarditis, and other infections. In the case of malignant endocarditis not only bacteria but large infected emboli may be carried to the kidney. The resulting infarcts quickly suppurate, and the large abscesses are found especially in the cortex; it is not always clear whether the abscesses depend on micro-organisms or on softened infarcts.

Another form of hematogenous infection makes yellowish lines in the pyramids, and the tubes there are filled with bacteria, leucocytes,

FIG. 268.

Caseous tuberculous nephritis. k. Renal tubule with caseous contents. $\times 12$.

and detritus. Probably the lesion is the result of excretion of bacteria by the kidneys, the germs lodging in the collecting tubes and setting up inflammatory reactions. This is called *nephritis papillaris mycotica*.

When the pyogenic organisms come from the urinary channels, the commonest source is a cystitis or ulcerative inflammation of the ureters, or a neoplasm of the tract which is breaking down. In all cases the mucosa of the pelvis is attacked, making a suppurative pyelitis, and from this a pyelonephritis develops which resembles the mycotic papillary lesion. With a common origin hydronephrosis and this form may coincide, as with calculi or carcinoma of the base of the bladder.

Infectious Granulomata. Tuberculosis of the kidney follows general infection or local disease of other organs, as the lungs, and is due to infection through the blood. Miliary and conglomerate tubercles result in the kidney.

Miliary nodules on the cortex and medulla accompany general infection, and less often pulmonary phthisis.

Less frequently conglomerate tubercles are associated with tuberculosis of the lungs, resembling the caseous miliary nodules, and resulting from fusion of many of these. They are commonest in the cortex, may be fibrous at their edges, and surrounded by fresh scattered tubercles.

A third form of renal tuberculosis begins in the papillæ or the calyces and spreads along the urinary tubules toward the cortex. There are then fewer circumscribed tubercles, but lines, and later masses, of caseous material in the medulla, which may join and reach a large size. This is called papillary tuberculous nephritis. The mucosa of the calyces and ureters may be involved in caseous ulceration, and in time the pelvis becomes wide and necrotic, with more or less necrotic contents—*phthisis renalis tuberculosa*.

Possibly in many of these cases the infection comes from the ureters or lower in the tract, but in most cases it results from hematogenous infection, perhaps during excretion of the bacilli. The urine regularly contains the bacilli in these lesions.

Syphilis of the kidney may occur as gummata or granular atrophy from disease of the vessels. Amyloid changes are common with it.

Tumors. **Epithelial carcinoma** is uncommon in the kidneys, most of the neoplasms considered as such are really hypernephroma, sarcoma, or endothelioma. Fibroma is also common.

Many of the *adenomata* of the kidney begin in scattered portions of adrenal tissue, which usually lie under the capsule and make small circumscribed tumors which resemble the cortex of the adrenal. Microscopically this resemblance is demonstrable, and the cells are apt to be so fatty at times as to resemble lipoma. The name *struma lipomatodes aberrans renis* (Grawitz) has been given to these neoplasms. They may resemble angioma because of their dilated vessels. The tumor may reach a large size and become malignant, breaking into the veins and forming metastatic growths. Other tumors which resemble these in the gross are composed of cylindrical endothelia, investing blood spaces which are filled with blood, and fatty degeneration of the cells is frequent.

Congenital *adenosarcoma*, or the same tumor developing early in life, is not rare. It may be due to scattered germinal tissue of the embryo, or be derived from the kidney by metaplasia. Metastatic carcinoma and sarcoma occur, and fibromyoma of the capsule is at times encountered.

Parasites. *Echinococcus*, *cysticercus cellulosæ*, and *filaria* are at times observed in the kidney, the latter passing out with the urine.

B. DISEASES OF THE URINARY PASSAGES.

Doubling of the renal pelvis and of the upper end of the ureter, entrance of the ureter into the seminal vesicle, or the urethra or other abnormal places, congenital hydronephrosis from stricture of the ureter, imperforate and bent ureters, and those provided with valves, are the commonest malformations.

Concretions in the renal pelvis may be formed there or excreted from the kidney, and if large they may reproduce the branching calyces like a piece of coral. (See *Calculi*, p. 432.) Such concretions cause pyelitis calculosa and pyelonephritis, paranephritis, and perforation into the intestine; if on both sides, hydronephrosis and uremia may result.

Tumors are usually carcinoma from the uterus and elsewhere, which invades the ureters secondarily, and a large percentage of women with uterine cancer die thus of retention and uremia.

Bladder.

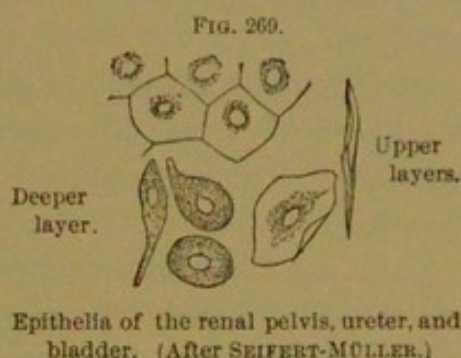
Hemorrhage may be due to injury of the vesical wall by calculus, or the presence of a papilloma or carcinoma, or fracture of the pelvic bones and injury to the bladder, or hemorrhagic diatheses and vesical hemorrhoids.

Catarrhal Inflammation. Acute cystitis is often the result of decomposition of urine by the action of bacteria, as the *bacillus proteus*. They enter the bladder with the introduction of instruments. Chemical substances used for washing the bladder, or excreted, as cantharidin, may also cause the lesion. Other bacteria come from the urethra and irritate the mucous membrane or set up fermentation of the urine, and thus cause cystitis. Retention of urine is very apt to be followed by such fermentation.

With acute cystitis the mucosa is hyperemic, often ecchymotic, the epithelium is cloudy and desquamating and proliferating, and its cells

are found in the urine mixed with pus cells and many bacteria. The reaction of the urine may be acid or alkaline. With purulent catarrh a thick, ropy mass of altered pus cells is found in the alkaline urine, together with crystals of triple phosphates and ammonium urate.

The chief cause of **chronic cystitis** is retention from diminished urethral lumen, calculi, or paralysis of the bladder from central nervous lesions; in all of these cases fermentation occurs in the stagnant urine by the entrance of bacteria, and these set up inflammation. Chronic cystitis accompanies vesical tumors also. The mucous membrane becomes thick, indurated, and pigmented, and papillary outgrowths occur. Erosions and deeper ulcers may accompany the process, while hypertrophy and dilatation of the bladder are common. The secretion from the inflamed bladder is mucopurulent, and the pus cells are altered into a slimy mass.



Diphtheritic cystitis has the same characters as any such inflammation of a mucous surface, and leads to similar destruction. It may occur with trauma, calculi, and in the course of severe general diseases.

Phlegmonous cystitis and abscesses in the bladder walls may follow purulent catarrh or diphtheritic inflammation, or ulcerating neoplasms, or injuries. Perforation into the peritoneum and adjacent structures, pericystitis and paracystitis, and various fistulae may be the results.

Urinary Calculi. Normal urine, though clear when passed, may soon deposit a sediment which varies with its composition. The uric acid occurs as neutral sodium urate in normal urine, and is easily soluble in water. After standing, a so-called acid fermentation splits this into acid sodium urate and uric acid. Alkaline fermentation may occur in the bladder with pathological conditions, and results in splitting urea into carbonic acid and ammonia. The ammonia forms triple phosphates with magnesia, and ammonium urate with uric acid. The important sediments are:

1. Uric acid in acid urine, as crystalline forms of brownish color, "whetstone" and other shapes.
2. Acid sodium urate, red amorphous deposit, dissolved by heat and addition of potassium hydrate, in condensed urines of fever. The urine may be turbid when passed, or become so on cooling.

3. Ammonium urate, in "thorn apple" forms from decomposed urine. These three sediments give the murexid test.

4. Calcium oxalate, in envelope-shaped crystals, soluble in hydrochloric acid, insoluble in acetic acid, occurs in both acid and alkaline urines.

5. Calcium carbonate occurs in human urine, but in small quantity, as small spheres or biscuit forms, which dissolve with acids and form gas.

6. Calcium diphosphate and triphosphate, the former in neutral or weakly acid urine as colorless wedges with slanting bases, often grouped. The latter salt occurs in alkaline urine as a fine amorphous powder.

7. Ammonio-magnesium phosphate, triple phosphate, as large prismatic coffin-shaped crystals, soluble in acetic acid, characteristic of alkaline fermentation.

These sediments, beside the renal deposits mentioned, may form stones in the renal pelvis (*nephrolithiasis*), or in the bladder. The larger are called urinary calculi, the smaller gravel. All have an organic albuminous material which holds the mineral together. Such concretions form about dead epithelium, clots, mucus, or foreign bodies of various kinds, as fragments of catheters, lead-pencils, bits of bone, etc.

Primary calculus formation occurs in an undecomposed urine (usually contains uric acid and urates), and when the stone is increased in size by other deposits from a fermented urine, as ammonium urate and triple phosphates, it is called *secondary calculus formation*. The calculi are often thus distinctly laminated. Metamorphosed calculi are those which are altered by alkaline urine, which removes certain constituents and replaces them with others.

The vesical calculi may form in the bladder or be carried down from the renal pelvis. In shape they are oval, round, and irregular. General diseases, with impaired metabolism, and especially the uric-acid diathesis, favor the formation of calculi.

The most important forms are:

1. *Urate calculi*, of uric acid and its salts, hard, heavy, smooth, or rough, yellow or brownish, concentric layers, give murexid test; pure uric acid stones occur in acid urine.

2. *Oxalate calculi*, of calcium oxalate, mulberry or thorny, cause bleeding, may thus be covered with dark fibrinous matter.

3. *Phosphate calculi*, of calcium phosphate and triple salts, seldom form primary stones, but often deposit about uric and oxalate nuclei

after decomposition of urine, less dense than the former kinds, chalky, friable.

4. *Calcium carbonate*, rare, white, and chalky, common in vegetable feeders.

5. *Cystin*, pale yellow, smooth or granular, round, waxy, transparent.

6. *Xanthin*, white or brown, amorphous fracture, waxy on friction, in alkaline urine.

Large stones may be found at autopsy which have given no symptoms during life, but usually vesical calculi produce catarrhal cystitis, ulcerations, ascending pyelonephritis, hematuria, retention of urine, dilatation and sacculation of the bladder, and hypertrophy of its walls. Stones in diverticula from the bladder may become encapsuled and excluded from its cavity by inflammatory adhesions.

Dilatation of the bladder occurs with urinary stasis from temporary or permanent interference with the lumen of the urethra, or in a rapid form, with thinning of its walls, from central nervous lesions. Hypertrophy of its muscular layers is usually functional, and occurs with obstacles to the expulsion of urine, but it may follow the irritation of chronic cystitis and frequent straining efforts at urination. The bundles of muscular tissue make prominent trabeculæ under the mucosa.

Separation of the fibres of muscle allows the mucosa to protrude between them, and thus diverticula form. These occur with obstacles to the outflow, and may be multiple.

Vaginal cystocele is the prolapse of the wall of the bladder into the vagina from traction of the prolapsed uterus, or simple weight of the filled bladder. Inversion of the bladder occurs when its upper pole bends into the lumen of the viscus and appears at the internal or external meatus.

Traumatism may cause hemorrhage from the bladder. Overdistention may lead to rupture. Obstetric operations may cause pressure necrosis of part of the wall. Any lesion of the bladder may lead to urinary infiltration of its wall and the surrounding tissues, and this produces severe purulent inflammation in the pelvis and diffuse peritonitis. From injuries received during parturition vesical fistulæ may result, which open into the vagina or uterus, and ulcerations within the organ may have similar consequences.

Tuberculosis is usually connected with similar lesions of other parts of the urinary system, and does not differ from any such process in a mucous surface.

Among tumors of the bladder, papilloma and papillary epithelioma deserve mention because of the cystitis and severe hemorrhages which they excite. They are benign themselves, but lead by transitional forms to carcinomata. Vesical carcinoma may be either nodular or papillary, and is distinguished from benign papilloma by its extension to deep tissues, rapid ulceration, and invasion of other organs. They are unusual tumors, and are most often secondary to uterine and prostatic cancers. The ulceration leads to the establishment of various fistulæ between the bladder, uterus, vagina, and rectum.

Urethra.

Urethritis is in most cases of gonorrheal origin, and while limited to the urethra in the male, the vulva, vagina, and endometrium in the female, may become inflamed by the gonococcus. Intense superficial suppuration, with the secretion of thick yellowish-green pus, results from the specific action of the coccus, and the discharge may be mixed with blood. Severe infiltration of the subepithelial tissue occurs. Although often confined in the male to the fossa navicularis, the inflammation may involve the posterior urethra, the bladder, Cowper's glands, the prostate, vas deferens, epididymis, and testis. Mixed infection with pyogenic organisms causes periurethral abscess, and this may open into the urethra or perforate the corpus cavernosum. In the female later results may be salpingitis and pelvic peritonitis, and abscess of Bartholin's glands. Gonorrheal conjunctivitis of the newborn is due to infection from a specifically inflamed parturient canal. In some cases arthritis, endocarditis, and myelitis may complicate the local inflammation, but these effects are seldom to be considered as the work of the gonococci themselves, but rather due to mixed infection with other pyogenic forms.

The passage of an acute urethritis into a chronic gonorrhea is relatively frequent, and in men the posterior urethra is commonly the site of the lesion. The secretion lessens in quantity and becomes more mucous, the cocci diminish in number or disappear, and are to be found only in the so-called "clap-threads." A complication which is often observed with gonorrhea and is important in its results is stricture of the urethra, from scars in the mucosa and submucosa. These contracting fibrous tissues narrow the lumen of the urethra, cause urinary stasis and retention, cystitis and dilatation of the bladder, and at times pyelonephritis. At the site of the scars the cylindrical epithelium becomes flat and corneous.

Non-gonorrheal urethritis may be a symptom of severe diseases, or come from near-by inflammations, as vaginitis.

Other lesions of the urethra include chancre, ulcer molle, tuberculosis, rarely lupus, and papillomata from the irritation of gonorrheal secretions on the skin and mucosa.

Other strictures of the urethra follow periurethral abscess and diseases of the prostate.

Urethral injuries most often depend upon foreign bodies, as catheters, and the posterior portion may be torn, with resulting false passages and infiltration of urine. During parturition the urethra of the mother may suffer spontaneous or operative injuries, especially necrosis following long severe pressure.

Cowper's glands may present simple swelling, suppuration and induration, commonly associated with urethral diseases.

The Adrenal Bodies.

Simple atrophy, fatty and amyloid degeneration, often affect these structures, the latter with general lesions.

Circulatory disorders include hemorrhage from local and general causes. Inflammations are unusual.

Tuberculosis of the adrenals is an occasional miliary infection, more commonly a diffuse fibrocaseous inflammation which enlarges the part and also softens and destroys it. This is seldom a primary lesion, but follows pulmonary tuberculosis, and is bilateral. It has a relation to Addison's disease (p. 261).

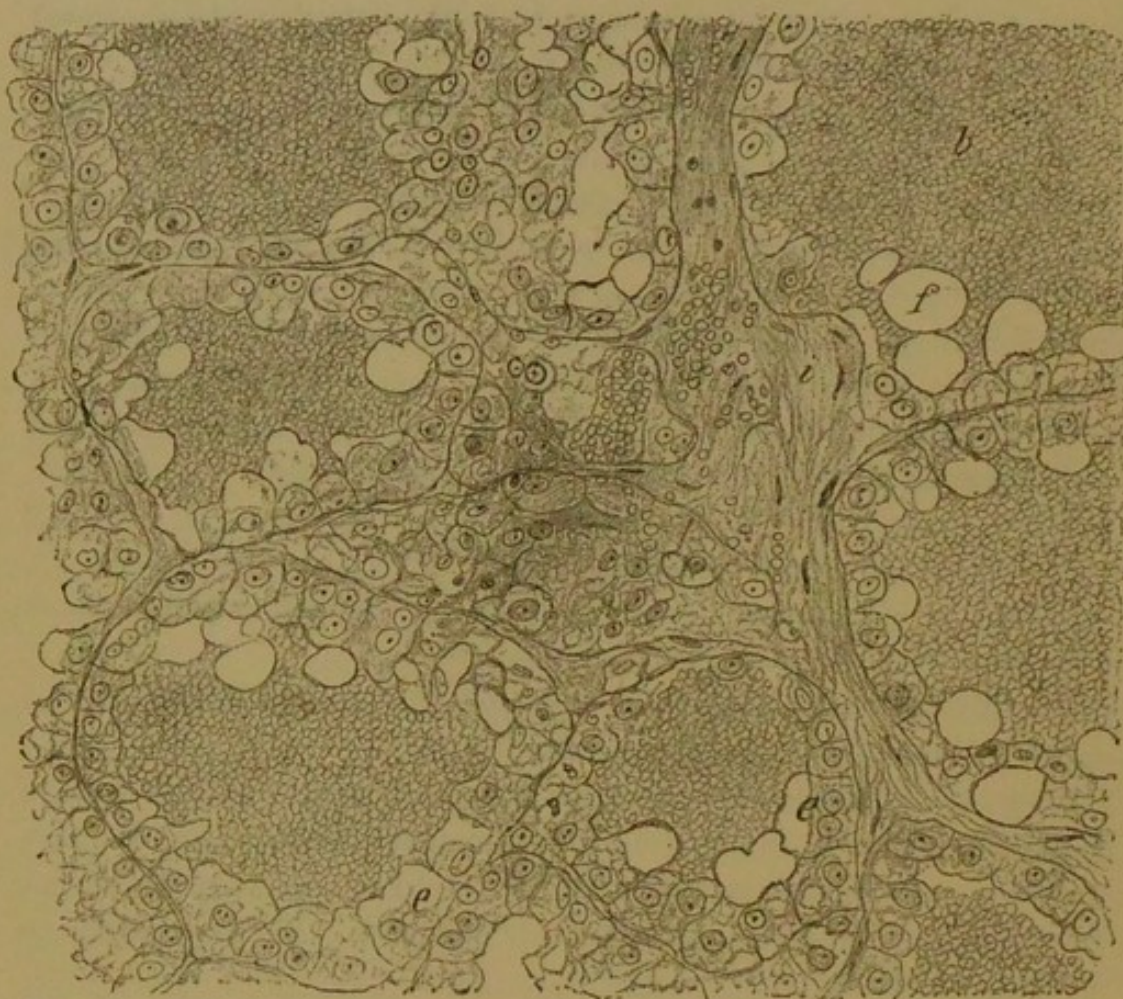
Tumors of the adrenal may be nodular hyperplasia, or adenoma, or struma, as circumscribed masses of the size of a cherry, which in the gross and microscopically reproduce the structure of the organ.

The adrenal is divided into cortex and medulla, the former displaying radiate markings and being of a yellow color, the latter having a grayish-red color. Microscopically the cortex consists of layers of epithelial cells with connective tissue between them, the upper called the *zona glomerulosa*, where the cells are in nests; the middle called the *zona fascicularis*, with cells in columns; and the inner in meshwork and called the *zona reticularis*. In the adult fat droplets are found in the middle layer within the cells.

The tumor known as struma, or hypernephroma, also consists of epithelial cells like those of the normal cortex, and like them may contain glycogen. Cavernous spaces may occur, filled with blood, and these tumors may be very malignant. Accessory adrenal glands some-

times occur in other abdominal organs and may be the starting point for hypernephromata.

FIG. 270.



Hypernephroma. *e*. Large epithelia from which fat has been extracted, leaving vacuoles, the cells arranged as in a gland. *b*. Red blood cells. *f*. Large spaces in which fat was held. *i*. Stroma.

Small-celled and large-celled sarcoma, carcinoma, and endothelioma, are also met with in the adrenals. Here and there a tumor occurs which is known as glioma.

CHAPTER XII.

DISEASES OF THE NERVOUS SYSTEM.

A. CONGENITAL ANOMALIES.

THE severest form of malformation, *cranioschisis* and *rhachischisis* have been noticed. Hernias of the central organs and their membranes may occur at the back of the head, the nasal suture, the base of the skull, along the spinal canal and elsewhere, the most important forms being as follows (pp. 187, 190):

1. **Hydromeningocele.** The sac consists of pia mater and is filled with fluid; the brain and cord do not enter the hernia. On the spinal column the dura may be one of the coverings.

2. **Encephalocele** and **myelocele** imply the protrusion of parts of either the brain or the cord. In most cases there is hydrops of the cerebral ventricles or the central canal of the cord. The wall of the sac contains nervous tissue, and in this case the protruding part is called *hydrencephalocele* or *hydromyelocele*, and the prolapsed organ is very rudimentary, forming simply a layer on the inner surface of the sac.

3. **Myelomeningocele.** With partial *rhachischisis* and simply an *area medullovasculosa* on the dorsal aspect of the open meninges, fluid may collect between the dura and arachnoid or between this and the pia, so that the pia with its rudimentary cord forms a hernia and the sac is formed by the membrane, having the nervous tissue on its outer surface. In this form the central canal of the cord both above and below the hernia opens on the dorsal aspect of the rudimentary cord, and hence can be entered directly from the exterior.

Certain anomalies are connected with lesions of the bony parts, as early closure of the sutures (**microcephalia**), by which the capacity of the skull is too small for the normal growth of the brain. Mechanical obstacles then cause a hypoplasia of the whole brain or parts of it. Internal causes not clearly understood may also produce hypoplasia, and fetal softening and hemorrhages may lead to the same result.

Micrencephalia, or smallness of the brain, may reduce the entire organ or parts of it, and certain lobes and structures may be lacking

from agenesis. External hydrocephalus *ex vacuo* may accompany such defects. (See *infra* and Chapter XIII.)

Porencephalia is a superficial defect, involving the cortex or reaching into the ventricles as a conical fossa, its walls lined with pia and its lumen filled with fluid and covered by arachnoid. Fetal hemorrhages and softening may be the explanation of some of these cases.

Various anomalies of the central nervous organs may be associated with idiocy and cretinism and psychoses, but there is no constant lesion with any special form.

Micromyelia, or small size of the cord, and hypoplasia of certain tracts may be observed, and the latter may be the foundation of later diseases. Congenital asymmetry of the cord, doubling of the cord, and heterotopic arrangement of the white and the gray substance have been described. Some of these are artefacts, due to imperfect methods of removal post-mortem. An important anomaly of the cord is hydro-myelia. (See Chapter XII., C.)

B. DEGENERATION AND ATROPHY ; SCLEROSIS.

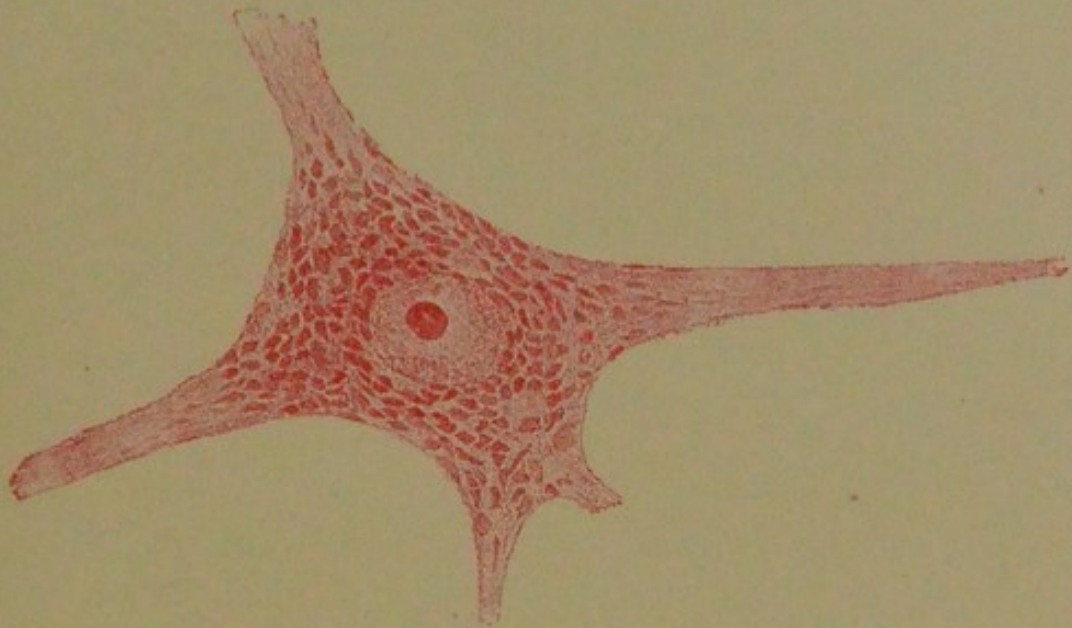
In the nervous system there are various diseases whose essential factor is the loss of nervous elements, both fibres and ganglia, while the neuroglia is either passive or increases. Lesions of this kind may affect the white substance or the gray. Degeneration is a term implying the destruction of the fibres and the collection of fatty detritus in their place. The medullary sheaths are broken and lost, and the axis cylinders show irregular swellings and division into segments, which then become dissolved into granular detritus.

The ganglion cells in the gray matter present peculiar forms of degeneration. The staining properties of both nuclei and protoplasm are altered, the cell body swells and becomes finely granular or fatty, pigment collects in it, and at last it calcifies. In severe lesions the nucleus suffers karyolysis or karyorhexis and is lost. The result of the process is atrophy of the cell, diminution of the cell body, and loss of its processes, or complete destruction. The reticular neuroglia, in whose meshes normally the ganglion cells and the fibres lie, appears as open spaces, filled at first with fatty material, and later by proliferation of the neuroglia, which converts the place into a mass of finely fibrillar tissue.

Macroscopically such lesions, if of any extent, appear of a yellow color as contrasted with the normal portions, so long as fatty fibres and granular cells are present. With the resorption of the softened

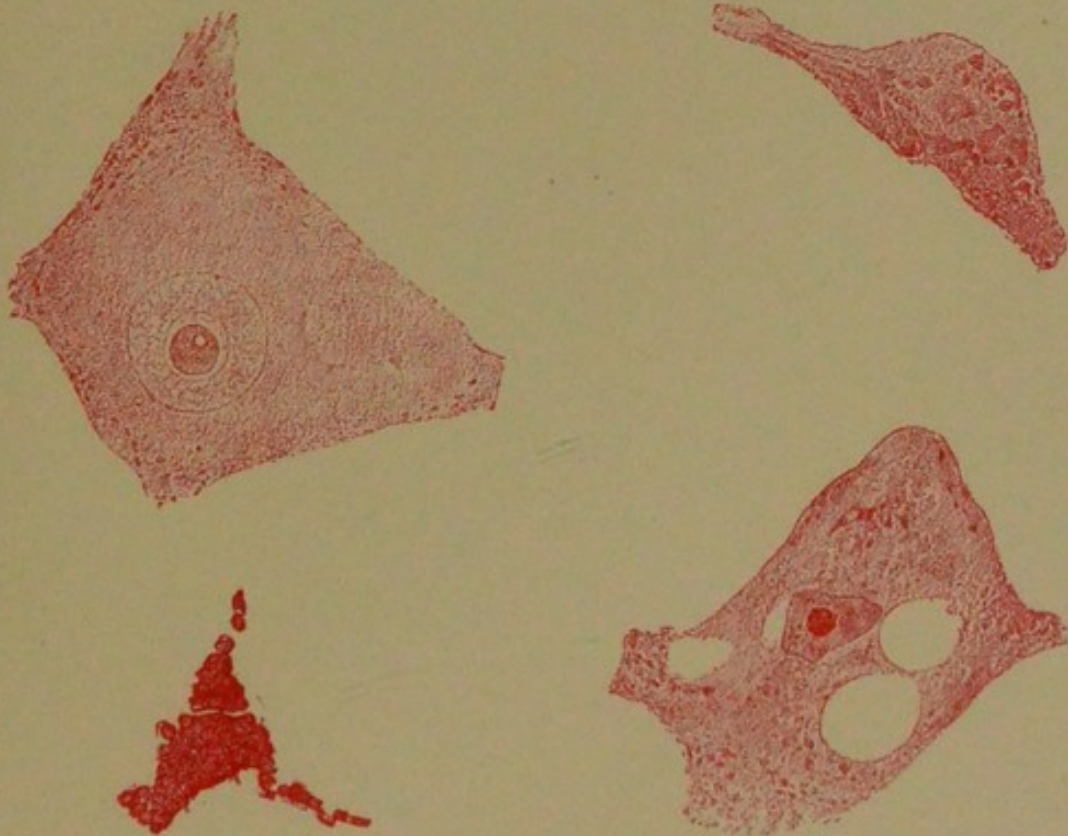
PLATE XXV.

FIG. 271.

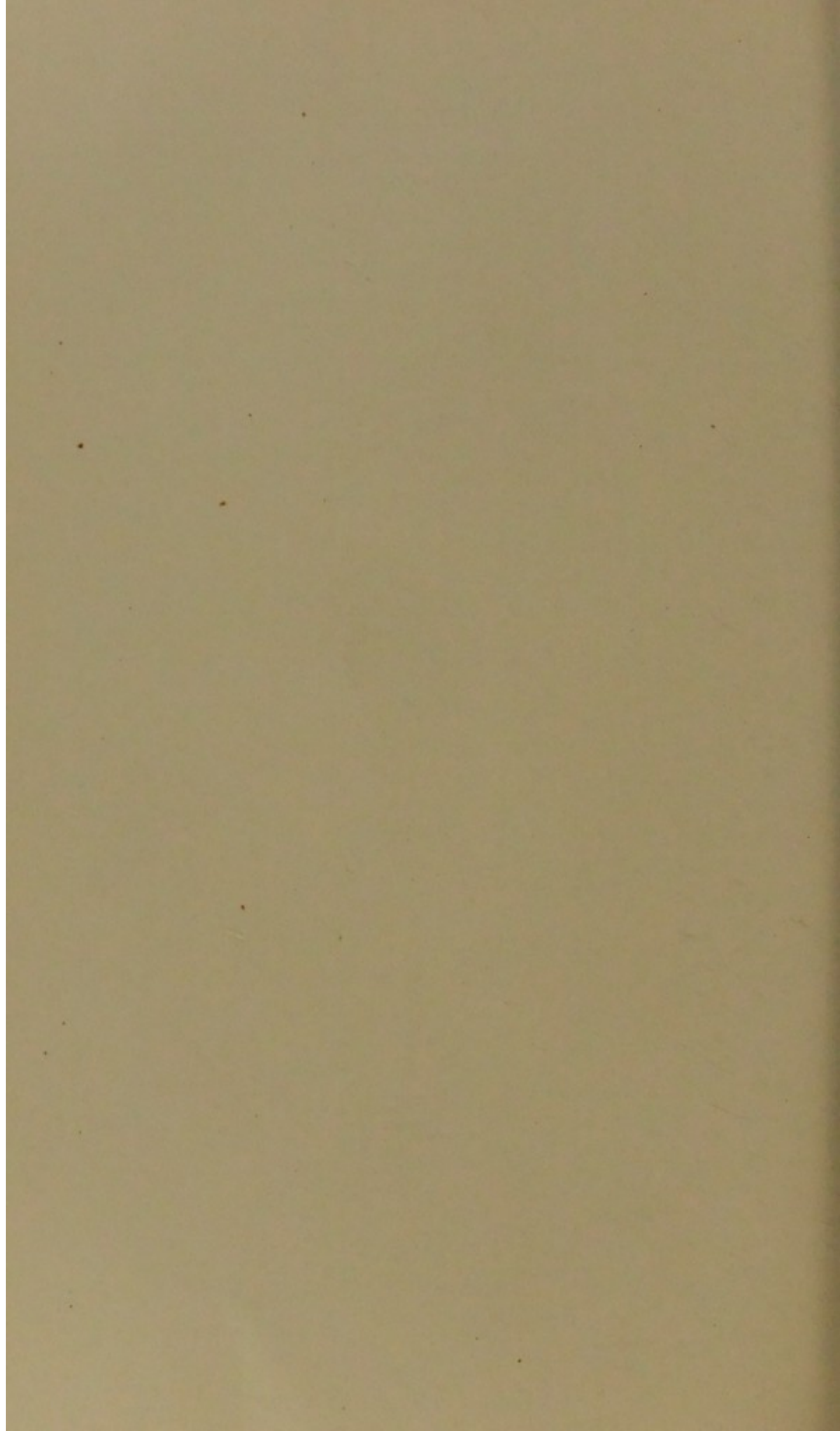


Cell from the Anterior Horn, Human Cord. Stained with Neutral Red.

FIG. 272.



Forms of Degeneration of Ganglion Cells.



tissues the color changes to a gray, and the consistence of the part becomes firmer. This is called sclerosis, or, in the white substance, gray degeneration, and it is a form of atrophy.

Other forms of atrophy may occur without fatty degeneration at any stage. If a portion of the fibres of a part slowly become fewer and more slender, and the part itself also shrinks, and the ganglion cells lose their processes and dwindle in size, it constitutes one form of atrophy, and the consecutive proliferation of the neuroglia is usually not observed.

The causes of atrophy are various. In some cases it is simply a senile involution, in others imperfect nutrition from diseases of the vessels, and in others infectious and toxic influences produce the lesion. Inflammatory conditions affect the nervous elements directly and also cause changes in the interstitial tissue, and together with transudation and emigration of leucocytes and proliferation lead to destruction of the nervous elements. Necrosis and fatty degeneration may follow traumatism, concussion, hemorrhage, and severe edema of the tissue. Finally, there is a certain relation and dependence between lesions of the ganglion cells and the fibres connected with them, which is expressed as so-called secondary degeneration and retrograde atrophy.

Secondary Degeneration. The entire nervous system consists of gray centres and tracts of communication, the former acting as points of origin for the latter, and also occurring in their course, chiefly represented by ganglion cells, and the tracts corresponding to medullated nerve fibres. The ganglion cells from which the fibres take origin possess protoplasmic processes—the dendrites. Another protoplasmic process which does not become more slender also takes origin from the prominent part of the ganglion cell, receives the name axis cylinder or neurite, and corresponds to the medullated nerve fibre of a nervous tract. The dendrites and neurites divide into the finest branches, called the terminal tree, and these communicate in all

FIG. 273.

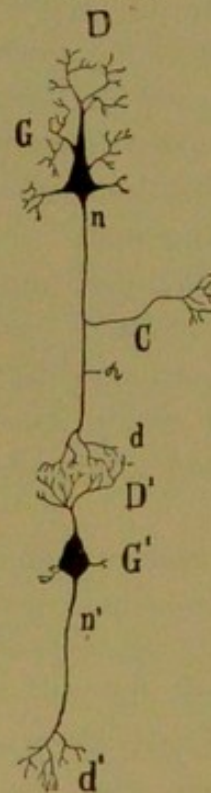


Diagram of two neurons. *G, G'*. Two ganglion cells. *D, D'*. Dendrites. *n, n'*. Neurites. *d, d'*. Terminal branches of the neurites. *C*. Collateral branch.

probability with similar branches from other ganglion cells. Collateral branches from the neurite repeat the branching process. Hence the simplest element of nervous tissue consists of a ganglion cell with its processes, and this is known as a neuron. (Fig. 273.)

It has been learned by experience that when a ganglion cell is injured all the processes suffer, the axis cylinder swells and splits into segments, the medulla is broken up, and fatty degeneration destroys it. This is called Wallerian degeneration. The ganglion cell, therefore, controls the nutrition of the entire neuron of which it forms the central point (trophic influence). When a nerve fibre is cut or injured the section which is separated from its ganglion cell degenerates. Thus in the diagram, section of the neurite at (*a*) would be followed by loss of the part reaching to (*d*), that is, to the processes of the nearest ganglion cell. This is called Waller's law.

Since now the communicating tracts are nothing but axis cylinder processes from ganglion cells, it follows:

1. That destruction of a ganglion cell implies destruction of the fibres originating in it.
2. That interruption of a nerve fibre is followed by loss of that portion which is separated from its ganglion cell.

The portion of the fibre still in communication with the ganglion cell does not remain intact, but suffers a slow and less distinct retrograde degeneration, and the ganglion cell shows a temporary or a permanent atrophy.

The degenerative and atrophic changes discussed vary in their results in the brain and cord according to their localization, extent, and intensity. If the entire brain is involved it is uniformly smaller, weighs less, and fills the cranium imperfectly. If the convolutions are atrophic they are more slender and have a somewhat triangular outline on section, while the sulci are wider. Serous fluid takes the place of the lost substance, and thus we find either external or internal hydrocephalus ex vacuo.

The most important forms of atrophy in the central nervous system are the following:

1. *Senile atrophy*, with general diminution in volume and weight. The cortex is especially reduced and replaced by fluid. The process may not be uniform, and then certain gyri are especially small. This may be explained by the fact that the atrophic changes are dependent upon atheroma, obstruction of vessels, and obliteration of their lumina, with perhaps local softenings in the cortex and cord.

2. *Progressive paralysis* depends in part on chronic degeneration of the cerebral cortex, and usually affects certain portions more than others, as the frontal, temporal, and insular cortex, and the occipital to a slighter extent. The gyri are small, sharpened, and divided by wider sulci. The ventricles are dilated with both external and internal hydrocephalus, and the consistence of the organ is increased. In recent cases the cortex may be spotted with hyperemic areas.

FIG. 274.

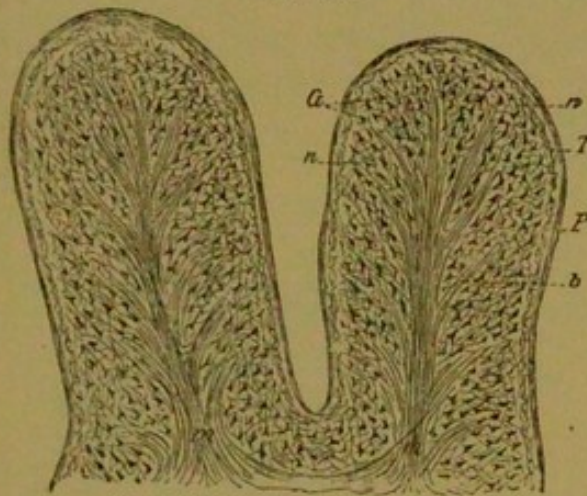


Diagram of two convolutions. *w.* White matter giving off the fibres, *m.* *b.* Branches of medullated fibres to the cortex. *n.* Network of fibres in the cortex. *T.* Tangential fibres. *P.* Pia. *G.* Ganglion cells.

Later on these areas are diminished, light or grayish yellow, and on section the division of the cortex into layers is lost. The pia is usually opaque and fibrous, with adhesions to the cortex, and on removal it tears off particles of nervous tissue. The adhesions are the result of chronic meningo-encephalitis which accompanies the interstitial lesions in the nervous tissue.

Microscopic examination discovers extreme degeneration in the ganglion cells even to complete destruction. The nerve fibres die from without toward the deeper portions. Proliferation of neuroglia and of the cortical vessels, hyaline changes in the intima, diminished lumina, cellular infiltration of the lymph sheaths, and dilatation of the veins, may also be found.

FIG. 275.

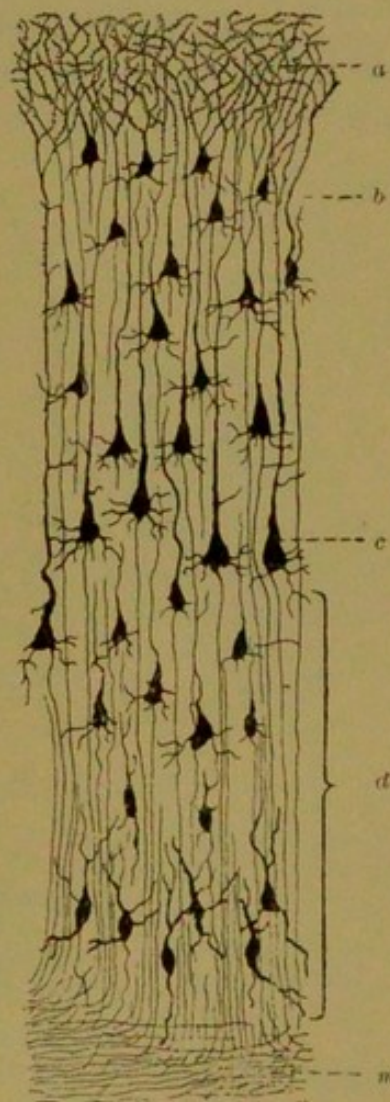


Diagram of the cortex. *a.* Superficial fibres. *b.* Layer of small ganglion cells. *c.* Large pyramidal ganglion cells. *d.* Deeper layer of ganglion cells. *m.* White matter. (After BÖHM-DAVIDOFF.)

FIG. 276.

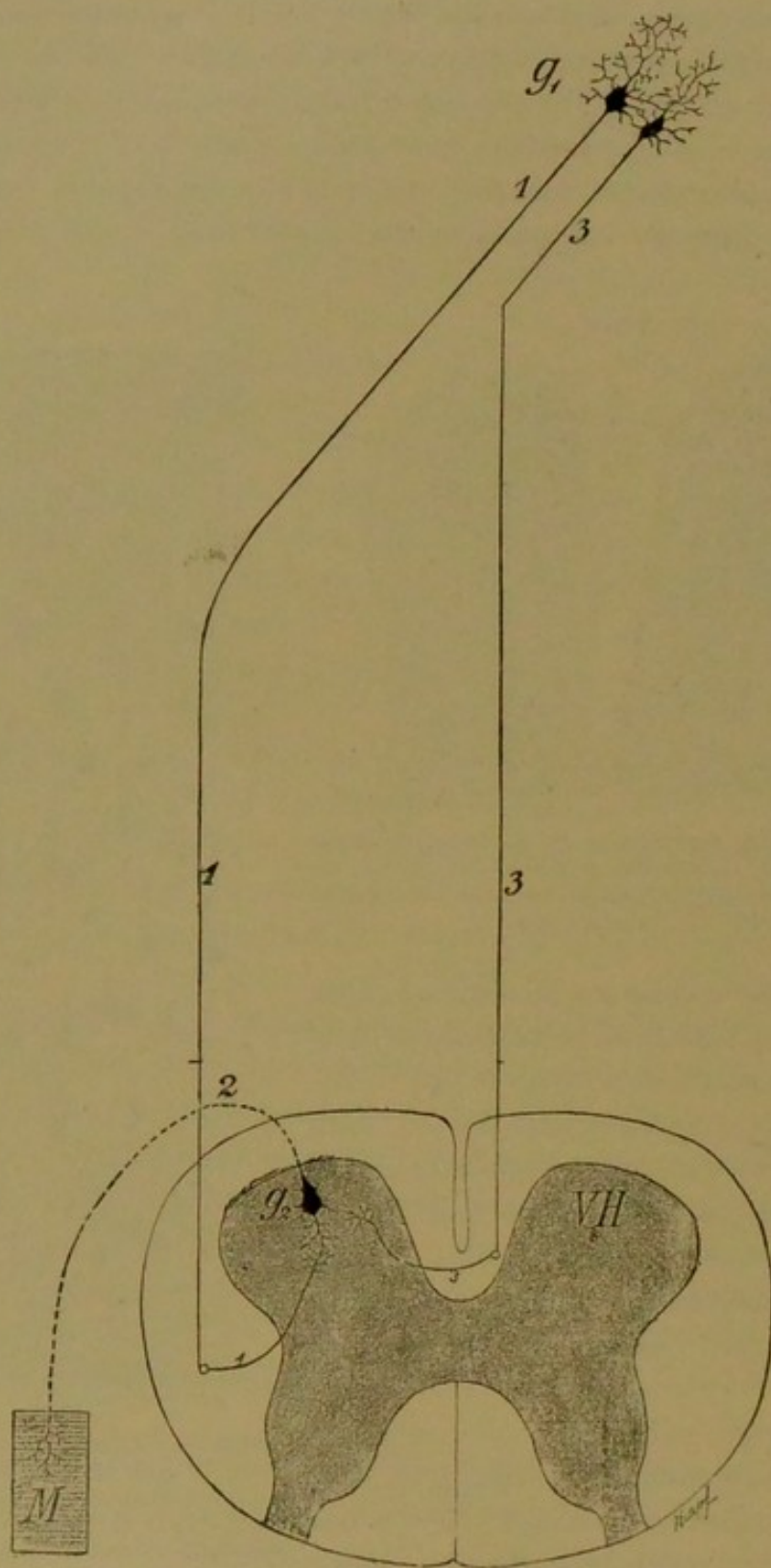


Diagram of the motor tracts. g_1 . Ganglion cells in the cortex of the brain. g_2 . Ganglion cell in the anterior horn of the cord. 1. Lateral pyramidal tract. 2. Motor fibre from anterior horn to anterior root and peripheral nerve. 3. Anterior pyramidal tract. M . Muscle.

Accompanying lesions are pachymeningitis interna hæmorrhagica, and degeneration of the pyramidal tracts and the posterior columns of the cord (tabetic).

As in progressive paralysis, degenerative processes of similar nature accompany chronic epilepsy, tabes dorsalis, carbon monoxide poisoning, and sunstroke.

In rare cases there is a general sclerosis of the entire brain from hyperplasia of the neuroglia, with contraction of the new tissue, diminution in size of the brain, and hydrocephalus. The lesion is common in children and youths, for example, in idiocy.

Secondary Degenerations. 1. **Motor System.** The centres for voluntary motion are situated in the central convolutions of the cortex,

FIG. 277.

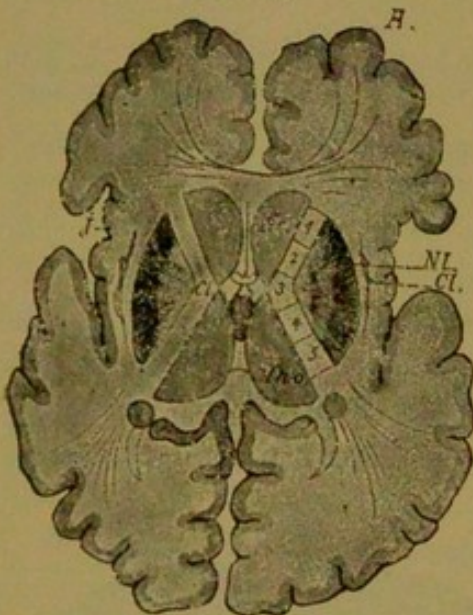


FIG. 278.

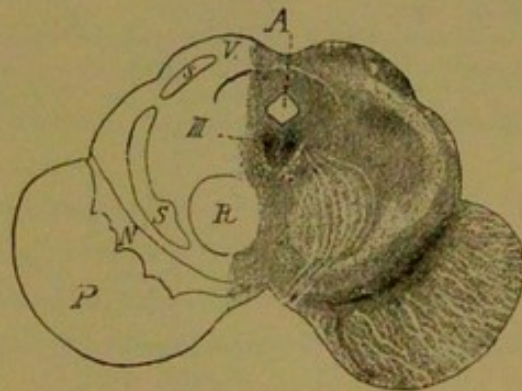


FIG. 277.—Horizontal section through the brain. *Nc.* Caudate nucleus. *NL* Lenticular nucleus. *Tho.* Optic thalamus. *Cl.* Claustrum. *Cl.* Internal capsule, in which the following tracts appear: 1. Optic tract. 2. To frontal commissure. 3. Motor tract. 4. Pyramidal tract. 5. Sensory tract. (Diagram after EDINGER and OBERSTEINER.)

FIG. 278.—Corpora quadrigemina and peduncles. *A.* Aqueduct of Sylvius. *V.* Corpora quadrigemina. *III.* Oculomotor nucleus. *R.* Red nucleus. *S.* Lemniscus. *s.* Upper lemniscus. *N.* Substantia nigra. *P.* Peduncle.

and from the pyramidal ganglion cells of this section the cortico-muscular tract takes its origin. The pyramidal tracts, containing motor fibres for the extremities, converge from the cortex, unite in a bundle, pass through the internal capsule, the peduncle, the pons, and gain the medulla, where they appear as pyramidal masses and take part in the decussation. Most of the fibres cross to the opposite side and descend in the cord as the lateral pyramidal tract. From here fibres pass to the anterior horn of the cord and divide as they approach the

ganglion cells of the part. A few fibres do not cross, but pass on the side of the anterior fissure of the cord as the anterior pyramidal tract, and also divide into fibrils connected with ganglion cells in the anterior horn. In this manner the central motor neuron is completed. From the ganglion cells of the anterior horn fibres go to the anterior roots

FIG. 279.

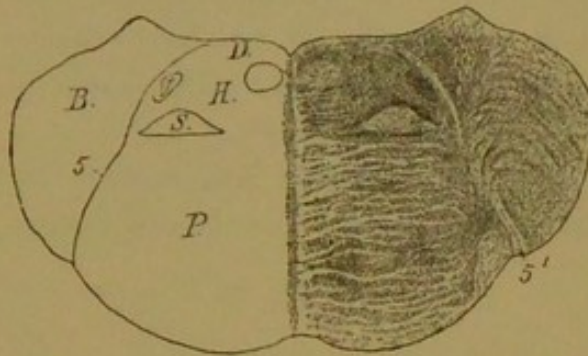


FIG. 280.

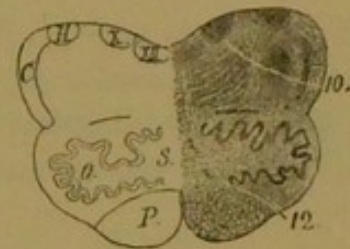


FIG. 279.—Frontal section of the pons. *D.* Gray tegmentum. *S.* Lemniscus. *V.* Nucleus of trigeminus. *P.* Peduncle. *5.* Root fibres of trigeminus. *B.* Outer portion of pons. *H.* Tegmental region.

FIG. 280.—Medulla oblongata, lower portion. *P.* Pyramid. *O.* Olivary nucleus. *S.* Fibres of lemniscus. *XII.* Nucleus of hypoglossus. *X.* Nucleus of vagus. *H.* Nucleus at upper end of posterior tracts (nucleus gracilis and nucleus cuneatus). *C.* Restiform body. *10.* Nucleus of vagus fibres. *12.* Nucleus of hypoglossal fibres.

of the spinal nerves, and thence to the muscles, in which they divide and end in the muscular end-plates, thus completing the peripheral motor neuron. These pyramidal tracts present the following secondary degenerations: (*a*) Lesions of the cortical motor area produce degen-

FIG. 281.



FIG. 282.

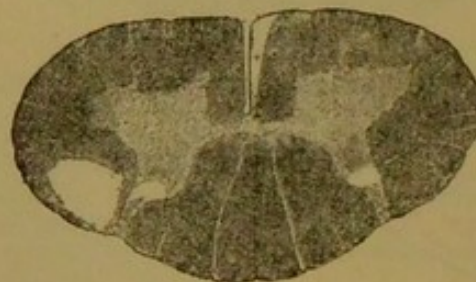


FIG. 281.—Descending secondary degeneration after transverse lesion of the cord. Both lateral and anterior pyramidal tracts degenerated.

FIG. 282.—Ascending secondary degeneration in the cord, with softening in the right internal capsule. The right anterior pyramidal and the left lateral tracts are degenerated.

eration of the whole group of fibres proceeding from here to the anterior horns. If on one side the entire motor area is destroyed, there is degeneration of the lateral tract of the opposite side and of the anterior pyramidal tract of the same side. (*b*) Similar degeneration follows interruption of the motor fibres at any part of their course

within the brain and above the decussation. (c) After total interruption, transverse lesions of the cord, degeneration of the pyramidal tract on each side occurs. (d) Any disease which destroys the anterior horn causes degeneration of the anterior root. (e) After lesions of the anterior root and the peripheral nerve the distal portion of the fibre degenerates.

2. Sensory System ; Centripetal. Tracing the sensory tracts from the periphery to the brain, it is found that they start from sensory end-organs in the skin or organs of special sense and pass in the nerves to the posterior roots of the spinal cord, entering through them into the cord. An intervertebral ganglion is interposed on the posterior root, from each of whose cells a process passes out and divides into two branches, of which one (dendrite) is the sensitive fibre of a peripheral nerve, and the other (neurite) passes into the cord. The posterior columns of the cord consist almost entirely of fibres from the posterior roots ascending, in great part, to the medulla. Within the medulla are two gray nuclei, the nucleus gracilis and the nucleus cuneatus, among whose ganglion cells the ascending fibres divide.

In addition to the long fibres mentioned shorter ones pass from the posterior roots to the motor ganglion cells of the anterior horn, called the reflex collateral fibres, thus uniting sensory and motor tracts; other fibres go to Clarke's column, and certain others ascend in the posterior column.

These sensory tracts together form the peripheral sensory neuron, their cells being represented by the ganglion cells of the intervertebral ganglia, their dendrites (afferent) by the sensory fibres of the peripheral nerve, and their neurites by the short and long fibres radiating from the posterior roots into the cord.

Sensory degenerations occur in these tracts as follows:

(a) After lesion of the peripheral nerve the distal portion degenerates because it is separated from its intervertebral ganglion. (b) Lesions of a posterior root cause degeneration of the fibres in the pos-

FIG. 283.

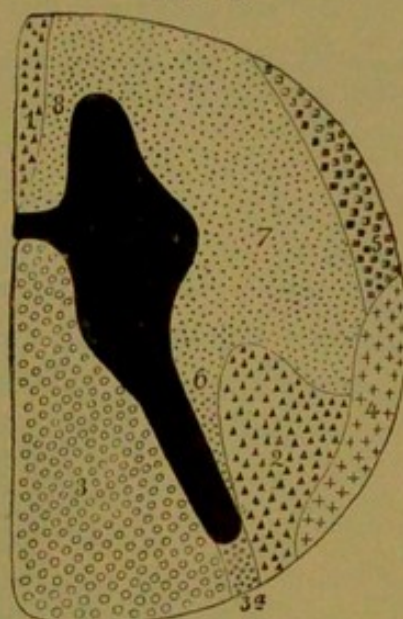


Diagram of the most important tracts in the cord. 1. Anterior pyramidal tract. 2. Lateral pyramidal tract. 3. Posterior column. 4. Cerebellar tract. 5. Gowers' column. 6. Lateral marginal tract. 7. Lateral column. 8. Remainder of anterior column. 3a. Lissauer's marginal zone.

terior column which come from it and corresponding fibres of the posterior horn. (c) Transverse lesions of the cord are followed by degeneration of the long fibres which have entered the posterior column

FIG. 284.

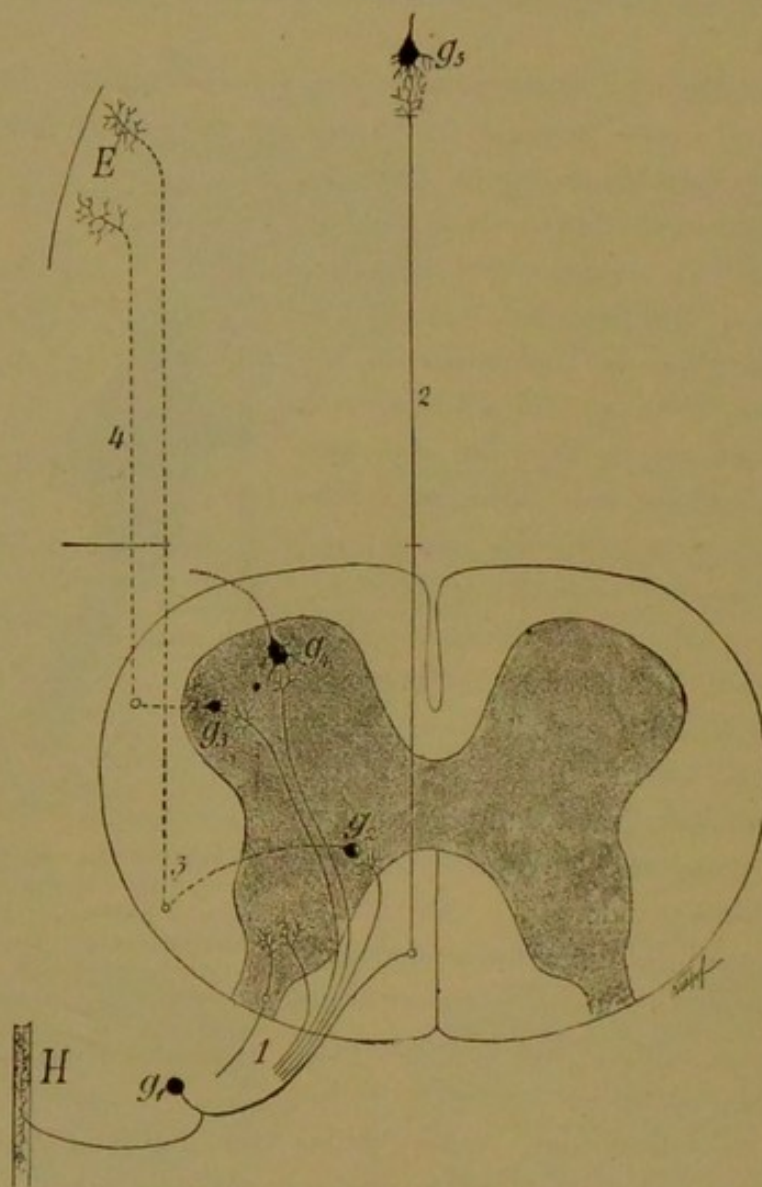


Diagram of the sensory tracts. *g*. Cell of spinal ganglion, with a process through the peripheral nerve to the skin, and one running in the posterior root. 1. Fibres of the posterior root, in part ascending in the posterior column, 2, in part passing to the posterior horn. *g*₂. Cell of Clarke's column, from which a fibre, 3, passes in the cerebellar tract to the cerebellum, *E*. *g*₃. Ganglion cell of gray substance with fibre, 4, ascending in Gowers' column. *g*₅. Cell of the nucleus gracilis in the medulla. From the posterior roots reflex collateral fibres pass also to ganglion cells of the anterior root, *g*₄.

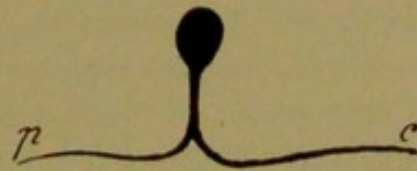
below the lesion. Since numerous fibres enter the cord as we go up it, the proportion of the degenerated fibres lessens from below upward. (Fig. 286.) (d) After lesions of the ganglion on the posterior root we expect degeneration in both directions.

From the gray substance of the cord other long centripetal tracts are derived. At the root of the posterior horn there is a group of ganglion cells, known as Clarke's column, from which fibres originate which pass through the posterior horn and lateral column and ascend in the margin of the latter to the cerebellum. This is called the lateral cerebellar tract. Slightly anterior to this lies the column of Gowers, which also ends in the cerebellum.

Transverse section of the whole cord must be followed by degeneration of all these tracts above the lesion.

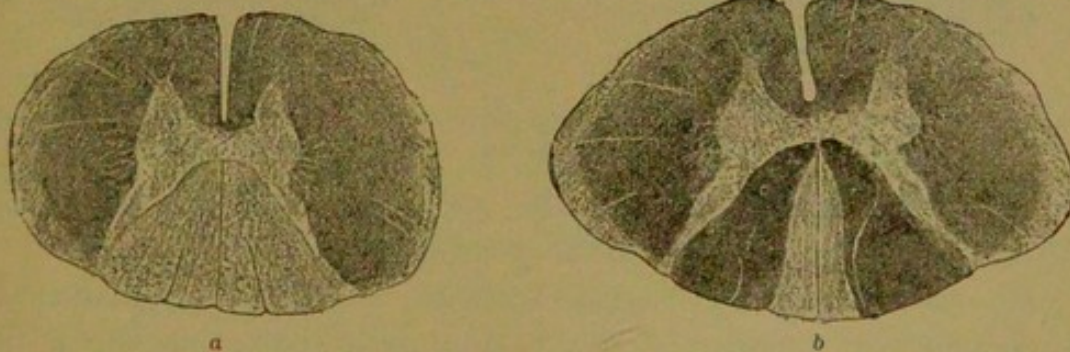
The cells of the nucleus gracilis and nucleus cuneatus send fibres toward the cerebrum which cross above and lie between the olivary bodies in the upper part of the medulla. Increased by many added fibres these form the lemniscus of each side, which passes through the pons, the cerebral peduncle, the internal capsule, and then radiates in the neighborhood of the parietal lobe to the cortex. Other fibres go to the corpora quadrigemina, others to the optic thalami and the lenticular nuclei.

FIG. 285.



Spinal ganglion cell with a process dividing into two fibres. (After OBERSTEINER.)

FIG. 286.



Ascending secondary degeneration after transverse lesion of the cord. *a*. Immediately above the lesion; *b*, higher up. In *a* the whole posterior column is degenerated; in *b*, only the columns of Goll. The degeneration on the edge involves the cerebellar tract and Gowers' column.

The sensory fibres of the cranial nerves present analogous but slightly modified relations; thus the Gasserian ganglion resembles a spinal ganglion.

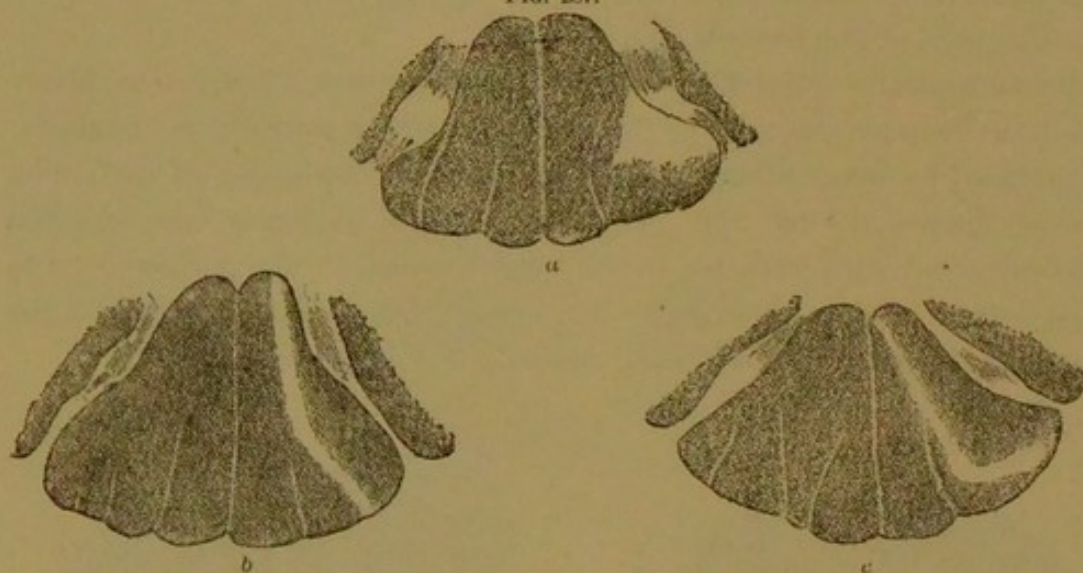
It is evident that degeneration follows the nervous tracts in the direction of their impulses, both in the motor and the sensory bundles.

In various parts of the central nervous system there are tracts which are called commissures, uniting different regions of the gray

matter with each other. Among these are association bundles, joining convolutions of the same side, the corpus callosum, the anterior white commissure, and others. In the cord fibres in the lateral and posterior columns join sensory centres, and in the lateral and anterior columns join various motor tracts. All these commissural fibres may degenerate, but because of their short course the process does not extend over long distances.

Histologically, secondary degenerations present nerve fibres in process of destruction, or replacement of these by glia tissue. (Fig. 287.) In the site of the fibres there are empty spaces and granular cells. The glia forms a network in which, when cut obliquely, there is an

FIG. 287.



Ascending degeneration of special bundles of the posterior column. *a*. Section at the entrance of the degenerated root. *b* and *c*. Sections higher up. (After PHILIPPE. Thèse de Paris, 1897.)

apparent fine fibrillation. In the glia tissue there are numerous Deiters' cells, with radiate pencils of fibrillæ.

Examples of retrograde degeneration are found after amputation of an extremity or a portion of one, both in the nerves of the stump, in the spinal roots, and in the cord. There may be only a trifling decrease in size and atrophy of the corresponding tract in the cord, or marked asymmetry of the halves of the cord on cross-section. The sclerosis which follows Wallerian changes is not often present in these cases. Experimentally removal of an eye in a newborn animal produces atrophy of the optic nerve and its occipital centre.

Primary Systemic Diseases.

Secondary degenerations play an important part in all diseases in which the gray substance suffers. Many of these are localized at

PLATE XXVI.

FIG. 288.



Wallerian Degeneration in the Cord of a Rabbit, six days after section. Longitudinal section from the posterior column. The nerve fibres are much swollen; in many the axis cylinders are broken and rolled up; in the yellow glia are free globules of medullary substance. $\times 350$. Formalin. (After VAN GIESON.)

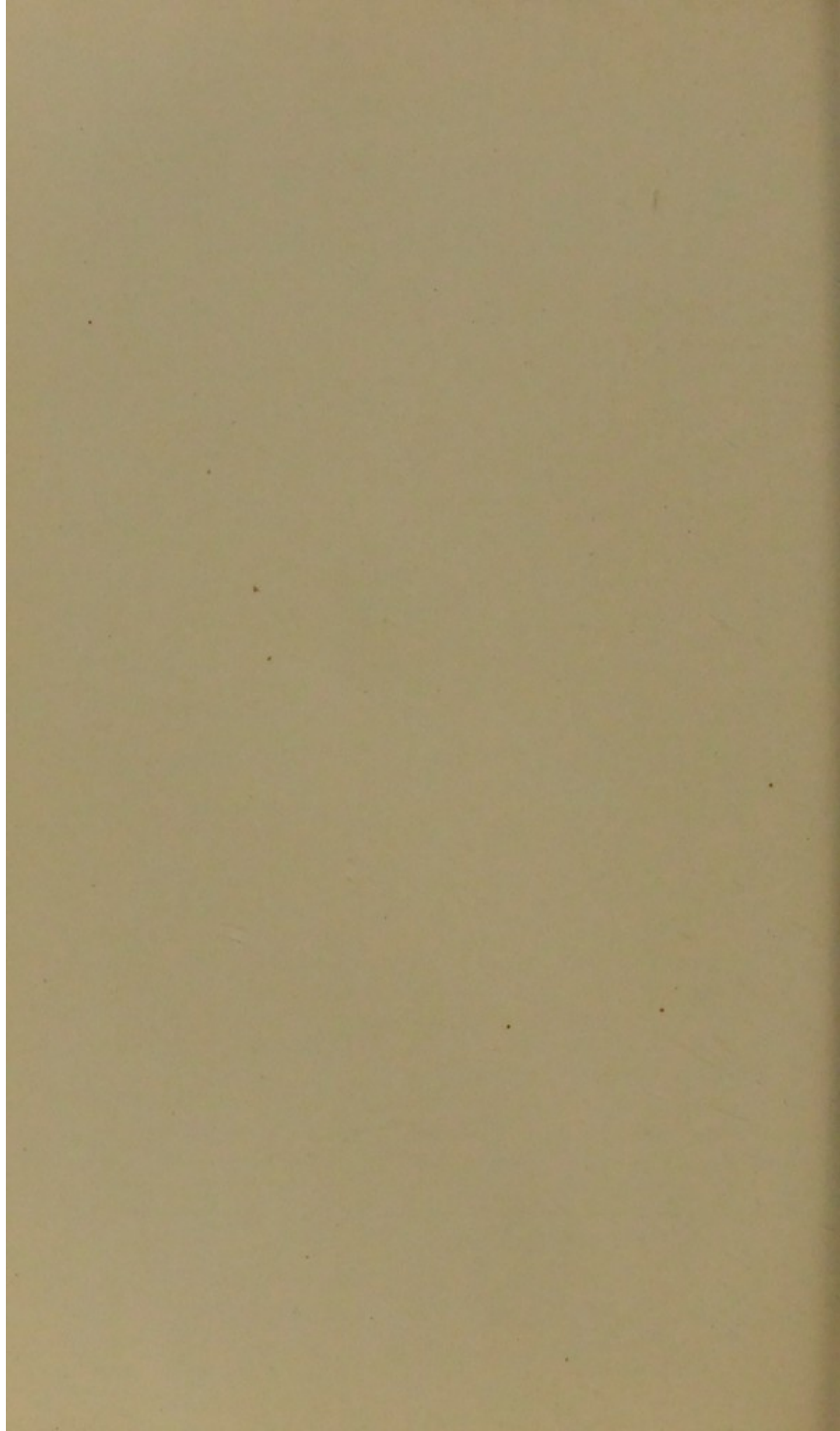
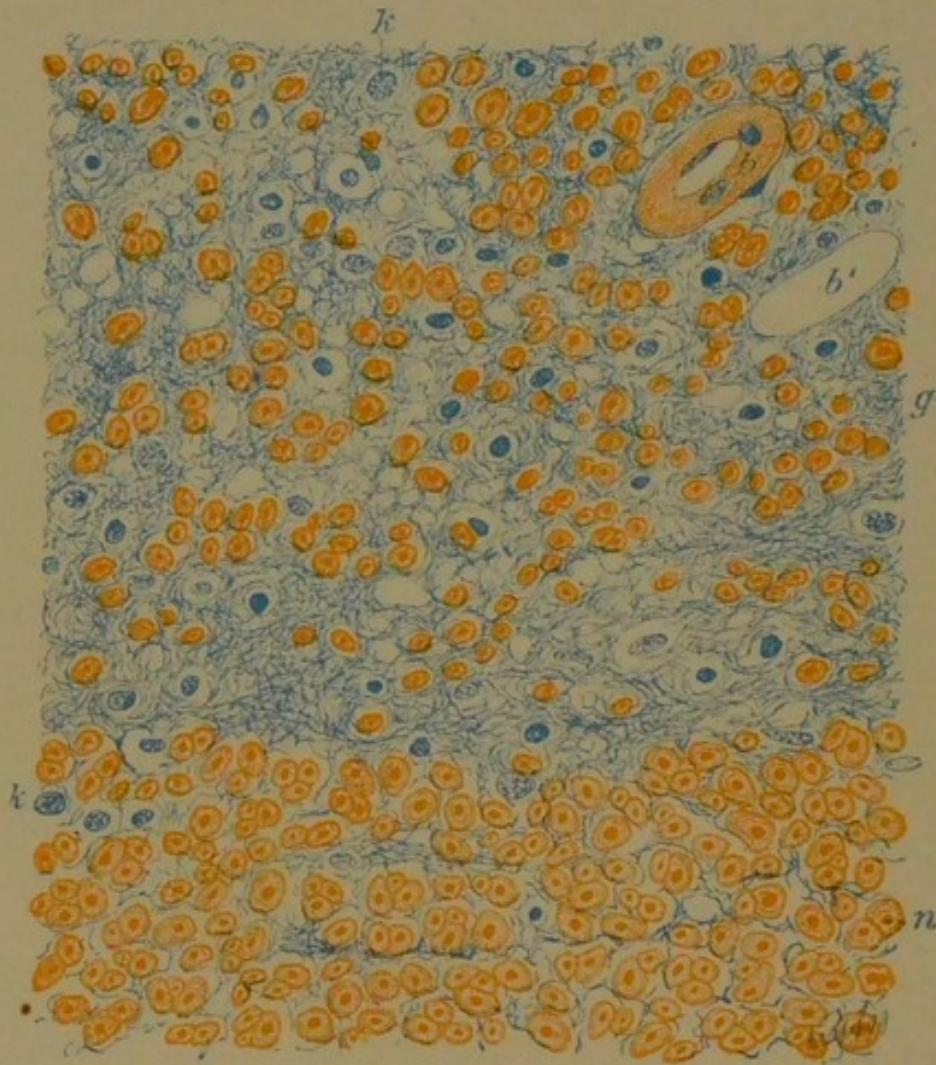




PLATE XXVII.

FIG. 289.



Gray Sclerosis of the Posterior Column.

g. Hyperplastic glia (stained blue) with a few fibres still preserved. *n.* Nerve fibres, yellow. *k.* Nuclei of the glia. *b, b1.* Bloodvessels. In the lower part normal fibres. Weigert's glia stain. $\times 350$.

special points, and cause a secondary change in the corresponding cells, their processes, and tracts. Thus the spinal form of progressive muscular atrophy depends upon a lesion of the cells in the anterior horns, and bulbar paralysis upon similar changes in nuclei of the medulla. But the nerve fibres may be primarily affected, and hence arise diseases which are called primary systemic affections, accompanied or followed by the secondary changes. The Wallerian degeneration does not involve the whole of the tract at one time, but gradually destroys fibre by fibre in much slower course, and both in the centres and tracts is followed by sclerosis. Hence the name primary sclerosis may be applied to these cases.

1. **Diseases of the Motor System.** These cause paresis or paralysis, often with irritative symptoms, and atrophic changes soon affect the paralyzed muscles. Degeneration in the anterior horns, anterior roots, and peripheral nerves, cause thus a peripheral paralysis, and the same may follow lesions of medullary centres and motor cerebral nerves. In general there is no muscular atrophy when the lesion is in the central motor neuron, for then the trophic centres of the cord are preserved. The paralysis may be complete or spastic, in the latter case the muscles offer some resistance to passive motion, and the reflexes are increased. Probably the latter condition depends on absence of the cerebral impulse, with increase of the muscular tonus, and transmission of sensory stimuli through the collateral reflex fibres. We expect, consequently, to find spastic paralysis with central lesions and complete paralysis with peripheral.

The following types occur:

(a) Primary disease of the muscles, dystrophy with atrophic paralysis. (See Chapter XIII., D.)

(b) Progressive muscular atrophy, in which both muscles and peripheral nerves are diseased. It may begin first in either or at the same time in both.

(c) Forms with degeneration in the anterior horns, the peripheral nerves, and the muscles. To these belong the spinal form of progressive muscular atrophy, in which it is assumed that the lesion begins in the anterior horns and attacks the peripheral parts secondarily. It is localized especially in the upper portions of the cord, is noticed first in the smaller muscles of the hand, and proceeds then to involve the muscles of the arms and trunk. The anterior horns atrophy, the ganglion cells are lost, and peripheral nerves and muscles atrophy. A similar affection is bulbar paralysis, with the lesion in the medulla,

and this may accompany the former disease. The nucleus of the hypoglossus, then of the vagus and spinal accessory are involved, the facial nucleus is attacked early, and those of the trigeminus and abducens less often. Because of the lesions in these nuclei and their nerves the familiar picture of labio-glosso-pharyngo-laryngeal paralysis results, and all the muscles supplied by the affected nerves undergo atrophy. Death is usually caused by aspiration pneumonia.

(d) Forms in which the entire motor neuron is involved, including the anterior horns and the pyramidal tracts. Among these is amyotrophic lateral sclerosis, which is accompanied by spastic paralysis and atrophy of the muscles. The degeneration can be followed to the decussation or even to the cortex; the anterior horns, anterior roots, peripheral nerves, muscles, and the commissural fibres in the brain and cord, all present similar lesions. It may be associated with bulbar paralysis, and this leads to a fatal termination. The disease specially affects the upper portion of the cord and the muscles of the upper extremities, and is distinguished from progressive muscular atrophy by

its more rapid course and the fact that it involves the muscles in certain groups of fibres and not as a totality.

(e) Unusual forms which affect only the pyramidal tracts, causing spastic paralysis without muscular atrophy.

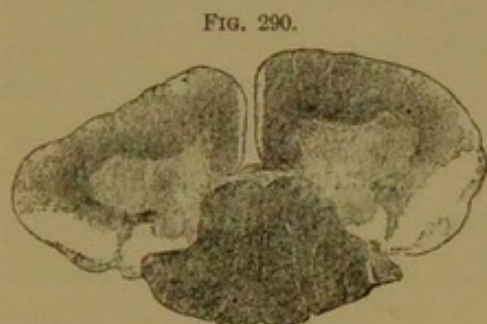


FIG. 290.
Amyotrophic lateral sclerosis. Both pyramidal tracts degenerated.

2. Diseases of the Sensory System. Tabes dorsalis is characterized by lesions of the sensory fibres of the

cord, especially of those which pass from the posterior roots inward, and the clinical symptoms are directly or indirectly referable to such lesions.

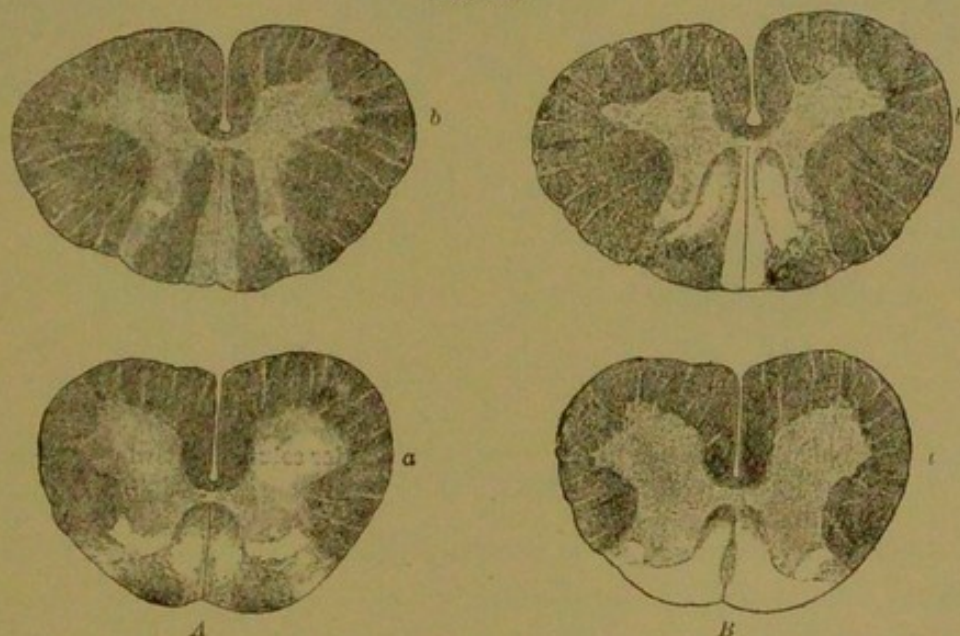
The fibres which enter the cord through the posterior roots lie in the posterior column near the edge of the posterior horn, and gradually become more median as they pass upward and new fibres come into the various segments. Hence the fibres coming from the sacral, lumbar, and lower thoracic nerves lie in the middle, near the posterior septum, separated laterally by the paramedian septum, and are known as the columns of Goll. The lateral portions of the posterior columns, containing fibres from the upper thoracic and the cervical roots, are Burdach's columns.

Tabes dorsalis begins, as a rule, in the lower thoracic and upper lumbar cord, and hence on section we find a degenerated area on either

side near the posterior horns, and higher up a similar lesion in Goll's column. If the remaining lower portion of the cord is involved, belonging to the lower lumbar and the sacral nerves, the entire posterior column is degenerated. When the tabes ascends higher the columns of Burdach may also be altered. The centre for the knee reflex lies at the first or second lumbar nerve, and as the collateral fibres are early affected this reflex disappears.

Tabes dorsalis is thus a degeneration of the posterior column, posterior horns and roots, and their radiations into the cord. In severe cases the lesion may be visible in the gross, the atrophy producing a flattening antero-posteriorly, and the degenerated parts appearing

FIG. 291.



Tabes dorsalis. *A*. Recent case. *a*. Lumbar cord with median degeneration. *b*. Columns of Goll, also affected. *B*. Older case. *a*. Lumbar cord with almost the entire posterior column degenerated. *b*. Columns of Goll and Burdach degenerated.

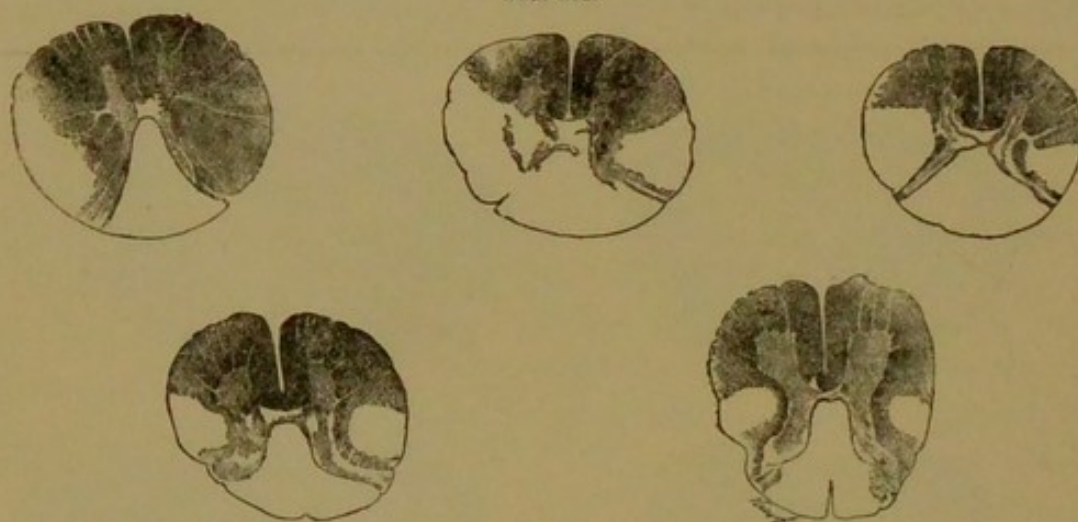
gray, firm, atrophic, and the posterior roots more slender. The pia may be opaque and thickened by chronic meningitis. The cerebral nerves and nuclei, especially those of sight, also share in the degeneration. The peripheral nerves and the sympathetic may suffer, and progressive paralysis may either precede or follow the tabes. The cause of the disease is supposed to be some toxic influence, which is in many cases syphilitic.

Degeneration of the posterior column may occur in other cases than tabes, where a toxic influence may be assumed. Poisoning by diseased grain (pellagra), by ergot, pernicious anemia, leukemia, diabetes, carcinoma, tuberculosis, and certain infectious diseases, may all be

followed by such lesions, and certain cases of auto-intoxication with cachexia, alcoholism, and lead poisoning, may be thus affected:

3. **Combined Systemic Diseases.** When several tracts together are diseased it is called a case of combined systemic degeneration, and such cases, with lesions of the cerebellar tract and Gowers' column, and of the pyramidal and posterior columns, are known as hereditary ataxia or Friedreich's disease, and occur in certain cases of tabes, spastic spinal paralysis, and progressive paralysis, and exist as diseases *sui generis*. Poisons and auto-intoxication furnish other cases.

FIG. 292.



Combined irregular degeneration in the anterior and posterior columns following concussion.
Post-traumatic.

The lesion may be primary in the gray matter of the cord, and this is probable where short commissural tracts are diseased, and in other cases the lesions are not strictly systematic but irregularly disposed, depending on vascular lesions in the cord.

C. DISORDERS OF THE BLOOD AND LYMPH CIRCULATION; HEMORRHAGE; ANEMIC AND HEMORRHAGIC SOFTENING.

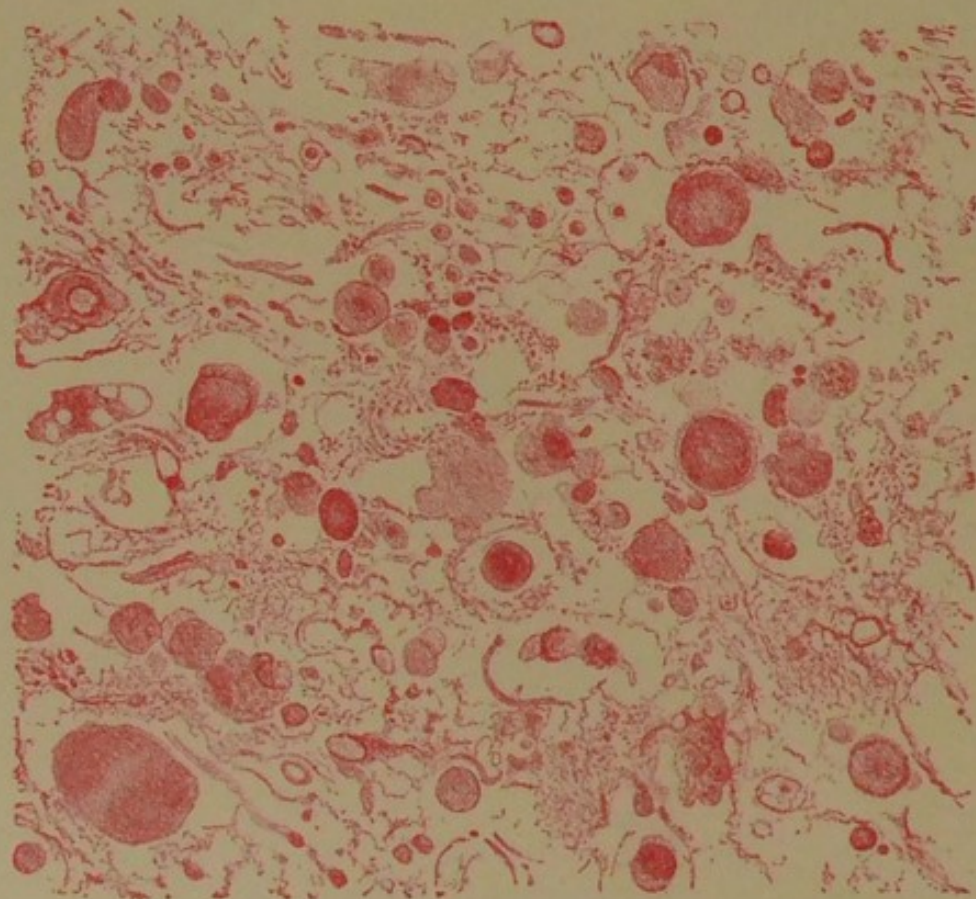
Anemia of the brain occurs with general anemia and after severe hemorrhages elsewhere, and a spastic form follows arterial contraction in small regions. The surface is pale as also the cut section, and on the latter there are but a few puncta vacuosa. Complete local anemia causes softening.

Congestive hyperemia precedes and accompanies inflammation. Stasis depends upon general conditions and on obstacles to the venous flow.



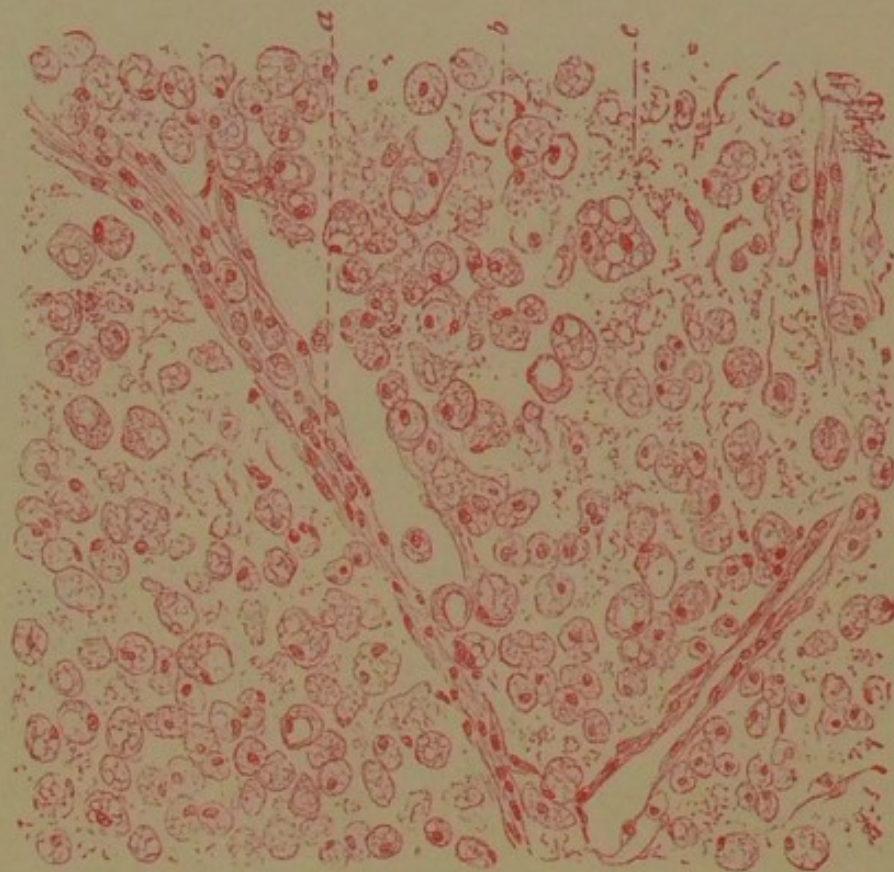
PLATE XXVIII.

FIG. 293.



Beginning White Softening from the Edge of a Recent Focus. In place of nerve fibres there are round and irregular swollen masses, the glia is loose and torn, and its meshes are large. $\times 250$.

FIG. 294.



Section from a Focus of Softening, about Fourteen Days Old.

a, Connective tissue persisting. b, Granular bodies minus their fat. c, Detritus. $\times 250$.

The former produces diffuse and mottled redness of the brain and its membranes. In the latter the superficial veins and the puncta vasculosa are prominent. Even in anemic brains gravity may cause the dependent veins, as with dorsal position of the cadaver, to fill with blood.

Local stasis is of three varieties: that due to occlusion of a venous channel, that due to thrombosis of a sinus, and that due to increased intracranial pressure.

Thrombosis of a sinus may extend to the veins of the pia and produce edema and passive hyperemia. At times it occurs in cachectic patients without apparent cause, perhaps from disordered nutrition of the wall of the vessel. At other times it is the result of phlebitis. Local softening and hemorrhagic infarction may follow in the cerebral tissue. Intense intracranial pressure compresses the thin walls of the veins, while the arteries remain permeable.

Softening. When a portion of the nervous tissue is suddenly deprived of its nutrition, as by closure of a vessel, it suffers a rapid liquefaction necrosis, or softening, for the dead tissue takes up water from the vicinity and melts to a thick semifluid mass. The axis cylinders soon show irregular swellings and break into short sections, and then become a fatty detritus. The medullary substance swells, separates from the axis cylinder or with the fragments of this forms globules of oval or irregular form, often with double contours, called myelin or axis cylinder droplets. The ganglion cells and glia also degenerate, and a frequent addition to the process is hemorrhage, either by diapedesis or after fatty degeneration of the vessels.

The tissue about the softened focus is usually edematous. The color of the lesion is red after hemorrhage, or without this of a white or gray or yellow tone; this is called white softening. Large admixture of blood produces a red softening if there are many capillary hemorrhages, or by the presence of red cells and imbibition of their coloring matter it may be a yellow softening.

Within forty-eight hours the focus may be filled with wandering cells, and in time the process of resorption and organization may lead to healing. The first leucocytes to enter the focus are polynuclear, and after these come numerous large lymphocytes. By taking up fatty matter these are converted to granular cells, and when filled with blood and its coloring matter they may be deeply pigmented. With large softenings the healing process is very slow, especially when the circulatory conditions are poor, from edema and senile disease of the

vessels. Secondary foci of softening may occur. The focus may become encapsuled and cystic or completely cicatrized.

The commonest cause of cerebral softening is closure of an artery, by thrombosis, embolism, or proliferation of its intima. This is called

ischemic softening. Thrombosis may be due to atheroma, emboli come from thrombi in the arteries of the brain, the heart, the arch of the aorta or the pulmonary veins, and syphilis and atheroma may obliterate the vessels of the brain.

The arteries most often involved are the great vessels of the base, especially of the Sylvian fissure and its branches which supply the large ganglia.

The focus of softening is often

in the neighborhood of the internal capsule, caudate and lenticular nuclei, and optic thalamus, less frequently in the pons, corpora quadrigemina, and peduncles. In size the softened area may be small as a hazelnut, or large as a hen's egg, or even include a great part of a hemisphere. The surface of the brain is depressed above the focus, and may be fluctuating on palpation. If the internal capsule is destroyed motor and sensory hemiplegia may follow, for the major part of the motor and sensory fibres pass through it.

When an artery which passes from the pia to the brain becomes occluded it causes circumscribed *softening of the cortex*, at times including several gyri and reaching to the white matter. Collapse of the convolutions and resorption may follow, with marked deformity, which may be increased by cicatricial contraction. The adjacent convolutions are usually atrophic. The artery of the Sylvian fissure gives off a branch to the lower frontal convolutions in which the speech centre of Broca is located on the left side; occlusion of this branch leads to motor aphasia.

Chronic softening in the brain may depend upon disease of the vessels, as atheroma and syphilitic arteritis, and the foci may be small and multiple. Areas which have had an acute origin may also extend by disorders of the circulation about them, both of blood and lymph, and further softening.

FIG. 295.



Teased preparation from a softened area about eight days old. *a, a₁*. Swollen axis cylinders. *b, b₁*. Naked axis cylinders. *b₂*. Granular swollen axis cylinder. *c, c₁*. Myelin drops. *d*. Fatty ganglion cell. *e, e₁, e₂, e₃*. Wander cells. *f*. Granular cell. *f₁*. The same, enclosing a fat drop. *g*. Wander cell with four red cells; *h*, with myelin droplet. $\times 250$.

Softening in the spinal cord is far less frequent than in the brain. Such areas of *myelomalacia* may be caused by syphilitic meningitis and meningomyelitis, and rarely by atheroma.

Hemorrhages in the brain are relatively common and of great clinical importance. Their usual cause is injury, or rupture of a vessel already the seat of hyaline or fatty degeneration, syphilitic or atheromatous lesions, or miliary aneurisms. Any of these processes will lessen the resisting power of the vessel and dispose to rupture. Diseases of the heart and kidneys, alcoholism, and other diseases which are accompanied by vascular changes are specially liable to produce cerebral hemorrhage. The immediate cause is frequently an increase of the blood pressure, as from muscular exertion, stasis with increased pressure within the abdomen, acute alcoholism, and emotional crises. A peculiar form of aneurism called the embolic may lead to intermeningeal bleeding at the base of the brain, where they commonly occur (p. 293). The hemorrhagic diathesis and septic conditions also may be complicated by cerebral hemorrhages.

In form cerebral hemorrhages may be punctate and capillary or, as in hyperemia about inflammations, and in hemorrhagic conditions and areas of softening, there may be an exit of red cells into the lymph sheaths of vessels.

Large masses of blood destroy the tissue and appear as dark-red areas of softened tissue and clot. Careful washing removes the blood and reveals the walls of the focus with projecting vessels and necrotic masses, and about it there are capillary hemorrhages and a zone of edema. After a time the dissolved blood pigment gives the part a yellow color. If of large size and near a ventricle this cavity may be perforated, and the blood then finds its way through the whole system of ventricles. After rupture of a vessel the bleeding continues until the external pressure equals the intravascular, and this pressure, transmitted through the brain, causes tightness of the membranes, dryness of them, flattening of the convolutions, and partial obliteration of the sulci.

Under the microscope the neighborhood of the hemorrhage is in a condition of red softening, and after a time absorption has occurred, and cells with granules and pigment are found. The color fades through brown and yellow and becomes much paler, and the end of the process is either a scar of fibrous tissue or a cyst with clear contents.

The commonest site of hemorrhage is about the great ganglia, especially with miliary aneurisms of the branches from the Sylvian artery.

With these as with emboli, the internal capsule is apt to be involved, causing hemiplegia. Other hemorrhages are found in the pons and medulla, and after trauma, either at the site of injury or on the opposite aspect of the brain (contrecoup).

Hemorrhage in the cord is rare, and usually follows injury. In most cases the bleeding is confined to the gray matter, and the histology resembles that given for the brain.

Disorders of the Lymphatic Circulation; Edema. An increased amount of transudate is found in the subdural and subarachnoid spaces, on the surface of the brain, in the ventricles, and the central canal of the cord, or generally throughout the substance of the nervous tissue. On the surface this condition is called *hydrops externus*, in the ventricle it is called *hydrops internus*, and in the central canal, *hydromyelia*. Edema of the nervous tissue refers to increased amounts of serous fluid in the substance of the nervous organs. In all these cases the condition is not always a mechanically developed dropsy, but often a serous inflammation.

Cerebral edema may be partial or general. If the former, the entire brain is large, moist, soft, and doughy, and usually anemic. On section it has a moist appearance, and the vascular puncta rapidly disappear. The increased pressure causes the convolutions to flatten and the sulci to be shallow.

Some of these cases may develop during the death agony, others accompany sunstroke as a serous apoplexy, others are found with acute exanthemata, especially in children. Some cases depend upon venous stasis, and others occur during chronic nephritis as part of a general hydermia.

In both brain and cord local foci of edema, affecting both the glia and the nerve fibres, may appear as soft and succulent regions, of red or anemic hue according to circumstances. The tissue may be semi-fluid. The axis cylinders are found irregularly swollen and thickened, homogeneous or granular, and frequently broken into short lengths, while the medulla remains or shares in the fragmentation. These swollen fibres lie in distended portions of the glia. The ganglion cells show swelling and granulation. In such cases, especially with senile atrophy, the lymph sheaths of the vessels may be cystic with the increased fluid, and this appearance of large vacuoles on section, especially in the large ganglia of the brain, has received the name *état criblé*.

Such conditions result from stasis of lymph, and accompany other focal diseases, as tumors, hemorrhages, etc., in a zone about the

primary lesion, and in the latter case it is probable that the lymph channels have been compressed by inflammatory congestion. In many cases a plainly inflammatory origin may be discovered for the edema, as when such lesions from the membranes invade the tissue of the brain, and in others the condition accompanies infectious edema and death from insolation. Anemic, diabetic, and other cachexias may be complicated by edema.

The circulatory conditions within the cranium determine the intracranial pressure. Physiologically the cerebro-spinal fluid exerts a certain amount of pressure upon the brain, which must not be confounded with the pressure within the blood-vessels, and when this pressure is increased the characteristic symptoms result which are included under compression of the brain. This may be due to increased

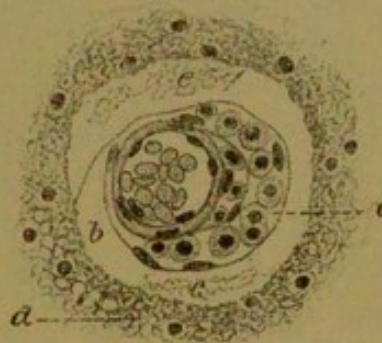
blood pressure, diminution of the space within the skull by tumors, hemorrhages, and similar processes, and up to a certain point compensation is possible by outflow of the cerebral fluid. Beyond this limit the brain is pressed against the bones, and the following conditions are observed: dura tense, both dura and pia anemic, convolutions flat and broad, sulci shallow.

D. INFLAMMATION.

Acute inflammatory processes in the central nervous system are compounded, as elsewhere, of hyperemia, increased transudation, and emigration, to which degenerative changes of the parenchyma are added. In the mildest grades of *encephalitis* and *myelitis* the inflammatory edema causes swelling of both glia and nervous elements, and this may result in degeneration, but in more severe cases there is also an infiltration of the part with white cells which at first affects the lymph sheaths of the vessels and then the adjacent and more distant nervous parenchyma. At the same time the irritation attacks the nervous elements and produces more or less marked degeneration.

The cause and the intensity of the process determine its final stage, either as *restitutio ad integrum* in the mild forms or as degeneration of

FIG. 296.



Perivascular and adventitial lymph spaces distended in a case of myelitis from compression. a. Adventitial lymph space with granular cells. b. Perivascular space. c. Clot in same. d. Glia about vessels. (After FICKLER.)

the tissue and replacement by fibrous scars. Hence sclerotic areas may be found similar to those described above (p. 448). The most severe lesions are accompanied by edematous softening and cellular infiltration, and entirely resemble marked anemic softening, unless there is a distinct purulent element present. The termination of these cases is usually by formation of cysts and scars.

In many cases the inflammatory character yields in its importance to the degenerative lesions, and thus transitions of all varieties occur between these two pathological conditions, and the gross and microscopic pictures differ accordingly.

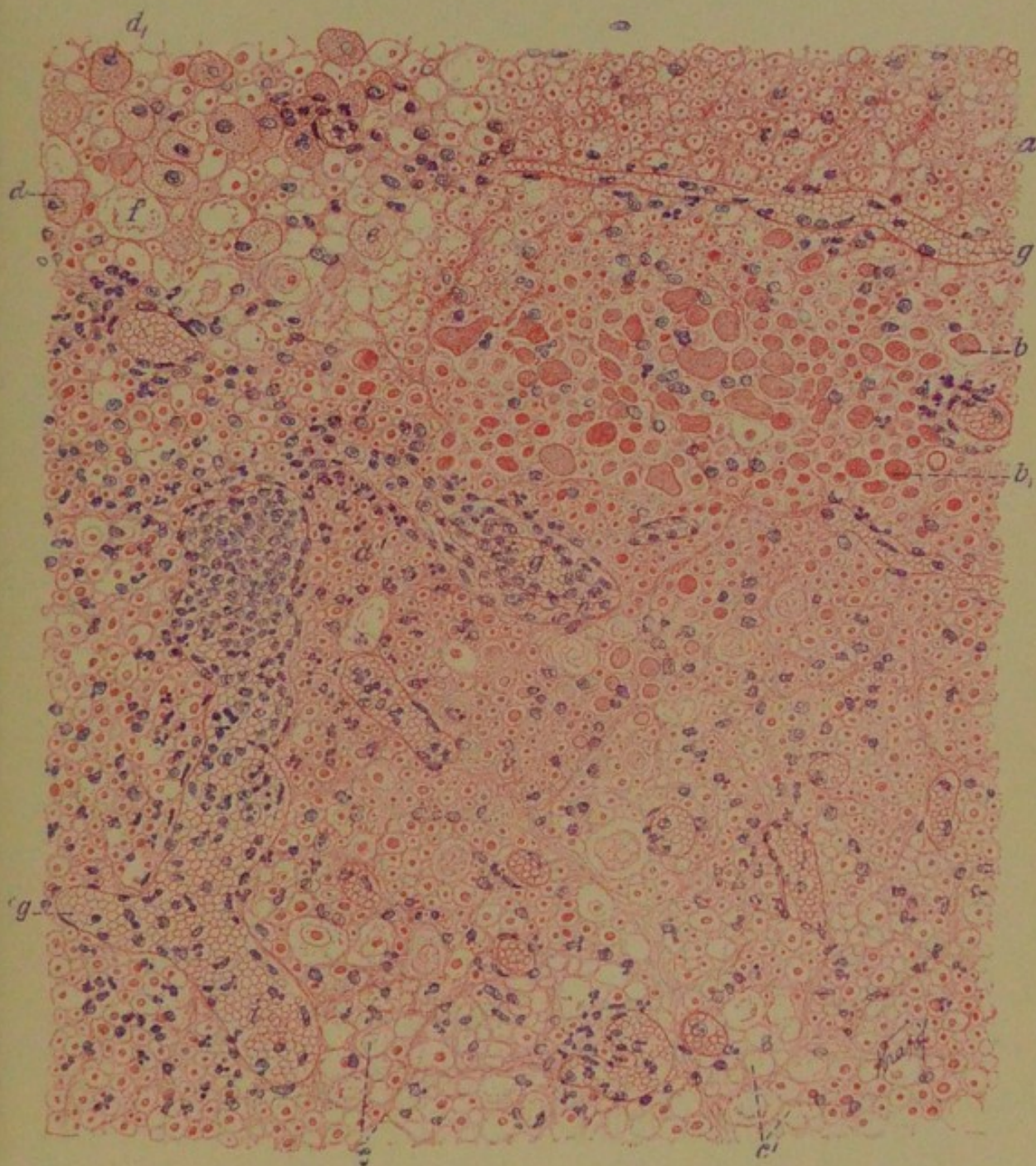
The causes of inflammation in the central nervous system are commonly of infectious nature or toxic. General diseases as scarlet and typhoid fevers, measles, arthritis, rabies, and, in a chronic form, syphilis, are often complicated by such inflammations. Encephalitis and myelitis may accompany poisoning either as idiopathic or secondary conditions. In the infectious cases it is reasonable to suppose that the toxic element is furnished by the organism causing the infection. In many cases there is a mixed infection, as when the nervous lesion follows the termination of another disease. At times the toxic influence selects particular regions for its action, as in poliomyelitis anterior.

The location and extent of these inflammatory lesions may vary greatly, the parenchymatous degenerations and sclerotic processes, and also those with much cellular infiltration and resulting softening and scars, may involve a large portion of a cerebral lobe or the whole of a spinal segment, producing *encephalitis diffusa* or *myelitis transversa* as the case may be. When the gray matter is especially the site of the lesion it is known as *poliencephalitis* or *poliomyelitis*. In many cases of encephalomyelitis the lesion follows the distribution of the blood-vessels, and only certain ones, and at times only a special branch, may thus localize the inflammation. When disposed in the course of the artery of the anterior fissure of the cord the disease is called *poliomyelitis anterior*. These sulco-commissural arteries take origin from the anterior spinal at regular intervals, enter the anterior fissure and pass alternately to the right and left, supplying the anterior horns and the white substance adjacent. According as many of these branches or only a few are attacked the focus of inflammation varies in extent, appearing either as longer or shorter regions of destruction, confined to the anterior horns or involving the white matter also.

Anterior poliomyelitis is an infectious disease, accompanied by fever, and is seen most frequently in children. It begins with extensive

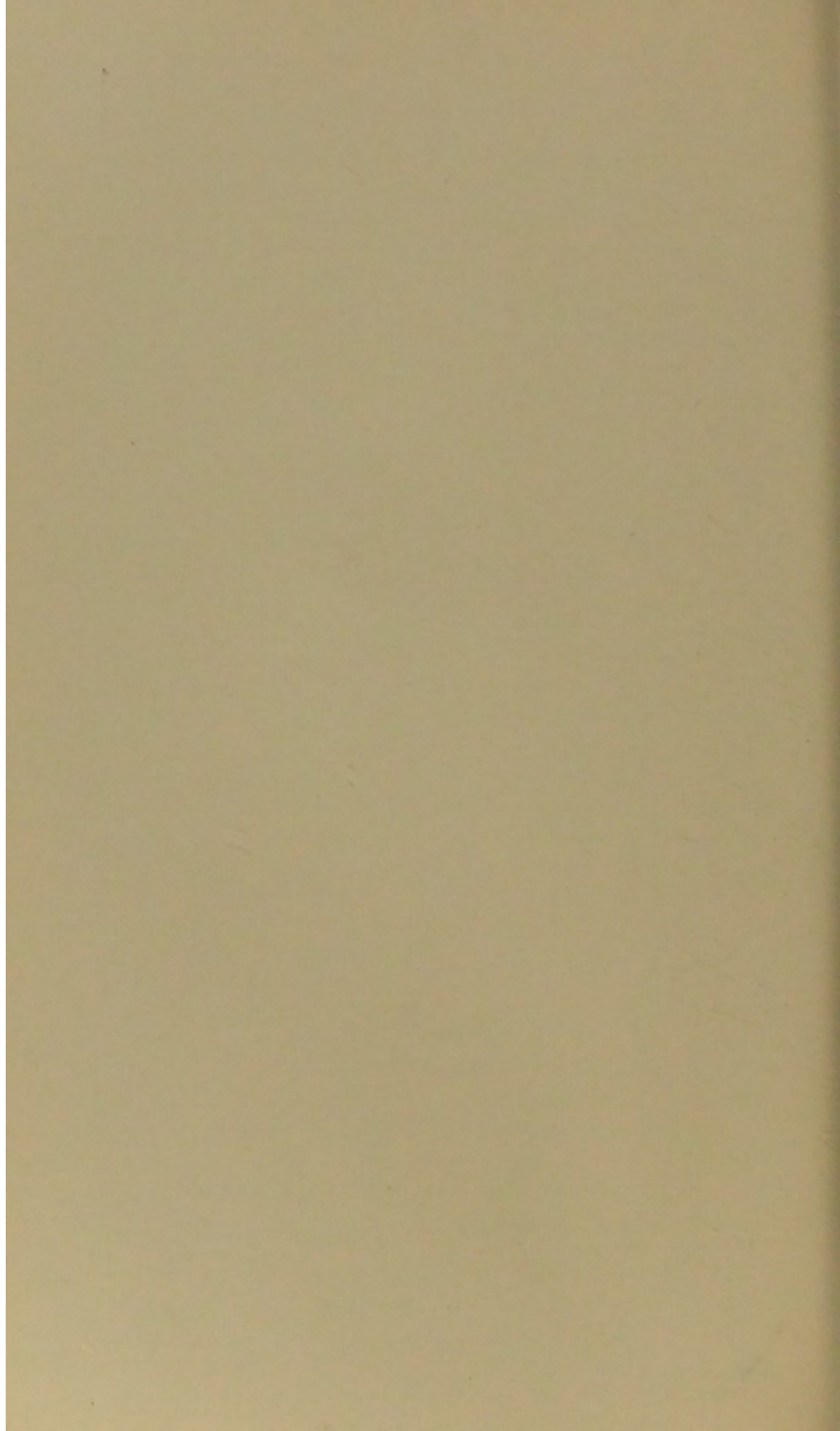
PLATE XXIX.

FIG. 297.



Acute Myelitis, Infiltrating Form.

a, a₁. Less altered tissue. *b, b₁.* Swollen fibres. *c, c₁.* Distended spaces in the glia, with loss of fibres. *d, d₁.* Granular cells with their fat removed. *f.* Remains of destroyed nerve fibre. *g.* Vessel with many red and white cells. To the left of the picture the tissue is infiltrated with cells, especially in the lymph sheaths.



paralyses, which may improve and leave only paresis of certain groups of muscles, and these undergo a degenerative atrophy later. The disease does not often end fatally, and hence the lesions are seen only after it has long since terminated. In recent cases there is well-defined cellular infiltration in the region affected, with degeneration of the ganglion cells and the anterior root fibres proceeding from them. In many cases the infiltration is unimportant, and the degenerative changes are pronounced. Sclerotic contraction is the final stage, and this diminishes the size of the anterior horn or the whole lateral half of the cord. The ganglion cells are lost, in groups or entirely, the motor fibres degenerate, and the corresponding muscles atrophy.

A chronic form of anterior poliomyelitis occurs which differs only in its course from the acute type described.

Analogous lesions in the medulla are found in bulbar paralysis, and in the brain with the cerebral form of infantile paralysis. The inflammatory character of many of these lesions has not been fully determined, especially as many of them cannot be studied immediately.

A more extensive poliomyelitis, involving large sections of the posterior horns and columns, may at times be observed with general infections, as variola, rabies, pyemia, influenza, and typhoid fever. In many cases severe functional disturbances may be caused by toxic influences without apparently leaving any anatomical alterations in the cord and brain; an example of this is called *acute ascending paralysis* or Landry's paralysis. Where the gray matter of the cord is generally involved the disease is known as central myelitis. All these forms of inflammation produce an interruption in the nervous tracts and may be followed by secondary degenerations.

When inflammatory processes extend from the membranes of the brain and cord to these structures, or in the contrary direction, the process is called *meningo-encephalitis* or *myelitis*.

Disseminated inflammations affect scattered foci and afterward extend to the entire mass of the brain and cord, and in some cases the lesion follows the bloodvessels. Acute disseminated encephalomyelitis may be primary, but usually follows some other disease, as an infectious disorder of childhood, appearing as an acute ataxia and ending in either resolution or multiple sclerosis.

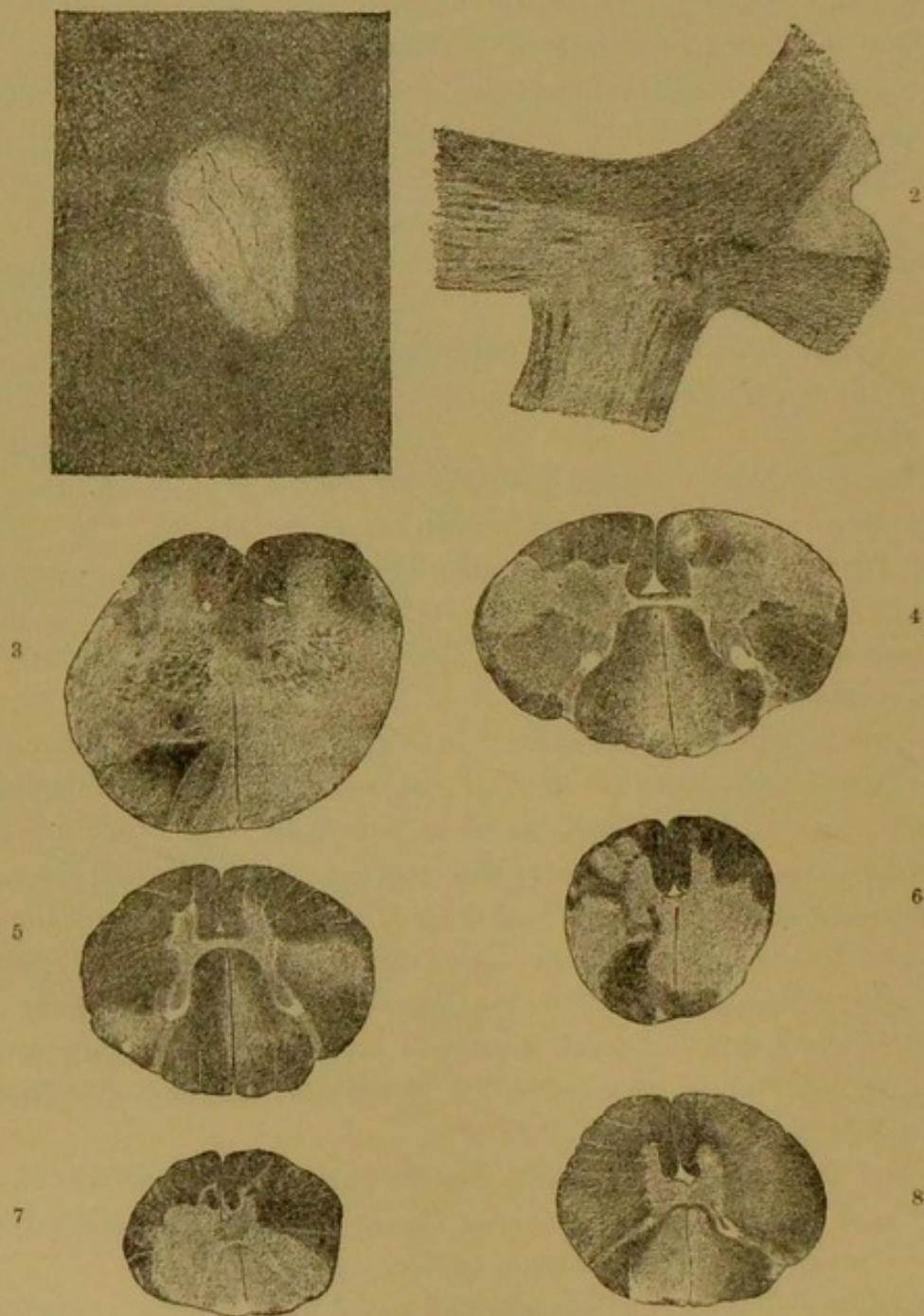
FIG. 298.



Section of the cord after acute anterior poliomyelitis. The left half of the cord diminished, especially in the anterior horn, where a white necrotic spot is seen.

Multiple sclerosis presents lesions which are soft, grayish red, almost gelatinous and full of granular cells, when the disease has been rapid or an exacerbation of a chronic form. But, as a rule, the lesions are

FIG. 299.



Multiple sclerosis. 1. From the centrum ovale. 2. From the optic chiasm. 3. From the decussation in the medulla. 4-8. From the cord. Magnified with a hand-glass.

hard and gray, even creaking when cut, and are sharply circumscribed from the rest of the tissue. The irregular distribution of these lesions throughout the nervous system is characteristic, but they present a

certain relation to specially affected regions, as the centrum ovale, the walls of the lateral ventricles, the pons and the white matter of the cord. In general the lesions may be confined to the brain, the medulla, or the cord.

Microscopically there is an absence of nervous elements and a hyperplasia of the neuroglia, but in some cases there are naked axis cylinders also, persisting after the atrophy of the medullary substance, and perhaps with this may be connected the fact that secondary degenerations may be lacking in multiple sclerosis. Many other areas show transitions to more diffuse lesions, and may involve an entire cerebral lobe. The cause of these lesions may be a preceding degenerative inflammation, or a toxic influence with infections and poisons, or disorders in the circulation of blood and lymph, or disease of the vessels, so that the same anatomical picture may have many origins.

Suppurative inflammation differs from other softenings of the nervous tissue by the presence of true pus, seldom made up of large nucleated wander cells, but of polynuclear leucocytes and those with fragmented nuclei.

Suppurative encephalitis, or cerebral abscess, forms a collection of yellow or yellowish-green pus in the hemisphere, of small extent usually but at times very large. The wall of the abscess is made of necrotic nervous tissue which is infiltrated with pus and shows an irregular outline. Hemorrhage, which is rather infrequent, causes the focus to assume a redder color. About it there is a zone of edematous infiltration in which capillary hemorrhages may be found. Microscopically the edge presents detritus from nerve cells and pus cells, cholesterol crystals, fat, and fatty granular cells.

Cerebral abscess may be due to the direct entrance of pyogenic bacteria from outside the body or from adjoining structures or through the blood. The former is the case with injuries which perforate the cranium and the brain, and so introduce infection. Complicated fractures of the cranial bones and sometimes injuries of the soft parts without fracture may be attended by abscess of the brain, the organisms gaining entrance probably through the lymph channels. In some cases the path of entry is clearly indicated by a pachymeningitis or sinus phlebitis, with purulent meningitis, and then abscess formation. Caries of the ethmoid and the temporal bone, empyema of the antrum of Highmore, and similar purulent conditions in the cranium may lead to cerebral abscess, with or without phlebitis of the sinuses and meningitis.

General infections and pyemic conditions, embolism with infected material, and metastasis from purulent bronchitis, bronchiectatic cavities with suppuration, and phlegmonous foci are responsible for other cases, and according to the character of the primary lesion the abscess simply contains pus or is also gangrenous. Certain other cases are called cryptogenic because their origin cannot be explained.

The case may be rapidly fatal, especially when there is extensive purulent meningitis or perforation of a ventricle and internal hydrocephalus. Edema and cerebral compression may also lead to death. At other times the process is slow in its course, and remains for a long time localized, being then more or less encapsuled by a fibrous membrane. The contents of the abscess may thicken and dry, but it is always possible that the pus may perforate elsewhere.

The site of the lesion depends on the trauma, and usually corresponds to it, or, if due to caries, is found in the temporal lobe or the cerebellum of the same side.

In the cord suppurative inflammation is usually due to metastasis with pyemia or to caries of vertebræ or suppurative spinal meningitis.

E. INFECTIOUS GRANULOMATA.

Tuberculous and syphilitic lesions in the brain are so intimately connected with similar affections of the membranes that they will be discussed together. The commonest and most important form of tuberculosis is tuberculous meningitis.

The name *basilar meningitis* is often used for this affection because of its tendency to involve the basal surface of the brain, especially about the optic chiasm. In the majority of cases there is another tuberculous lesion elsewhere in the body to which the meningitis is secondary, either of the pleura, the lung, the bones, or the middle ear. In other cases the disease is associated with conglomerate tubercles of the brain. A hematogenous origin is the commonest, and hence the lesion is part of a general miliary tuberculosis, and it is possible that it may affect the brain through the lymph channels.

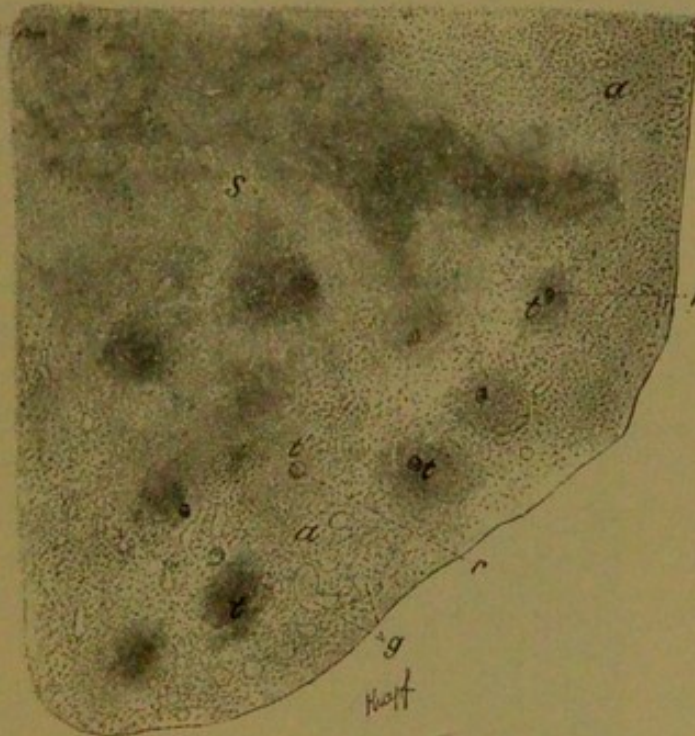
From the meninges the process passes to the brain substance, causing edematous swelling, infiltration, anemic or hemorrhagic softening in the gray or the white matter, and on the walls of the vessels which enter the part there may be tubercles.

The termination of acute tubercular meningitis is generally fatal, but it is claimed that cases may present evidence of healing, with

diminution of the exudate, and fibrous changes in the tubercles and thickening of the meninges. It is uncertain how much of this process is reparative, but without doubt such lesions may be subacute or chronic and of a fibrous nature rather than destructive.

The membranes of the cord may present lesions like those described in the cranium, and the cord itself may be affected. The original lesion may be tuberculosis of the vertebrae. Simple tuberculosis of the membranes also occurs without involving exudative and productive changes.

FIG. 300.



Conglomerate tubercle in the brain. *t, t'*. Resorption tubercles with giant cells, *r*.
a. Infiltration with small cells. *g*. Vessels. $\times 12$.

When the tubercular foci are numerous in the nervous organs the name *disseminated tuberculosis* is employed. More commonly in the brain there are solitary or conglomerate tubercles which may attain a large size, and about them resorption tubercles are noted. The surrounding tissue is edematous or the seat of granulation and fibrous hyperplasia. Clinically the symptoms may be those of tumor and compression, and, if the lesion is in the cord, paralysis and secondary degeneration occur.

Cerebro-spinal syphilis may occur within a few months after infection, but usually it is the tertiary forms of the lesion which are found. There may be circumscribed gummata or a diffuse gummatous inflam-

mation with degenerations. The vessels play an important part in the lesion. The pia of the brain, and less often of the cord, is commonly affected, and most frequently as a gummatous meningitis. A proliferation of a very cellular and vascular granulation tissue on the inner side of the pia gives rise to grayish-red thickenings, semi-gelatinous and at times caseous, which tend to fibrous transformation and shrinking. Small areas may be completely absorbed, but the larger always leave firm scars. Less often caseous gummata occur, and the vessels are involved in syphilitic inflammation (p. 291).

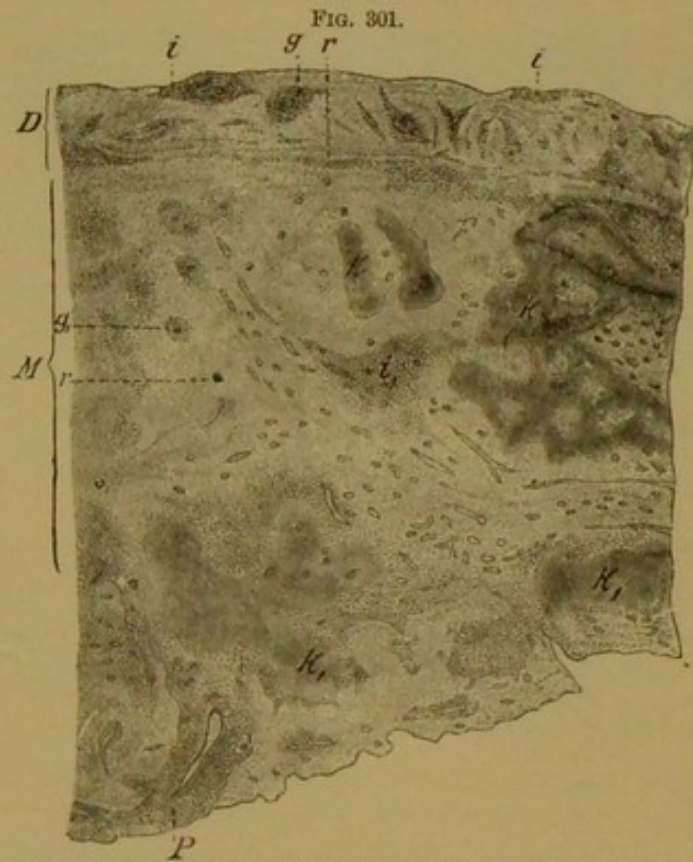


FIG. 301.
Syphilitic meningo-encephalitis. *D*. Thickened fibrous dura. *M*. Meninges. *g*. Vessel with syphilitic arteritis. *i*. Infiltrate in the dura. *i*₁. The same in the pia. *k*, *k*. Gummatous foci in the meninges, which are thick and fibrous with infiltrated vessels, *g*, and giant cells, *r*. *k*₁, *k*₁. Gumma in the cortex. *P*. Pia in a sulcus, its vessel infiltrated. $\times 250$. (After OBERMEIER.)

Gummata, which often form at the base of the brain and about the vessels and nerves, usually involve cellular infiltration and degeneration of the brain and cord adjacent to their sites, with resulting caseous or fibrous areas. This is called syphilitic meningo-encephalitis and myelitis. Circumscribed gummata sometimes occur within the central nervous organs independent of meningeal lesions, and may act clinically as tumors.

Compression symptoms may also follow the exudate because of its

thickness and pressure, and by occluding the vessels it may produce stasis and edema. In the cord the contraction of fibrous scars may have similar effects. These indirect results of syphilis may be controlled in many cases by appropriate treatment, and thus their recognition has a practical value.

Primary lesions of the vessels may be distributed over many small arteries as a gummatous inflammation, or involve a few larger arteries. The lumen may be occluded more or less completely, and softening results in the corresponding parts, or, in other cases, thrombosis and embolism, or weakening and rupture of the vessel, with hemorrhage.

Syphilis may cause simple degenerative lesions in the nervous parenchyma without inflammatory changes, probably because of the lessened blood supply and consequent impaired nutrition. Such lesions are commonly scattered in many small areas as degeneration and fibrosis, or, by direct action of the poison of syphilis, certain tracts present degenerations and sclerosis. Among the latter may be mentioned syphilitic lateral sclerosis, involving the pyramidal tracts, and also certain lesions of the posterior columns.

Certain other cases which cannot be recognized anatomically as syphilitic, are in all probability due to this cause in many cases; among these are tabes dorsalis and progressive paralysis, which are sometimes known as post-syphilitic or meta-syphilitic diseases. It may be that syphilis predisposes the individual to such lesions, or, after the syphilis is cured, a toxin derived from it remains in the body and causes the nervous disease.

Inherited syphilis may affect the nervous system during fetal life, childhood, or after puberty, and, including hydrocephalus, presents anatomical changes similar to those already described. An interstitial encephalitis neonatorum has been described by Virchow in syphilitic infants, which present yellow areas of softening in the white matter, in which numerous granular cells are found, as well as throughout the brain; but these cells may occur physiologically in the brain of the newborn child.

F. INJURIES OF THE CENTRAL NERVOUS SYSTEM; REGENERATION; COMPRESSION; CONCUSSION.

Incised and punctured wounds of the brain and cord are not common because of the protected situation of these organs, but experimentally they have been fully studied. The line of separation is at first filled

with serofibrinous exudate, but with deep wounds the edges gape, and in the cord complete division is followed by retraction of the segments. On the edges there is a broad margin where the tissue undergoes destruction, with swelling and degeneration of the nerve fibres, known as traumatic degeneration, so that even clean and smooth wounds have a relatively large extent. Secondary degenerations follow.

Without complications the wound heals by absorption of the softened parts and growth of granulation tissue from the pia and the adventitia of the vessels. Regeneration of nerve fibres within the central organs takes place to a very limited degree, for while the bundles of new fibres sprout from the stumps of the old, they have not the power of piercing the scar, and ganglion cells appear never to be regenerated.

On the other hand a regeneration of nerve fibres may take place when the supporting tissue and the vessels remain unimpaired, the new fibres growing along the lymph sheaths of the vessels and replacing the degenerated portion and re-establishing communications.

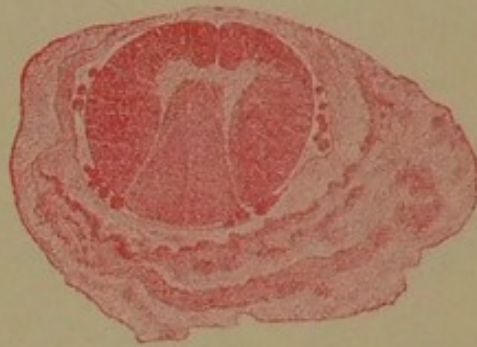
The commonest injury to nervous tissue is contusion or crushing, with escape of blood. In the brain this may be due to bullet wounds, blows with blunt instruments, or fragments of bone being driven in. The cord suffers with fracture or dislocation of the vertebræ and bullet wounds, and the destruction of vertebræ by caries or tumors. Hemorrhage in the cord is not common with such conditions, but in the brain there is usually a rupture of meningeal vessels and escape of blood into the subdural and subarachnoid spaces. The bruised tissue resembles the soft semifluid mass, mixed with blood, which is found with red softening. Extreme flexion and extension of the spine may cause stretching and tearing of fibres within it and hemorrhage, and temporary dislocation and twisting of the vertebræ may have the same effect, and at the autopsy some time afterward there may be no traces of the injury other than those in the nervous tissue. In the newborn similar trauma may follow difficult birth and vigorous methods of artificial respiration (Schultze's).

Commotio Cerebri. Extreme degrees of force, as blows and falls, acting upon the cranium, may cause lesions of its contents without injury to the bones. Severe hemorrhage may occur, evidently caused by unequal diffusion of the cerebro-spinal fluid and its compressing effect at certain places, and hence the lesion is often at the side opposite the point of impact, or on the walls of the ventricles or of the Sylvian aqueduct. In other cases concussion produces numerous capillary apoplexies from rupture of vessels by the strongly shaken fluid. Some-



PLATE XXX.

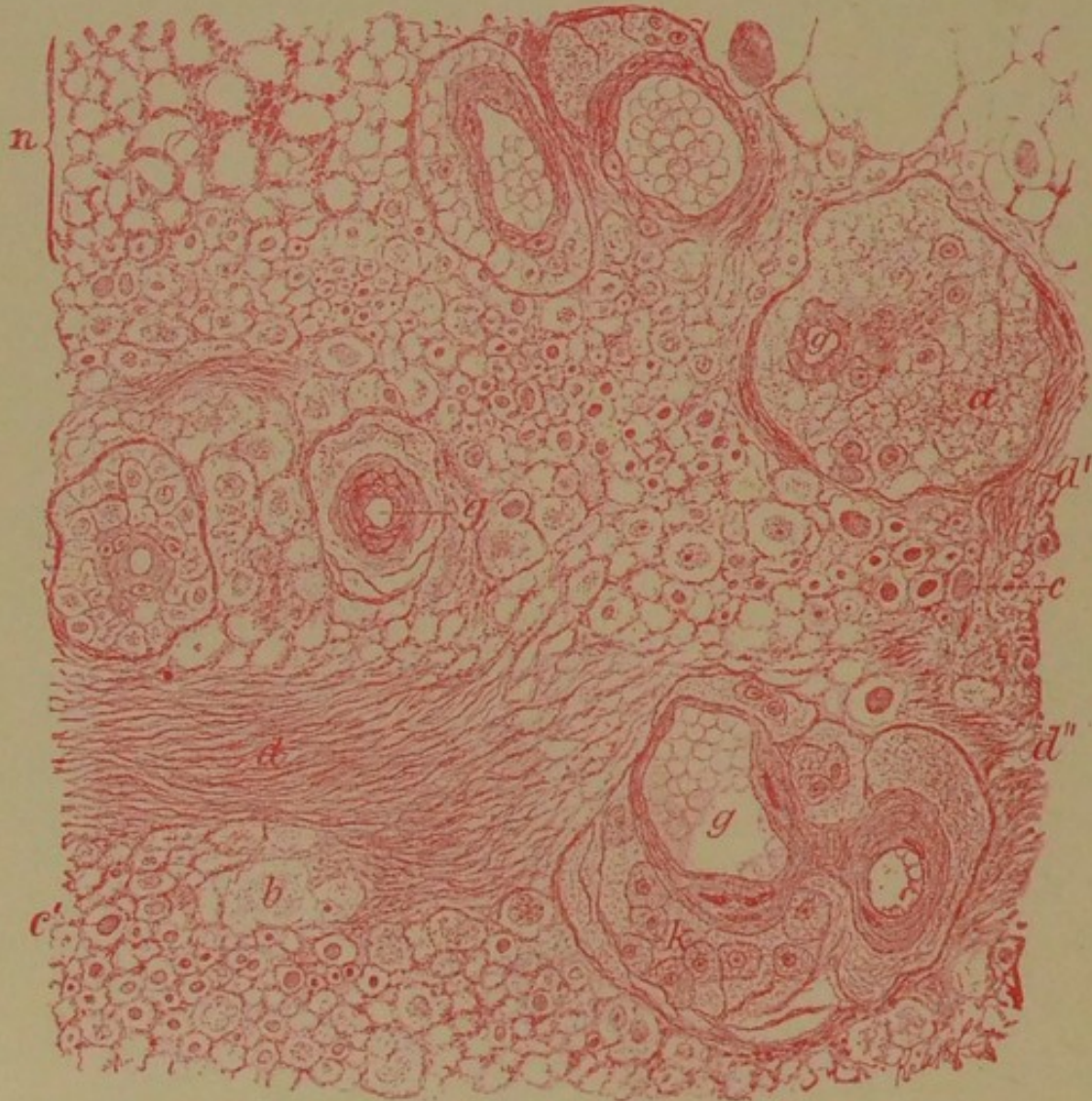
FIG. 303.



Epidural Tuberculosis.

The cord is tightly surrounded by the thickened dura. Magnified with a hand-glass.

FIG. 304.



Myelitis from Compression with Caries of Vertebra. Swelling, Degeneration, and Sclerosis in the Cord.

g. Vessels with distended lymph spaces, containing granular cells and detritus. *c, c'.* Swollen axis cylinders. *n.* Enlarged meshes of the glia. *d, d'.* Sclerosed parts of the glia. $\times 250$.

times, however, without gross lesions there is an alteration in the nervous tissues which may cause only temporary functional effects. All these conditions are grouped under the name of concussion of the brain or *commotio cerebri*.

Similar traumatism of the spine may lead to secondary degeneration, in many cases after hemorrhages or torsion and stretching of the cord.

Myelitis from slow compression of the cord may be due to exostoses, malignant tumors of the vertebræ, caries, and tuberculosis of these bones, and other invasions of the available space within the canal. With caries of vertebræ the bones gradually yield and an angle forms in the spine by which the affected vertebræ are slowly pushed backward. If the displacement occurs suddenly after vigorous movement or trauma a fatal termination is immediate from crush of the cord.

When the caries affects the upper cervical vertebræ slight movements of the head may cause a shifting of one upon the other, and the odontoid process is pressed into the medulla, causing sudden death.

With a gradual development of the kyphosis the compression of the cord is much slower, and it becomes flattened or fusiform at the site of greatest pressure. But because of the fact that the cord does not entirely fill the canal such results may be postponed for a long time. It happens rarely that an abscess under the periosteum lifts up the longitudinal ligament, projects into the canal, and compresses the cord.

In most cases the compression of the cord is due to proliferation on the external surface of the dura. With caries of the vertebræ a tuberculous process very soon invades the dura, spreading along the cellular tissue between it and the bone, and on the inner side there form large spongy grayish granulations, partly caseous and partly suppurating, which press upon the cord. Microscopically they consist of granulation tissue with giant cells and caseous foci, many of which tend to become fibrous. The condition is called *pachymeningitis tuberculosa externa*.

Compression by such a mass leads to occlusion of the large lymph spaces of the cord as well as of the veins, small lymphatics, and capillaries, and consequently there is a stasis of all fluids and edema of the cord. The nervous elements swell and degenerate, and later

FIG. 302.



Diagram of compression of the cord with caries of the vertebræ. The diminished vertebra, II, is pushed backward by I and III, and narrows the canal. (After STRÜMPPELL.)

the glia suffers. Possibly toxic products from the tubercle bacilli, and vasomotor disorders, as well as a mechanical irritation, also take part in producing the lesion.

At times the tubercular process invades the cord, and tubercles are found upon the pia and in the substance of the nervous tissue. As a rule, however, the changes in the nervous parenchyma are referable to the severe edema, and after a stage of degeneration and softening sclerotic changes follow. Embolism and thrombosis of spinal vessels may lead to the same effects. The cord is thinned and flattened, or still swollen with edema, or hard from the sclerosis, or in a condition of softening.

Even in severe degrees of vertebral caries reparative processes are possible, and the abnormally movable parts become ankylosed by fibrous and bony overgrowths, so that single bones may no longer be distinguishable. And in the cord the edema may disappear and the nervous elements to a certain extent be restored. Thus clinically improvement and even complete cure may be observed in some of these cases.

The part most often involved is the lumbar region, then the dorsal, and after that the cervical.

Osteomyelitis and tumors of the vertebræ and syphilitic spinal meningitis may have effects similar to those of caries with tuberculosis.

G. LESIONS OF THE VENTRICLES AND THE CENTRAL CANAL; HYDROCEPHALUS INTERNUS; HYDROMYELIA; SYRINGOMYELIA.

Internal hydrocephalus is the name given to accumulation of fluid in the ventricles of the brain, usually in the lateral, then in the third, and least often in the fourth.

Congenital hydrocephalus develops during fetal life or soon after birth, and is progressive, so that the quantity of fluid may exceed a litre. It is usually thin and serous, rich in albumin and clear, or at times turbid. The etiology is obscure. In many cases there is imperfect development of the brain, in others, perhaps, an early inflammation or a mechanical obstacle to the flow of the cerebro-spinal fluid. Both lateral ventricles are usually distended, but one alone may be involved or only a portion of it, and in the latter case the distended part is often shut off from the remaining cavity by adhesions.

The ependyma is often loose and macerated or thickened and sclerotic, and covered with granulations. Atrophy of the convolutions accompanies the process, so that the fluid may be contained in a very thin-walled sac. The surface is flattened, the corpus callosum may be lacking, the bones are at times pressed apart and the fontanelles increased in extent or closed by Wormian bones. Congenital hydrocephalus is often associated with idiocy, and other defects, like harelip, may coexist.

Acquired hydrocephalus may arise in acute form as an inflammatory exudation from the choroid plexus, and the fluid may be serous or more purulent and mixed with blood. When serous it is distinguished from normal cerebral fluid by containing more albumin and being turbid. The plexus and the wall of the ventricle may show hemorrhages. The commonest source of this variety is the extension of a suppurative or tuberculous meningitis through the transverse fissure of the brain along the pia which passes into the ventricles.

Acquired hydrocephalus of chronic form may be a transudate from the choroid plexus and tela because of obstacles to the venous flow from the brain, by reason of tumors in the cerebellum or other pressure on the great veins of Galen. These veins collect the blood from the deeper veins of the brain, and consequently their occlusion leads to marked stasis throughout the organ. Similarly closure of the communications between the ventricles, as the foramen of Monro and the Sylvian aqueduct, may lead to distention of the ventricles. This may be the effect of scars and inflammatory exudates or chronic meningitis. In many cases the disease coincides with rhachitis and seems to be idiopathic. Atrophy of the brain is followed by external hydrocephalus, especially in the aged.

The symptoms of the lesion are those of increased intracranial pressure, and the form of the brain corresponds. When the condition develops early enough the form of the head is distorted also, but not to such severe degrees as with the congenital type.

Escape of blood into the ventricles may be due to perforation of a hemorrhagic focus or traumatism, as during difficult births.

Among the chronic changes which occur here are especially the fibrous thickening of the ependyma during old age, which appears as smooth, hard areas or granulations of small size, on the floor or the walls of the lateral and fourth ventricles.

The *tela choroideæ* of the third and fourth ventricles are folds of pia mater which enter between the corpus callosum and the corpora

quadrigemina, and between the cerebellum and the medulla, respectively, and at certain points present vascular processes, from 1 millimetre to 2 millimetres in length, of dilated capillaries arranged in lobules and covered with cubical epithelium. The epithelium is the remnant of the ventricular wall pushed before it by the pia.

In this tissue *corpora amylacea* and concretions of lime are frequent, and sometimes we find large tumor-like masses filled with lime salts in masses; these are called psammomata. In the old the choroid apparatus becomes cystic by collection of fluid between the layers of pia. From the epithelium of the plexus or of the ventricle carcinoma may develop, and from the other elements, endothelioma and sarcoma.

Inflammation occurs with meningitis, and may be of any character and lead to hydrocephalus. Tubercles in the part are common.

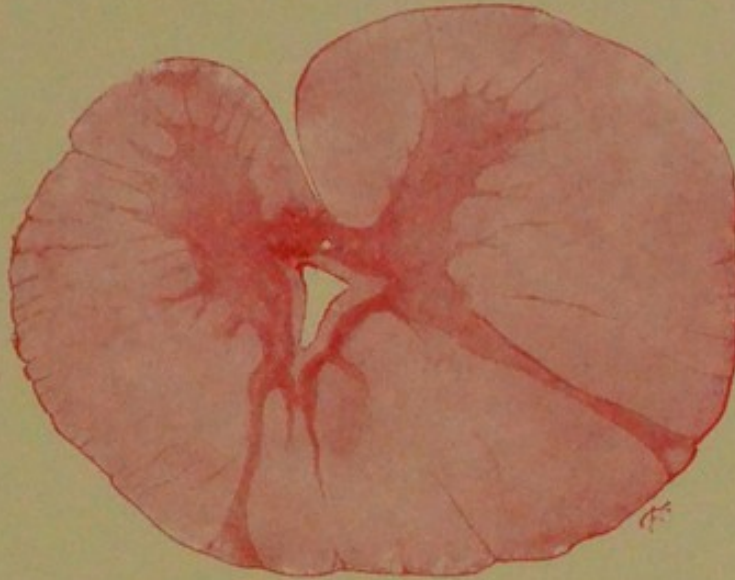
Syringomyelia. This term is given to fissures and dilatations in the cord, either confined to the medulla and the upper cervical region or extending through its length. The cavity begins in the central canal or near it, and in the most pronounced case the cord remains as a thin investment of a long tube, of greater volume than the normal cord, filled with serous or colloid material and collapsing after its removal. At first the wall is composed of gray substance, and later of white, and various diverticula may be found along its course. It may be softened or sclerosed. When the cavity is plainly due to distention of the central canal the name hydromyelia is applied, and this may be congenital when there has been a defect in the closure of the medullary plate. In other cases it is acquired and depends upon causes similar to those which produce hydrocephalus internus.

Other cases of syringomyelia are due to hemorrhages or lymphatic transudates or softening over a linear course, but these are not strictly considered as syringomyelia. Many of these cases are connected with the development of glioma, and such a tumor may be found, involving a long segment of the cord, increasing its size and forming a long cavity by softening. In other cases a gliosis of the gray matter develops which does not increase the size of the cord, and is distinguished from true glioma by its larger proportion of fibrous stroma and smaller proportion of cells, but it forms similar fissures. Other cases may be due to anatomical congenital conditions or hemorrhage, softening, and traumatism, ending in progressive softening.

The Hypophysis. In its anterior lobe this structure is glandular, in its posterior lobes it consists of vascular connective tissue and often contains colloid cysts. Hyperplasia of the anterior lobe may occur as

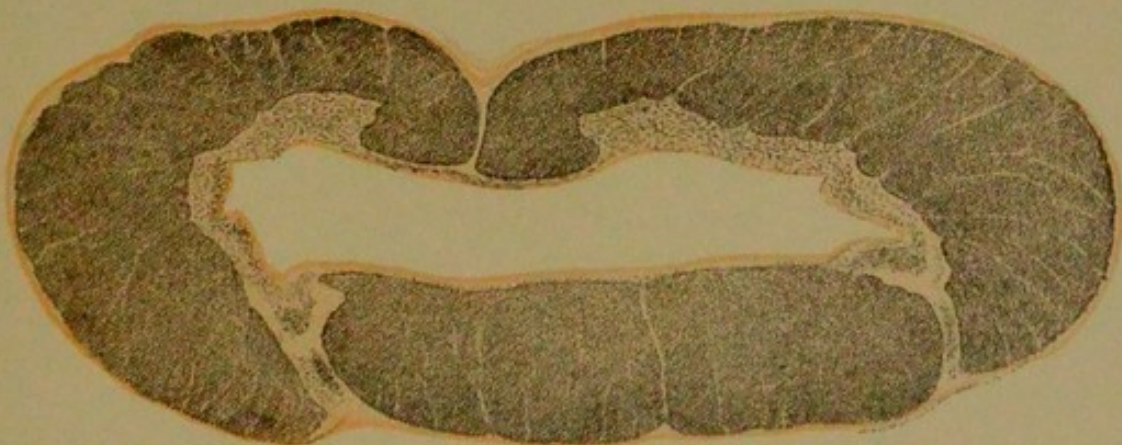
PLATE XXXI.

FIG. 305.

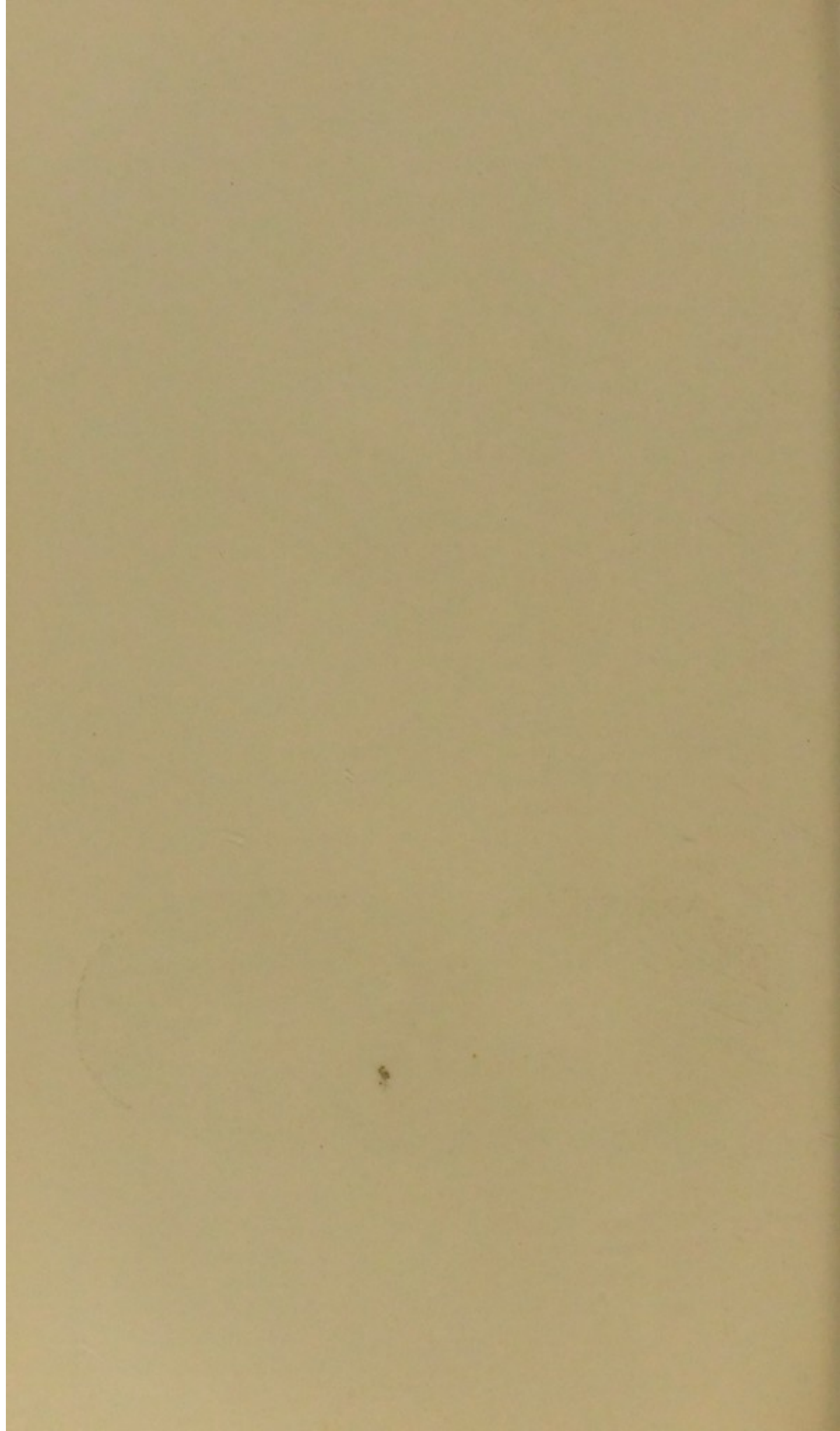


Syringomyelia. Fissure behind the central canal when there has been a defect in the closure of the medullary plate. In other cases it is acquired, and depends upon causes similar to those which produce hydrocephalus internus.

FIG. 306.



Hydromyelia. Weigert's Stain.



adenomata of the size of a hen's egg. Other tumors are uncommon. The pineal gland often contains a large amount of "brain sand" (calcareous material), or it may be hyperplastic, cystic, or the seat of tumors.

H. TUMORS AND PARASITES.

Small tumors of the brain which grow slowly may be wholly without symptoms. In other cases they produce general and localized disturbances. The general results are due to compression, of which the descriptions already given will suffice. Parts of the brain may also be distorted or atrophied by the pressure, or edematous. The tumor may be encapsuled by thickened glia. Malignant forms, especially gliomata, are usually infiltrating, and cannot be sharply separated from surrounding tissue, extending further and growing also by apposition. Usually the severest effects of pressure are not observed.

Clinically, parasites and conglomerate tubercles, neoplasms of the skull and the membranes, and hematomas of the dura, also act as tumors. Of the true proliferative tumors glioma is most common and may be very large; sarcoma, angioma, lipoma, fibroma, and mixed forms also occur. Glioma may begin in the retina and follow the optic nerves to the base of the brain and the neural canal.

Tumors of the cord are not common, but of them all glioma is most frequent, as pseudosyringomyelia. Cholesteatoma, sarcoma, lipoma, and fibroma are sometimes found. These may cause pressure and distortion, edematous distention of the cord, or complete interruption of the tracts, with secondary degenerations, both ascending and descending. Secondary carcinoma from the vertebræ and sarcoma from the meninges may be diffuse and very extensive. The latter occurs as metastases in the brain, and less often in the cord.

Animal parasites in the brain are uncommon. *Cysticercus* may form multiple and numerous vesicles, at times racemose, most often in the membranes and the ventricles, and in the latter place they lie free in the cavity. If large they cause compression. In the cord this form is extremely rare, but rather more common in the dura than in the nervous tissue.

Echinococcus may be single or a group of several vesicles on the surface of the brain, or within its mass, or in a ventricle. In the cord it may be extradural or intradural or primary in the vertebræ. From the subpleural and subperitoneal tissue the cyst may grow into the spinal canal through the anterior foramina, as is true of certain tumors.

I. DISEASES OF THE MEMBRANES OF THE NERVOUS ORGANS.

In the pia and arachnoid lesions are observed similar to those of serous membranes, and with these the nervous tissues are apt to be affected also.

Among circulatory disorders hemorrhages are common after cortical injuries in the newborn when the cranial bones are made to glide over each other, and thus vessels are torn, and, to a smaller extent, with both active and passive congestion. Most of the larger meningeal hemorrhages in the spinal membranes may be referred to trauma.

External hydrocephalus is a collection of fluid between the pia and the arachnoid. The pia follows the inequalities of the cortex, while the arachnoid is attached only on the summits of the gyri and bridges over the sulci, hence the fluid collects at first in the sulci and widens them, and at last lifts the arachnoid off the convolutions. The condition accompanies stasis, inflammation, and atrophy of the cortex. In the latter form hydrocephalus ex vacuo occurs over local depressions from scars and softening, and generally when the brain is imperfectly developed and does not fill the cranium.

Inflammation is called **leptomeningitis** and may be exudative, in the various forms, or productive.

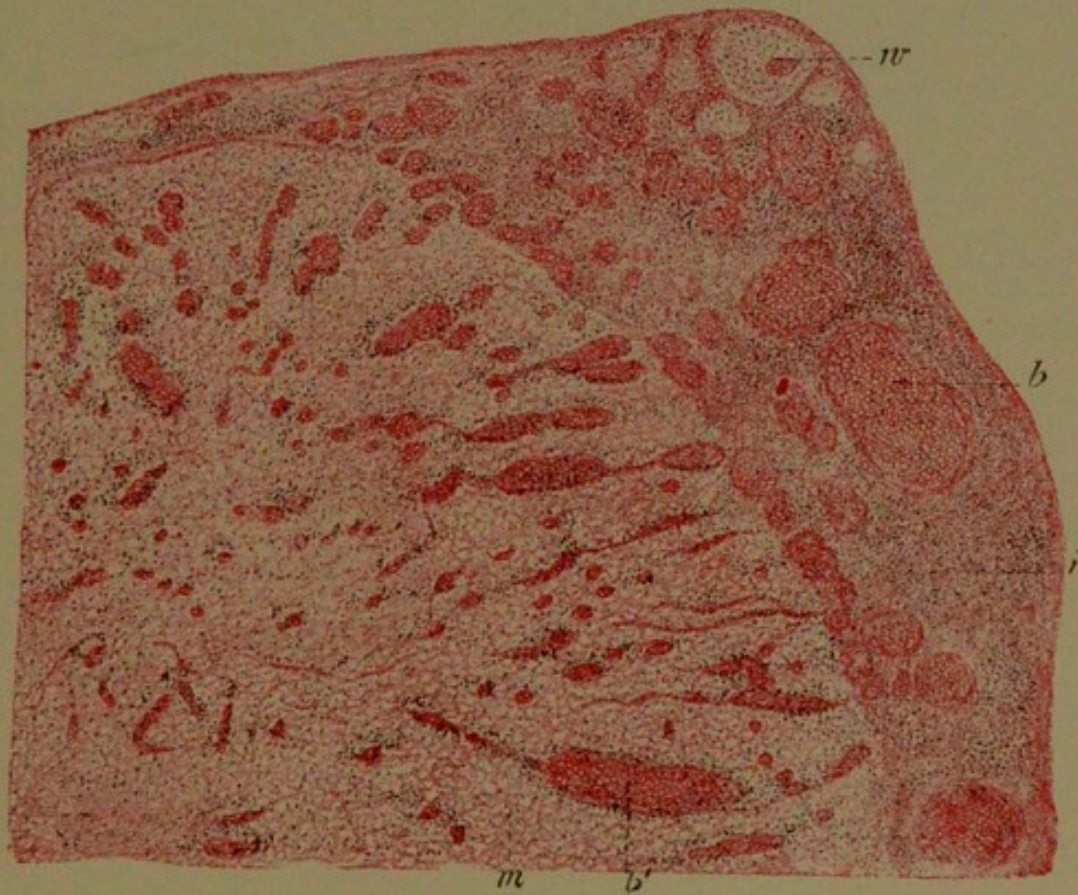
Serous meningitis, or **inflammatory hydrocephalus externus**, consists of acute hyperemia, increased transudate, and edema of the surface of the brain, and occurs with infectious diseases and as a stage of other forms of meningitis. It is observed also with sunstroke.

Primary purulent meningitis may be sporadic, endemic, or epidemic, and it is often impossible to say how the infection arises. The epidemic form commonly involves the membranes of the cord also, and is called epidemic cerebro-spinal meningitis. Post-mortem a purely suppurative or a fibrinopurulent exudate is found in the meshes of the pia and arachnoid which gives these tissues a yellow color. The convexity of the brain is more frequently involved than the base. Microscopically the exudate is made up of fibrin and pus cells, the vessels are the seat of purulent infiltration, and hemorrhages are common.

In the brain there may be a general or a cortical edema, or foci of inflammation and softening, or acute inflammatory hydrocephalus from extension to the choroid membranes of the ventricles. These cavities are then filled with serous or seropurulent exudate, and the ependyma is swollen and loosened and infiltrated with round cells.

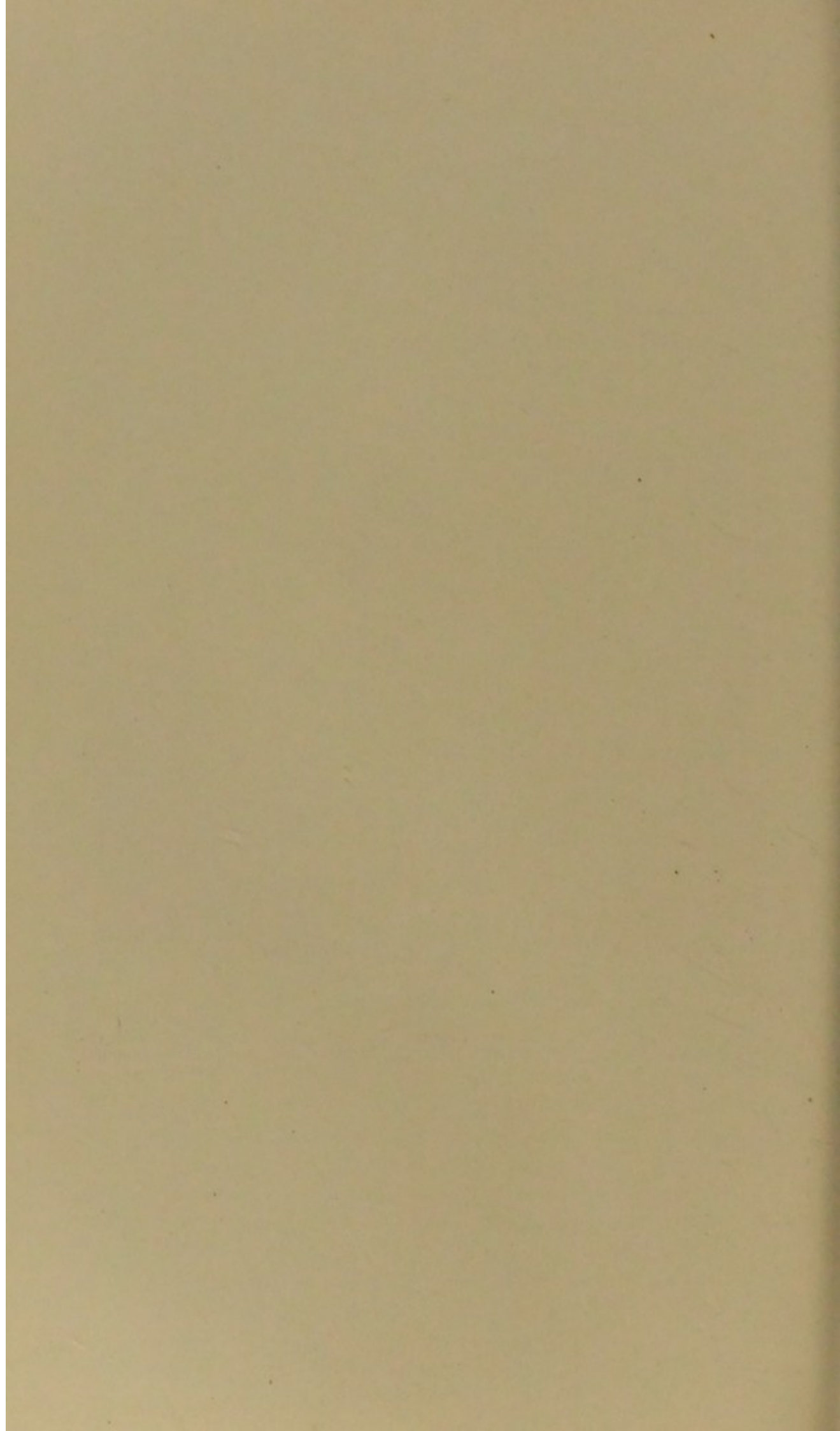
PLATE XXXII.

FIG. 307.



Acute Infiltrating Meningitis and Myelitis.

m. The cord, covered above and to the right by the strongly infiltrated membranes. *w.* Nerve roots enclosed in the latter. *b, b'.* Vessels congested and surrounded by small-celled infiltrate. $\times 50$.



The foci of inflammation in the cortex may be markedly edematous or show simple, hemorrhagic, or purulent softening, and large abscesses may develop. As a rule, the course of the disease may be followed along the vessels which enter from the membranes. The symptoms may be those of cerebral compression. At times the substance of the cord is also involved in inflammatory edema, and on the margins the

FIG. 308.



Junction of meninges and cord with mild meningitis of chronic type. *w.* White matter; between its septa of glia the nerve fibres have a dark axis cylinder and a lighter medullary zone. *r.* Glial margin. *i.* Inner layer of thickened pia. *a.* Outer layer. *b.* Vessels. $\times 250$.

fibres are strongly swollen and degenerated. In other cases there is a small-celled infiltration about the arteries entering from the membranes. In very intense lesions there may be areas of softening, hemorrhage, and pus in the medulla. These cases are known as *meningo-encephalitis* and *meningomyelitis*.

The cause of such inflammations may be pyogenic cocci, Fränkel's diplococcus and other forms, and as one port of entry the ethmoid sinuses have been recognized in many cases. Metastatic forms occur with infectious diseases of all varieties. Other causes are wounds of the cranium and the membranes, caries of the temporal bone and other parts, which may at first cause a localized purulent pachymeningitis and a later invasion through the lymphatics, purulent processes in the orbits, frontal and nasal cavities, and primary abscesses of the brain. Similar conditions may be observed as the origin of spinal meningitis.

Chronic meningitis includes a series of diffuse or regional thickenings and cloudings of the membranes which under the microscope are due to hyperplasias of the connective tissue. These may be the traces of more acute processes, especially of purulent meningitis, or develop in a chronic form from the beginning, as is frequently seen in psychoses, alcoholism, and chronic renal diseases. If the nervous tissues are not involved the condition is called *leptomeningitis superficialis*. Similar conditions accompany all sclerotic lesions of the cortex and surface of the cord, such as progressive paralysis and tabes, and the usual result is such strong adhesions between nervous tissue and meninges that the latter cannot be removed by gentle force. This is termed *leptomeningitis profunda*, or *meningo-encephalitis* and *myelitis chronica*. Superficial areas of softening present such adhesions as yellow plates (*plaques jaunes*), in the membranes, of firm consistence, yellow and often pigmented, and entering the nervous tissue as a scar of some depth. Similar adhesions between dura and pia occlude the lymph spaces and lead to stasis of lymph with hydrocephalus and hydromyelia.

Chronic leptomeningitis of the convexity regularly presents numerous Pacchionian granulations along the great fissure. These consist of fibrous hyperplasia in the arachnoid and often grow through the dura and into the longitudinal sinus. They may be mistaken for tubercles. In the pia of the spine, at times also of the brain, meningitis ossificans sometimes causes the formation of bony plates in the membrane.

The Dura Mater. Among circulatory disorders of this membrane thrombosis of its sinuses may be mentioned, occurring in marasmus of all kinds, with infectious diseases and after injuries. Stasis and edema of both brain and membranes follow, and hemorrhagic infarction of the former is not uncommon.

A peculiar form of chronic fibrinous inflammation of the dura is called *pachymeningitis interna hæmorrhagica*. In general its course is

composed of an initial fibrinous exudate on the inner surface of the membrane; then a granulation tissue develops from the dura and replaces the fibrin by young connective tissue very rich in vessels; then repeated small hemorrhages occur from these vessels on the inner surface and stimulate new hyperplasia of connective tissue, and as the process continues there are found various layers, of a rusty brown red, presenting older and more recent bleeding and organization of the clots. The first exudate may be very small and thin; the final mass may be thick and tumor-like, made up of many pigmented layers, and constituting the so-called hematoma of the dura. Rupture of the hematoma may cause fatal bleeding into the subdural spaces.

This lesion is found with many cerebral diseases, among which may be cited various insanities, and atrophy, and it occurs also with diseases of the heart and kidneys, in hemorrhagic diatheses, with alcoholism, and after injuries to the cranium. An analogous process called *pachymeningitis hæmorrhagica externa* rarely occurs on the outer surface of the dura mater.

Purulent meningitis appears as a layer of pus and fibrin on the inner surface of the dura, and in a simple or gangrenous form may follow infected wounds of the head and caries of the bones.

Thrombophlebitis of the sinuses often accompanies suppurative lesions of the dura, either in a primary or a secondary relation, the lesion passing through the walls of the sinus from the dura or arising first in the sinus from caries of the bones. In either case large abscesses of the brain and widespread, purulent meningitis may be observed and be the immediate cause of death. In other cases the lesion complicates erysipelas of the face and head.

The dura acts as the internal periosteum of the cranium, and has the power of making bone. Hence *pachymeningitis ossificans* leads to the formation of osteophytes on the inner side of the skull and plates of bone in the dura, especially in the falciform process. Productive fibrous inflammation, with adhesions to the brain and the cord, has been mentioned.

Tuberculosis and **syphilis** of the pia and arachnoid have been treated with similar lesions of the nervous tissues. In the dura tubercles are infrequent, except that the spinal dura becomes involved from the development of such lesions in the epidural fat. Fungous and spongy nodules are found, of a grayish or yellowish color, more or less caseous, of varying extent and with a tendency to fibrous changes, and when the dura is invaded adhesions between it and the cord result, and

on the inner surface of the membrane there may be discrete or confluent tubercles.

Syphilitic pachymeningitis, on the other hand, is more common over the cerebrum, and usually takes its origin from the cranial bones or the pia, and attacks the dura secondarily. It occurs as a diffuse infiltrating inflammation or as circumscribed granu-

lomata with fibrous or caseous tendencies, scars, and adhesions between the membranes and the bones. Starting in the dura, it may progress to the bone or the pia. In the affected part the vessels are the seat of syphilitic arteritis.

Hypertrophic cervical pachymeningitis is due to a chronic inflammation, usually syphilitic, which surrounds the cord with a thick fibrous ring and produces myelitis by compression. The dura shares in the lesion, but is not the starting point of it.

Sarcoma and endothelioma (*fungus duræ matris*) sometimes occur in the dura, the latter developing from the lymphatics. They may break through the bone or involve the brain and cause compression. Psammoma of the dura is relatively frequent, and is either a sarcoma or an endothelioma which contains masses of lime salts.

In the pia and arachnoid various tumors occur, including epidermoid (cholesteatoma), endothelioma, sarcoma, fibroma, and others. A diffuse form of sarcoma sometimes involves the entire length of the cord, from the medulla to the cauda equina, as a flat mantle of varying thickness, entirely surrounding the cord or entering its substance also. It is usually of the small round-celled variety. The mem-



Sarcoma of the cord and spinal pia. (After BRUNS.)

branes may be involved secondarily by tumors of the bones adjacent or by metastasis from a distant neoplasm.

K. DISEASES OF THE PERIPHERAL NERVES.

Degeneration and Neuritis. The peripheral nerve fibres may be regarded as neurites or dendrites, protoplasmic processes from nerve cells of the anterior horns, the spinal ganglia, the cerebral nuclei, or perhaps also from the end organs of the nerves; consequently they suffer secondary degeneration when separated from their ganglia.

Division, compression, and contusion of the nerve may be followed by Wallerian degeneration of the peripheral portion with the same microscopic changes which have already been described, including swelling and fragmentation of the axis cylinder, breaking up of the medullary substance, and loss of the sheath of Schwann. The fat which results is gradually absorbed by wandering cells. The central stump undergoes a retrograde degeneration of milder type, which may pass through it into the cord and at last the proximal part becomes atrophic.

Beside the degeneration due to mechanical causes, similar lesions may be found in general infections, as diphtheria, from the action of toxic products. With degeneration there may be cellular infiltration and fibrous changes ending as an induration. The condition is termed neuritis. In beriberi and polyneuritis such lesions are the principal element in the case. In diseases of the brain and cord, as tabes and cerebro-spinal syphilis, similar neuritis is common, and, among the intoxications, saturnism and alcoholism frequently lead to it.

Nerves which happen to lie in foci of suppuration undergo infiltration and degeneration or purulent and necrotic changes.

Within the central nervous organs regeneration of fibres is extremely rare, but the peripheral nerves are very capable of renewal. Both after degeneration of single fibres and after entire division of the nerve a regeneration is possible if the ends are not too far retracted or tough fibrous tissue does not intervene. At present the process is thought to begin in the central portion with the formation of a new axis cylinder, which grows distally and in time becomes invested by medullary sheath and neurilemma. According to other views, the regeneration begins in the peripheral part by proliferation of the nuclei of the neurilemma to long strands, which acquire a protoplasmic envelope and after union differentiate to an axis cylinder.

Tuberculosis and syphilis involve especially the roots of the nerves at their passage through membranes similarly affected, the granuloma distorting and destroying their fibres. Leprosy causes nodular and fusi-

form enlargements of the nerves (*lepra nervorum*), in which cellular infiltration and degeneration may be found.

Tumors include fibromata which start from the perineurium and the endoneurium, and usually contain no nerve fibres, sarcomata, myomata, and other forms. Fibroneuroma often occurs in multiple form, but is seldom a true neuroma. After amputations the divided nerves form new fibres throughout their stumps and also become involved in the cicatricial tissue and form large nodules of tangled nerve fibres and connective tissue.

CHAPTER XIII.

DISEASES OF THE ORGANS OF LOCOMOTION.

A. THE BONES.

BONES consist of an outer compact layer, covered by fibrous periosteum, and an internal spongy substance, and within the spaces of this contain a soft marrow. The compact tissue and the trabeculae of the spongy are formed by a calcified ground substance which encloses small dentate cavities provided with processes called the osseous corpuscles and containing the bone cells. The processes are in communication with each other, and thus form a system of canals throughout the bone called canaliculi, and certain large spaces of this kind in the compact bone carry vessels and nerves and some connective tissue, and are called Haversian canals. About these the compact substance is arranged in lamellae more or less concentric. The lamellae consist of fibrous tissue joined by cement substance and permeated with lime salts. From the periosteum certain fibrous bundles, known as Sharpey's fibres, enter the bone, and in young specimens are easily demonstrated.

Since bone is not a dead tissue it undergoes pathological processes like any other tissue, but those connected with the compact portion are usually of regressive nature and those of the medulla and periosteum are often progressive.

Degenerations.

The marrow of the bones in a growing individual, up to about puberty, is red and lymphoid, characterized by profusion of cells and vessels. It contains marrow cells, giant cells, nucleated red blood cells, and others enclosing red corpuscles. At puberty the marrow of the long bones becomes fatty, contains fewer cells, and these enclose fat globules; in the short and flat bones it remains red. In many degenerative and cachectic conditions and in the aged the fatty marrow becomes colloid or mucoid, and loses its yellow color for a grayer tint.

(a) **Loss of Osseous Tissue by Lacunar Arrosion.** Resorption of bone in most cases is connected with the formation of small cavities

along the otherwise smooth edges of the spongy trabeculae and superficially under the periosteum. These portions which become hollowed out are called Howship's lacunae, and in them are large cells resembling myeloplaxes which probably absorb the bone, and are hence called *osteoclasts*. With a numerous appearance of these lacunae the parts become irregularly toothed and eaten, in the microscopic picture, and may in time disappear.

Atrophy of bone is usually of this variety. If the entire bone is involved the condition is called *rarefaction* or *osteoporosis*, and is characterized by enlargement of the canaliculi and loss of spongy trabeculae; the bone is then lighter in weight, porous, and fragile. If the bone as a whole becomes smaller from external absorption it is spoken of as *concentric atrophy*, and proceeding from within *eccentric atrophy*. These processes may involve a single bone or the entire skeleton, the latter being common in senility and cachexia and specially marked in the flat cranial bones and the lower jaw in old age. In the diploe of cranial bones there is a condensation preceding the atrophy.

Inactivity and pressure may cause the atrophy of single bones, as when a central nervous lesion or disease of a joint prevents the use of a limb, and also in a stump after amputation. An example of atrophy from pressure is given by the Pacchionian granulations and the thin bones of the hydrocephalic skull.

Atrophy from loss of function in a paralyzed limb is called neuro-paralytic atrophy. In certain cases it accompanies nervous lesions without paralysis of muscles, and is then called neurotic atrophy.

(b) **Atrophy with Halisteresis.** *Osteomalacia* is a slow softening of all the bones of the body, in which the essential feature is the removal of mineral salts from the tissue and persistence of the ground substance, as osteoid tissue. It differs from the lacunar absorption; here both bone salts and framework suffer together. In the spongy parts the process starts in the medullary spaces, and in compact bone from the Haversian canals, as an osteomalacic margin, free from salts, but still connected with calcified portions. The margin appears homogeneous or in places lamellar and fibrous, with transitions to the systemic lamellae of the tissue. The canals either disappear or persist as small oval vacuoles. Probably the process is a chemical solution of the mineral matter by the fluids circulating through the bone.

The process begins with the appearance of holes and fissures in the bony tissue which are due to solution of the cement substance, and hence are disposed longitudinally in the course of the fibres. Then

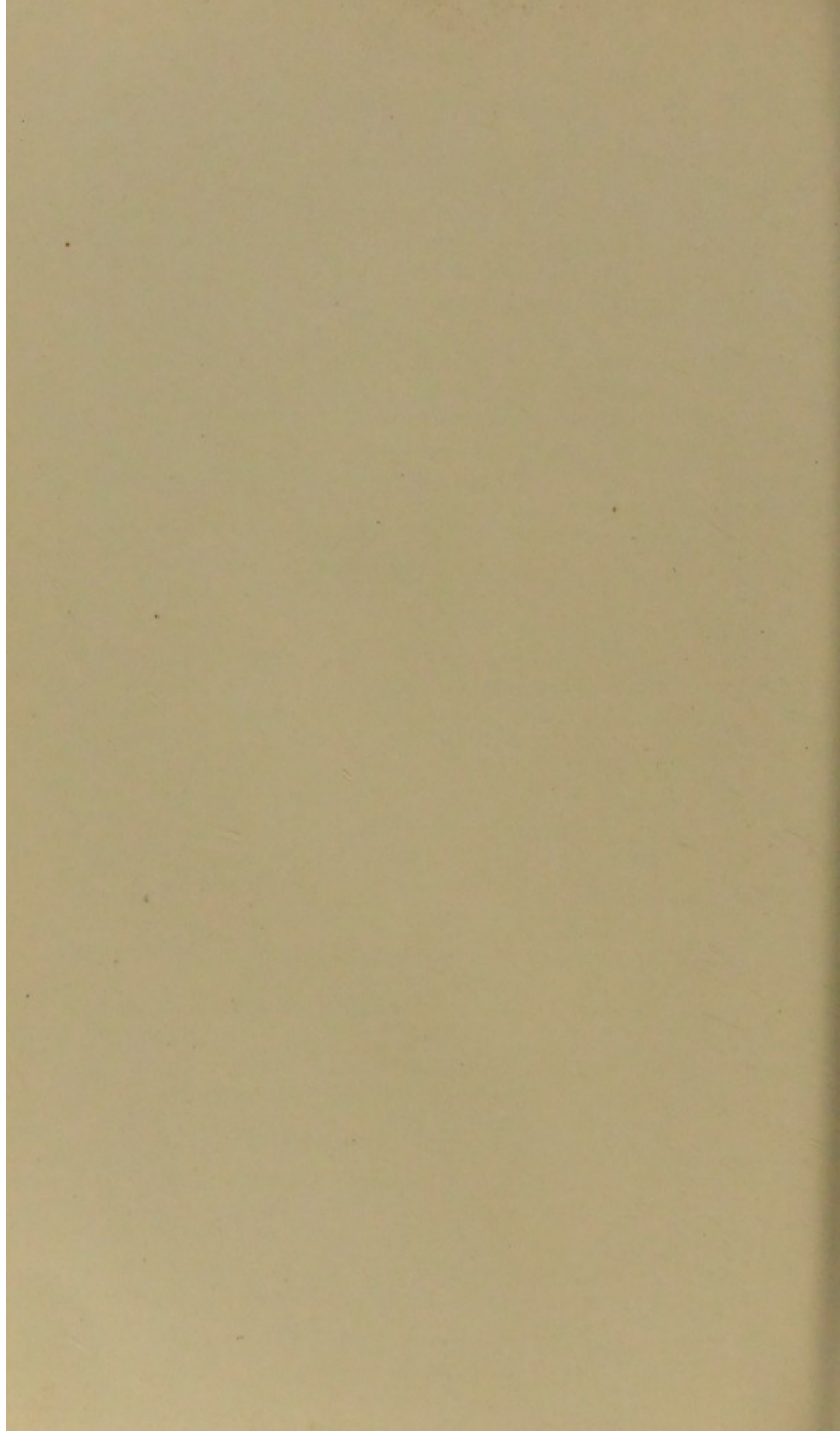
PLATE XXXIII.

FIG. 310.



Section from a Pronounced Case of Osteomalacia
of the Femur.

M. Marrow. *R.* Margin of bone. *K.* Trabeculae of bone, nearly decalcified and much narrowed, with edges completely decalcified and rounded excavations, lying in a fibrillary ground substance. Embedded in paraffin and cut without further decalcification. $\times 350$.



peculiar "lattice-work" spaces develop, star-shaped, feathery, and retiform, from irregular widening of the canaliculi. They are not uniformly distributed, but occur most numerous along the softening margin. Granular areas are found, due to the solution of cement substance and fragmentation of fibrillæ. Few Howship's lacunæ are found in osteomalacia, but many perforating canals.

The osteoid tissue is either dissolved, split up into fibrillæ, or replaced by medullary and fibrous tissue in which islands of osteoid and bony material may persist. Later it may undergo mucoid degeneration and even become fluid. The bone is rarefied, its spaces are enlarged, and after the compact substance, which resists the process for a time, also becomes affected, there remains a reddish pulpy mass in which no trace of bony structure may be recognized.

The marrow may be red and lymphoid or fatty or mucoid, and pigment and hemorrhages are frequent in it.

Essentially osteomalacia is not, like rhachitis, an imperfect calcification of new bone, but a removal of mineral salts from bones already formed; but at the same time certain bones, like the femur and the vertebræ, may show new formation of imperfectly calcified bone which renders them much thicker than normal. Fractures occurring in the course of the disease may show a free formation of callus. In the early stages the bones are fragile, and hence are frequently broken, in the later they are pliable, and hence variously bent and distorted.

The most important changes are observed in the bones of the pelvis and the lower extremities. In the pelvis the weight of the trunk on the sacrum bends it forward and pressure from the femora drives the symphysis forward, in a beaked form, and these two changes are characteristic of the osteomalacic pelvis. The spine suffers various curvatures. The lower limbs present bendings and infractions which may heal by fibrous or osseous tissue, or not at all, and when they heal angular deformities remain. Chemically, the affected bones are rich in organic matter and lacking in inorganic, and the osteoid tissue does not resemble the ground substance of true bone in its composition.

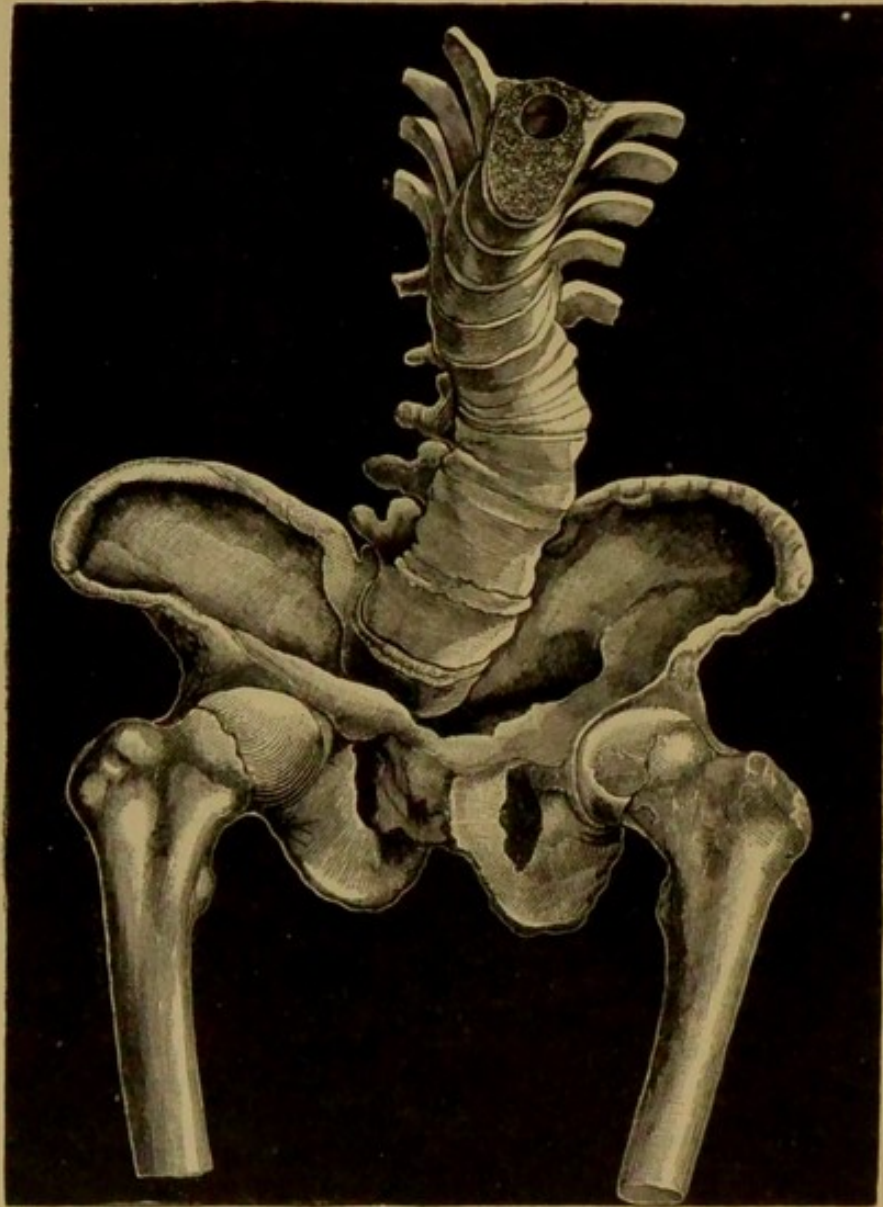
FIG. 311.



Lattice-work figures in haliteresis. (After V. RECKLINGHAUSEN.)

Puerperal osteomalacia is distinguished from the non-puerperal. The former begins in the pelvis, the latter in the legs or the cranium, but both are almost confined to the female sex. The puerperal form accompanies pregnancy, and, while its course is variable, it is usually worse in succeeding pregnancies. Recovery in any case is rare.

FIG. 312.



Laterally bent osteomalacic pelvis with scoliosis of the vertebral column.

The etiology of the disease is undetermined. It has been ascribed to the action of lactic acid, and the bones and urine may contain this acid, but its appearance is not constant. The disease is unusual, but endemic in certain places, as along the Rhine in Germany, and sporadic cases occur elsewhere.

Halisteresis occurs in senile osteomalacia, with free formation of new bone, with tumors of the bones, and in osteitis deformans and fibrosa. Very mild degrees of a similar process are common in pregnancy, and it has been suggested that the disease is but an exacerbation of a condition which normally accompanies pregnancy.

Regeneration of Bone.

New osseous tissue may be formed from the periosteum, or from the marrow by osteoblasts in linear series, which become calcified and are succeeded by others, except a few which remain as bone corpuscles ;

FIG. 313.

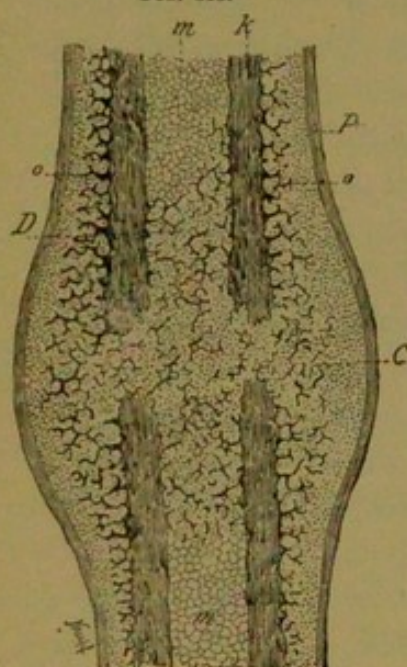


FIG. 314.

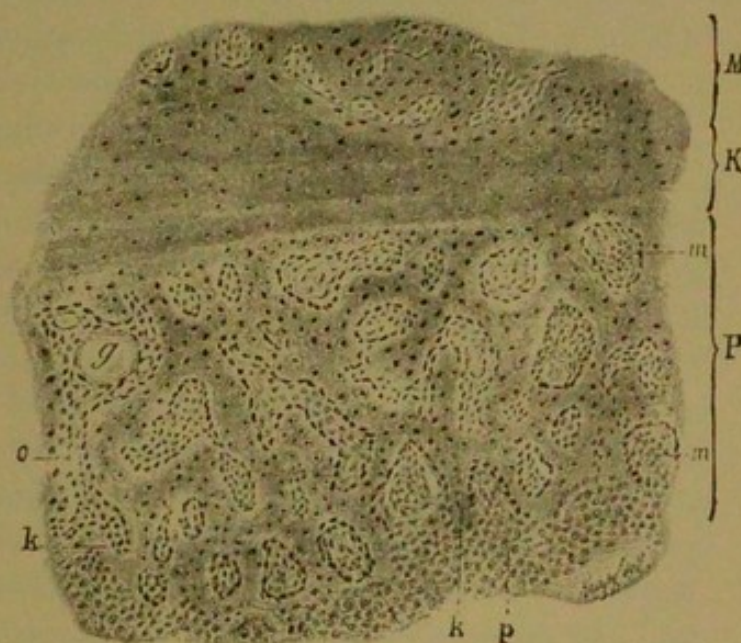


FIG. 313.—Diagram of healing fracture. From a guinea-pig, ten days after injury. *K*. Ends of the bone. *m*. Marrow. *c*. Periosteal callus. *d*. Medullary callus. *o*. Osteoid tissue. $\times 6$.

FIG. 314.—The same preparation. *M*. Myelogenous callus. *P*. Periosteal callus. *K*. End of the bone. *k*. Osteoid trabeculae. *o*. Osteoblasts in rows. *p*. Thickened periosteum. $\times 250$.

the row of formative cells resembles cylindrical epithelium in appearance. Beside this appositional method new bone may be formed as trabeculae, which arrange themselves in groups and apparently excrete finely fibrous osteoid tissue between them, in which calcification occurs later. A third formation occurs by direct calcification of bundles of the periosteum, and further growth by apposition of osteoblasts. Physiologically a fourth method is general, namely, the endochondral, mineral salts being deposited in the ground substance of cartilage.

Productive and regressive lesions commonly involve both resorption and new formation of bone, and the two may go on at opposite sides of the same trabecula.

Repair of Fractures. In simple cases without much separation of the fragments there is a reaction which prepares for the absorption of blood and splinters of bone. The ends become united by osteoid tissue, which is formed partly by the periosteum and partly by the marrow, and this *callus* is hence distinguished as the medullary and the periosteal. In both the osteoid tissue is arranged in strands which enlarge by apposition. If the ends are separated by an interval an intermediate callus forms between them. Thus about the site of the fracture there is a large fusiform swelling which joins the ends and closes the medullary canal. The development of the callus requires from two to ten weeks, and after that time the mass begins to become more porous, decreases in size, superfluous bone is removed, and in time the medullary canal may again become patent.

If conditions are unfavorable the union may be merely fibrous, which is the case in old age and cachectic states, but certain fractures, as of the patella, always heal by fibrous repair. When the fibrous bands are loose the ends of the bones may become smooth and a false joint form (pseudarthros).

Transformation. The finer structure of bone corresponds to its function, for the trabeculae are arranged according to the mechanical conditions of stress and weight. If pathological processes alter these relations the bone affected undergoes a readjustment to suit the new requirements by the aid of resorption and new formation of trabeculae, and this process, which is called *transformation*, is frequent in callus after fracture, ankylosis of joints, and persistent luxation. In general, the whole mass of a bone varies according to its functional needs.

Inflammation and Hyperplasia of Bones.

Active inflammatory changes in bones occur in the periosteum, the medullary canal, the spaces of the spongy parts, and the Haversian canals, the compact tissue and ground substance remaining passive. The results are either absorption of old bone or formation of new, and hence the process may be divided into destructive and productive lesions. Essentially both removal and formation of bone resemble the corresponding physiological processes, and are frequently combined.

(a) **Destructive Forms.** Among the most destructive lesions of bones are those with suppuration in the medullary cavity or under the periosteum and the formation of granulation tissue, as occurs in chronic inflammations and tuberculosis. The bone undergoes lacunar arrosion and becomes rarefied, and when this occurs on an inflammatory basis it is called inflammatory osteoporosis. Granulation tissue which enters the spaces of spongy bone and Haversian canals has a marked power of thus melting down the compact tissue. Perforating canals form at the same time, by the development of new vascular channels between spaces in spongy tissue and between Haversian canals in compact bone, which thus perforate the bone in various directions and assist in its rarefaction.

Beside their perforation the trabeculae break into molecular fragments, owing to interference with their nutrition, and lie as free "sand" among the granulations.

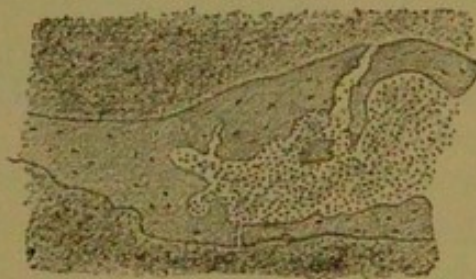
At the site of the lesion the bone is not only rarefied, but also breaks down in mass and leaves large defects. This is called *caries* or ulceration of bone. In the gross such carious defects are either depressions on the surface or cavities communicating with the interior, and filled with granulations or pus according to the nature of the case. The wall of the cavity is made of markedly rarefied bone, or it may have become secondarily thickened. Small lesions of this kind are called erosions.

When large sections of the bone undergo death from conditions which produce the same effect in single trabeculae it is spoken of as *necrosis*, and the dead fragment is called a sequestrum. This separates by demarcation from the bone. Necrosis develops with infectious diseases, after injuries, especially fractures with splintering, near bed-sores, and with gangrene of the extremities.

The varieties of inflammation in bones include periostitis, osteitis, and osteomyelitis, according as the enveloping membrane, the compact bone, or the medullary cavity is involved; but since these combine in many cases the name suggests the starting point of the process rather than restriction to a part of the bone.

Acute periostitis may be serofibrinous or purulent. In the former case the membrane is swollen and red; in the second case it is also

FIG. 315.



Trabeculae of bone with perforating canals. $\times 50$.

infiltrated with pus, and yellow. Large collections of pus under the membrane are called subperiosteal abscesses, and these cause similar lesions of the soft part and caries of the bony surface, or even invade the cavity by way of the nutrient canal. Necrosis and exfoliation of a part of the bone may occur.

The lesion accompanies many cases of osteomyelitis and follows injuries with infection, and suppuration of adjacent soft parts. When of a chronic type it is often associated with the formation of new bone, as osteophytes and hyperostoses (*periostitis ossificans*).

Acute osteitis and osteomyelitis are usually the result of infection and are commonest in the long bones, as the femur and tibia, but may invade the small bones also. The cause is frequently the staphylococcus. Infection occurs through the blood from the skin, the lungs, or the intestine, and injury predisposes the bone to the lesion. It begins in the medullary canal or the spongy tissue, and passes to the compact bone and the periosteum. Severe hyperemia and bleeding change the color of the marrow to bright red, and where it has been fatty it becomes lymphoid. Gradually this color turns to grayish red or yellowish, and the marrow becomes purulent or "pyoid." When the canals of the bone and enveloping membrane are involved the bone becomes rarefied, or carious, or necrotic. Necrosis occurs in a peculiar way. The diaphysis of a long bone may die and the sequestra may lie centrally or superficially (cortical), or involve the entire thickness of the shaft; hence they are called central, peripheral, and total sequestra. Usually they are thin and flat, with sharply toothed margins. After demarcation they lie as loosely attached or free bodies in purulent fluid.

The periosteum behaves as in primary purulent periostitis, but in addition masses of new bone are formed and the osteophytes often surround and partly hide the sequestrum. Perforation of the bone and escape of pus externally form cloacæ and fistulæ. Sclerotic changes in the bone may go on with the destructive lesion, and the canal may thus be closed; this is to a certain extent a protective process. After removal of the sequestrum recovery may follow. If it remains the dead portion may be enclosed by osteophytes and remain as a foreign body. In some cases the osteomyelitis is not a primary disease, but the expression of localized infection with a general disease, as typhoid and scarlet fevers, pneumonia, measles, etc. Such mixed infection is usually due to pyogenic organisms which attack a part weakened by the previous disease.

Caries of the temporal bone is usually associated with otitis media, which may cause deep ulceration and destruction of the local mucosa, and may include the formation of cholesteatoma. The cause is usually a pyogenic coccus, but tubercle bacilli seem to produce the inflammation at times. The ossicles of the ear and various parts of the wall are destroyed, and wide necrosis and sequestrum formation may occur in the temporal bone. The accompanying *cholesteatoma* consists

FIG. 316.

FIG. 317.

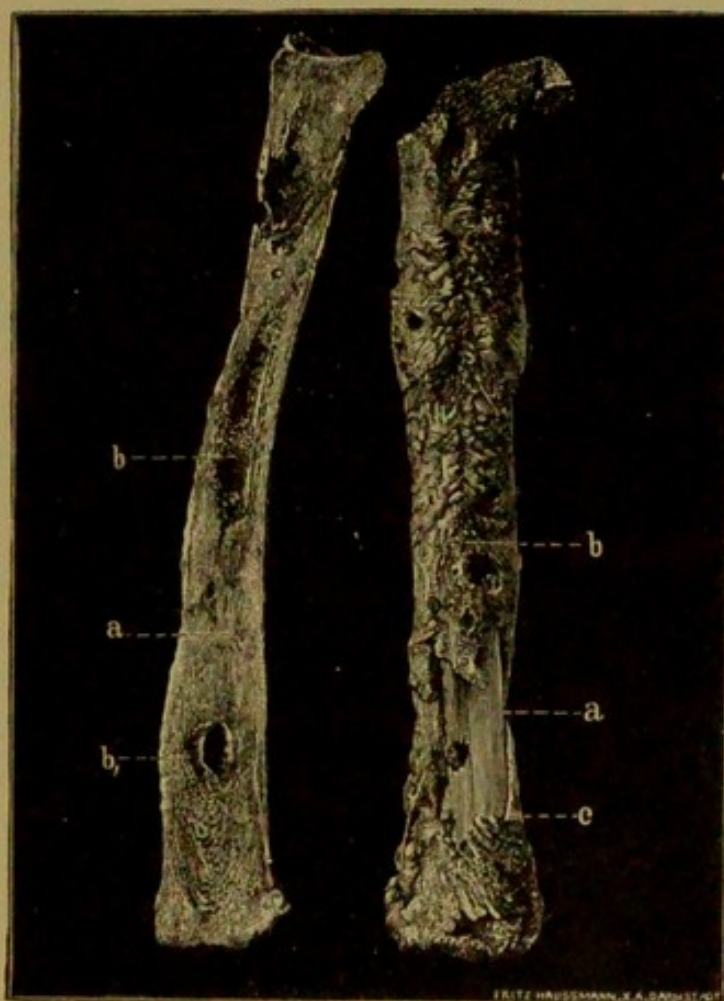


FIG. 316.—Sclerosis of the medullary cavity after osteomyelitis.

FIG. 317.—Suppurative osteomyelitis with necrosis, and sequestrum formation and osteophytes.

of masses of pearly, concentrically arranged material which forms a solid cast of the middle ear. Microscopically cholesterin, crystals of fatty acids, and epithelium are found. The mass is formed from proliferating squamous epithelium over the granulations on the inflamed wall. The pus may rupture through the tympanum into the cranial cavity, and, with or without actual perforation, set up a secondary abscess of the brain.

Phosphorus Necrosis. Workers in match factories and other trades where phosphorus is used frequently suffer a purulent or ossifying periostitis of the lower jaw, with necrosis of the entire bone or large portions of it. Pyogenic organisms are associated with the disease, and the point of entry is commonly found in carious teeth. Other bones may be invaded later.

(b) **Productive Forms; Hyperplasia.** Productive processes in bones start in the spaces of the spongy portions, the Haversian canals, and the periosteum, and either follow acute destructive lesions and repair the damage, or accompany chronic forms until they exceed them, or arise spontaneously. The latter case is simple hyperplasia, and frequently leads to the formation of bony tumors.

Productive or ossifying periostitis is often part of an acute inflammation, and causes the deposit of new layers of bone under the membrane. It is observed also about sequestra, with osteomyelitis and caries of the bones and joints. In other cases there is persistent venous stasis, or the lesion starts about an inflammatory area, as an ulcer of the leg, and in the course of chronic diseases of the heart and lungs it produces enlargement of the finger-tips. The new bone resembles the osteoid tissue of callus, and is at first spongy, but growth by apposition thickens the trabeculae as in the latter case. The new material may be flat or rounded, dentate, foliate, and acicular, and after a time becomes firmly attached to the old bone beneath. Such new formations are called *osteophytes*. More diffuse thickenings are called *hyperostoses*. During pregnancy delicate folia of new bone may form on the inner side of the cranium; these are to be connected with the absorption of bone which occurs at this time. Other cases of periosteal new-growths may be fibrous or cartilaginous.

The formation of new bone in the spongy tissue increases the trabeculae and diminishes the spaces, so that the part in time may resemble compact bone and even the entire medullary canal may be closed. This condition is known as *osteosclerosis*. Localized areas of this kind are sometimes called *enostoses*.

Osteosclerosis occurs in the following circumstances:

1. Without apparent cause, or as part of a senile change, in the diploe of the flat cranial bones, sometimes combines with porosis, and, if syphilitic, with hyperostosis.
2. Bone which has been inflamed and rendered porous may later on become sclerosed.
3. Circumscribed sclerosis about carious bones is very common,

PLATE XXXIV.

FIG. 318.

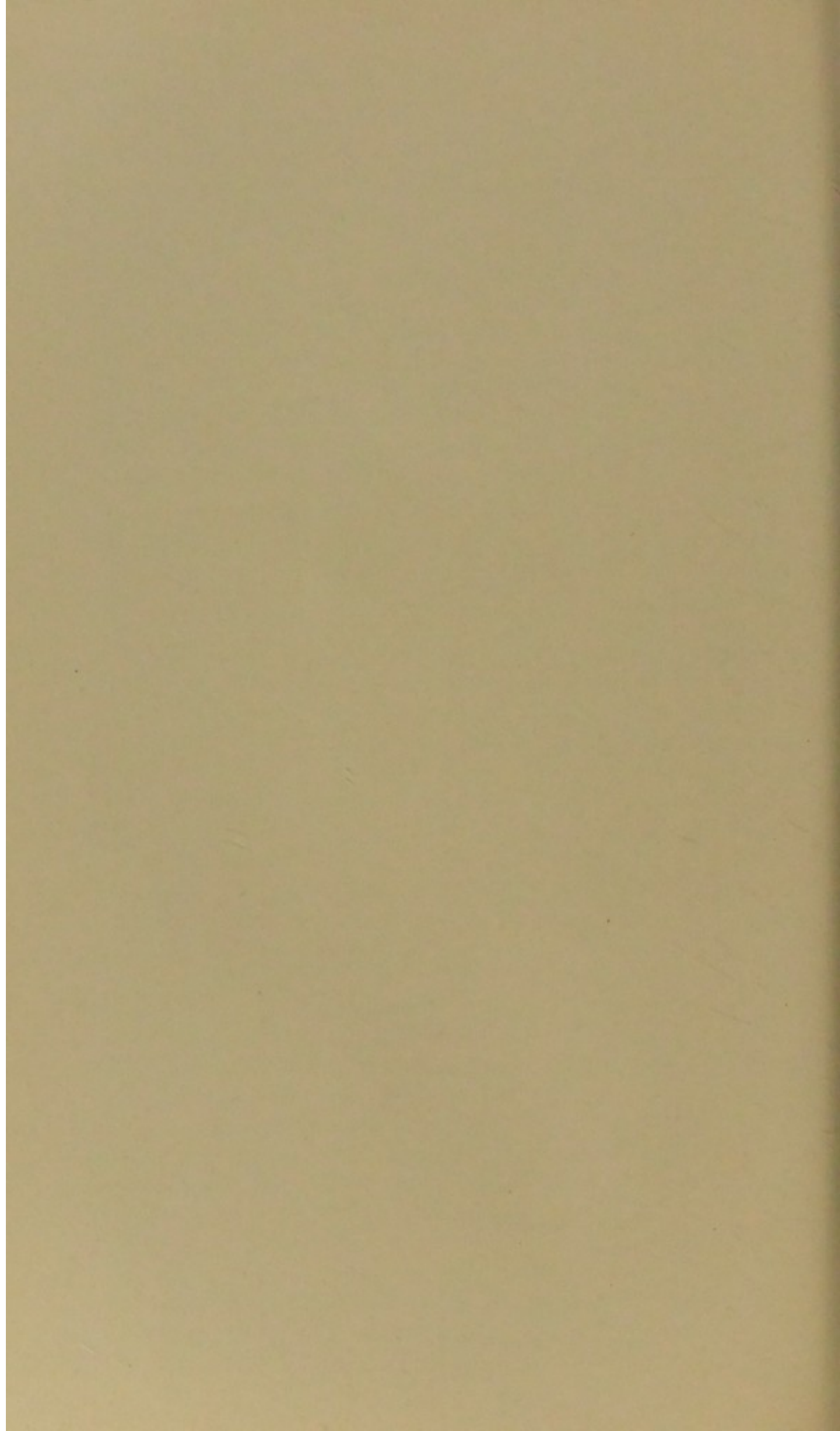


Osteoporosis of the
Cranium. $\times 6$.

FIG. 319.



Osteosclerosis of the
Cranium. $\times 6$.



protecting the remaining bone by a thick wall of compact substance. Tuberculosis, syphilis, destructive tumors, and ulcerative lesions of the joints are frequently limited in this manner.

4. In the formation of sequestra the same process helps to form the bed in which the dead bone lies, and as eburnation it converts ordinary bone into an unusually hard and voluminous tissue, with distortion.

In the young, hyperostosis of the facial and cranial bones at times occurs, which depends upon the formation of new osseous tissue, and may diminish the orbits and other cavities of the face and also of the cranium. This is termed *leontiasis ossea*. In *acromegaly* a similar process develops under nervous influences, and other cases comprise partial and general giantism.

Osteitis deformans or *fibrosa* is an infrequent regressive and productive lesion of old age which affects many bones at once. It attacks parts which bear special burdens, and leads to thickening and osteophytes, while at the same time *halisteresis* occurs in neighboring parts. In the end the bones may be very much distorted, and the disease resembles *arthritis deformans*.

Infectious Granulomata.

Tuberculosis. One of the commonest diseases of bones is tuberculosis occurring in childhood, as part of severe *scrofula* or independently, and at times as an inherited condition. Infection occurs through the blood from other organs, or directly from adjacent tissues, as from the pleura to the ribs or from joints to the bones forming them.

If the infection comes from without, as from the pleura, the periosteum becomes caseous, and the bone beneath carious after a time, and at last the infection reaches the medullary spaces. From a joint the spongy tissue is first attacked, with the periosteum lying nearest, and, as a rule, hematogenic infection starts in the spongy bone rather than in the medullary canal.

Tubercles of gray color and a spongy mass of granulation tissue develop in many foci and steadily enlarge by the formation of new foci. In the granulations microscopic and macroscopic and somewhat sharply limited tubercles occur. The canals of the bone are invaded by the granulations, and lacunar *arrosion* and typical caries are the result. Large masses of bone may die and lie free in the exudate. Sequestra are usually small, and have rounded edges of irregular

outline. Large wedge-shaped sequestra may form by occlusion of nutrient vessels, resembling anemic infarcts in other organs.

Caseation, with or without softening, and fibrous hyperplasia, are the succeeding steps in the lesion, and their proportion determines the further course of the case. Profuse spongy granulations cause total resorption of the bone and give rise to the fungous type of tuberculosis of bone. Massive caseation with enclosed particles of dead bone may be observed in other cases. In others there is softening and liquefaction of the mass, and it then appears as a puriform

FIG. 320.



Tuberculous caries of a vertebra.

fluid. True suppuration may also be noted, and, as a consequence of both, large cavities may be left.

At first the tuberculous areas are not clearly defined from the remaining tissue, but by fibrous and suppurative changes they may undergo demarcation and lie as large sequestra in a cavity, with osteophytes along the edges.

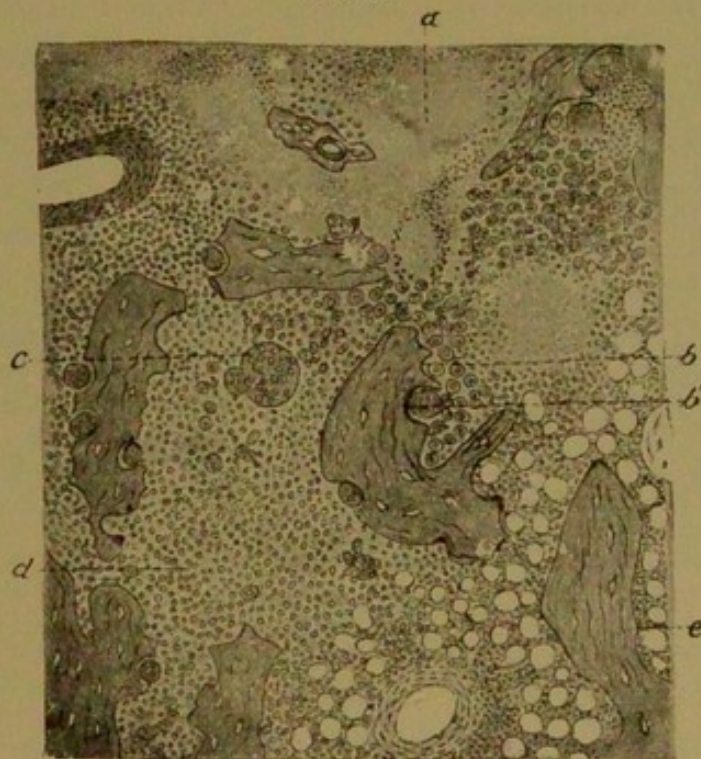
From within the process makes its way to the periosteum, and causes suppuration and perforation, with further progress in various directions and formation of fistulæ. If the adjacent soft parts are involved the pus may follow muscles and fascia and point at distant regions. Thus caries of the lumbar spine causes psoas abscess, which

points in the inguinal region, and pus from caries of the cervical vertebræ follows the muscles of the back.

Ossifying periostitis and sclerosis, with fibrous changes, may slowly bring about a repair after tuberculous tissue is removed, and in some cases this occurs spontaneously. Other cases present a gradual and continuous progress, with more and more destruction of the bones, consequent deformities and fractures, and the formation of osteophytes.

Tuberculosis of the bones is not apt to set up secondary lesions in other organs, and may be confined to bones and joints. General

FIG. 321.



Tuberculous caries of a carpal bone. *a*. Caseous granulation tissue. *b*. Trabeculae. *b'*. Howship's lacunae with osteoclasts. *c*. Trabeculae still unchanged. *c*. Tuberculous giant cell. *d*. Lymphoid marrow. $\times 250$.

miliary infection from such sources has not yet been demonstrated, although commonly assumed as possible. Amyloid degeneration of the organs is frequently seen in these cases.

Of the various bones the epiphyses of long bones, the carpal and tarsal groups, the ribs, and the short tubular bones of fingers and toes, are specially liable to tuberculosis.

Tuberculous caries of the spine is called Pott's disease and leads to angular deformity. In the first two cervical vertebræ the lesion permits sudden displacement and death from compression of the

medulla. In the cranium the temporal bone is most often thus diseased.

A peculiar form of tuberculosis of the fingers and toes is called *spina ventosa*, and consists of osteomyelitis internally, with destructive changes and continuous formation of new layers of bone externally under the periosteum, so that the parts are much increased in size. The condition may heal without necrosis or perforation.

Syphilis of the bones occurs as a hereditary, a secondary, and a tertiary affection.

The so-called rheumatism of the second stage is usually due to slight exudation in the periosteum without severe alterations, and the lesion heals by absorption or with the production of new bone, forming syphilitic tophi. This lesion is found on the long bones and those of the cranium.

In the tertiary form gummata invade the periosteum and the bone directly or from similar lesions in the soft parts, as the skin and the nasal mucosa. Periostitis gummosa appears as flat and indistinct deposits on the bones, of soft and slimy consistence, or elastic, or caseous, due to the formation of syphilitic granulations and their subsequent caseous and fatty destruction. They may be absorbed and leave fibrous scars, or they may suppurate.

The commonest site of the lesion is the cranial dome or superficially placed bones like the clavicle, tibia, and nasal bones. Erosion and caries are frequently associated with the other lesion, and the bone may become porous and worm-eaten or entirely lost.

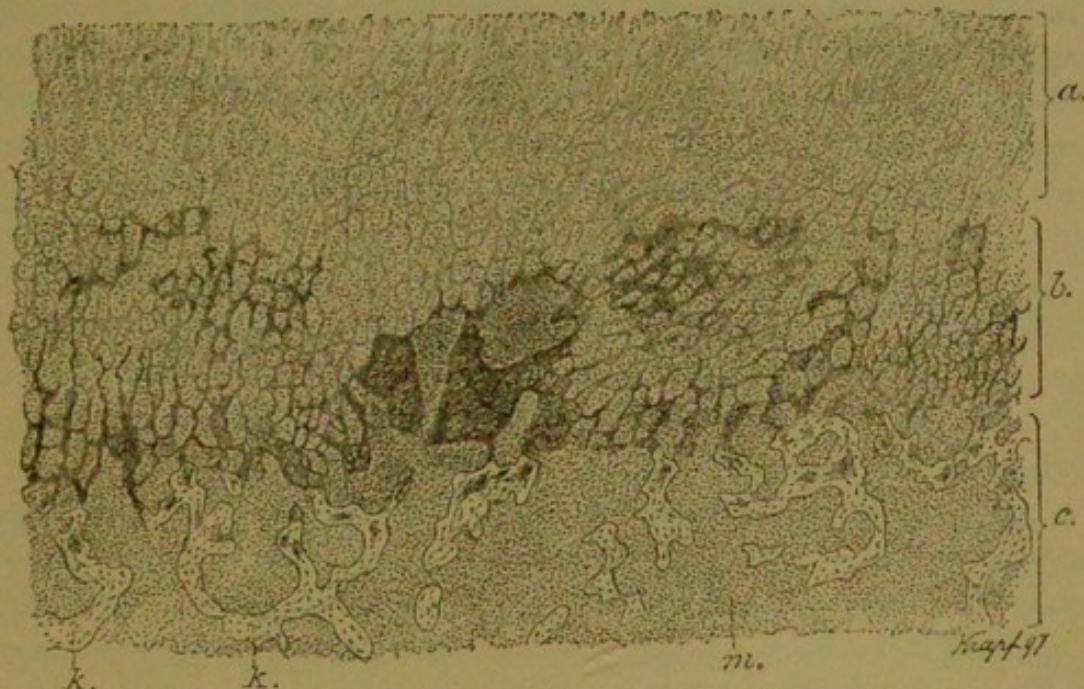
Osteophytes and diffuse periostitis surround the lesion with a wall of new bone, and the spongy tissue becomes sclerosed. Scar formation leaves scars and firm attachments between the sunken skin and the bony surfaces. Sequestra form in severe cases, and in the cranium meningitis may follow.

Syphilitic osteomyelitis may occur as discrete or diffuse lesions in the spongy parts, with further changes similar to those already given for simple lesions of this kind.

In hereditary syphilis there may be a pathognomonic *osteochondritis* at the epiphyses of the long bones and ribs, and no other lesions may be discovered. In slight degrees the ossifying zone is broadened irregularly, as tooth-like projections of calcified tissue reaching into the cartilage, and at other places calcification fails. Similar projections occur into the medullary canal, and the usual straight line between the medullary and the calcifying zone is lacking, and the

deposit of mineral salts is delayed. The trabeculae of the diaphysis are slender, the calcifying zone is white or pink, and has a peculiar soft and friable consistence. In the second stage the zone of calcification is enlarged and more irregular, and the projecting processes join and separate islands of cartilage. The whole growing zone is soft and gelatinous and bulging. In the highest degree, the so-called third stage, a reddish or yellow zone of granulation tissue forms in the layers nearest to the diaphysis, and at times purulent softening accompanies it. The epiphysis becomes loosened from the shaft, being held only by the thickened periosteum, or entirely free. The

FIG. 322.



Osteochondritis syphilitica. a. Zone of cartilaginous growth. b. Zone with irregular calcification, the calcified parts dark. c. Wide marrow spaces, *m*, with slender trabeculae, *k*, of the diaphysis. $\times 250$.

surface of the diaphysis, after removing the epiphysis, does not show the usual finely granular appearance, but is irregular, of various colors, and still retains portions of the calcifying and developing zone of the cartilage.

The most constant site of this lesion is the femoral epiphysis, which should always be examined in suspicious cases, but it occurs also in tibiae and ribs.

Actinomycosis occurs in the jaws, vertebrae, and ribs especially, and infection may occur through carious teeth. Periosteal suppuration accompanies necrosis of the bone in the human subject. In animals

new formation of bone causes immense thickening of the parts, and the lesion resembles certain neoplasms, as osteosarcoma.

Lepra causes deep ulcerations which may involve the bones, and the phalanges of the fingers, especially, suffer necrosis and caries. Leprous lesions of the nervous system cause trophoneurotic changes in bones. Lepra nodules and diffuse infiltration, with caries, occur within the long bones.

Tumors.

In the bones occur nearly all the tumors of the connective-tissue varieties, and mixed forms and metaplasia add to the multiplicity of the forms. The neoplasms arise from the periosteum, the marrow cavities, and the cartilages. Those from the periosteum are called peripheral, and those from the marrow cavity are called endosteal or central or myelogenous. The bone undergoes both inflammatory and carious changes, and also arrosion and necrosis, halisteresis and spontaneous fractures, and about the tumor hyperostosis and osteophytes and sclerosis are observed.

The reactive changes coincide with the carious, forming a protective wall which the neoplasm continuously endeavors to pierce. The proliferation of bone about the tumor surrounds it with a shell which is being steadily destroyed and renewed, and thus the tumor may reach an enormous size and finally rupture externally.

Within the tumor itself new bone may be formed. Apart from osteomata, which consist almost wholly of bone, fibroma, sarcoma, and chondroma may show this formation of new bone within them, and direct metaplasia of cartilage to bone also occurs. Osteoid tissue may develop similarly.

Destructive forms, like osteosarcoma, and metastatic carcinoma and sarcoma, are accompanied by both resorptive and formative changes in the bones affected.

Fibroma of the bones develops usually from the periosteum, and is rather rare. The fibrous pharyngeal polyps which develop from the basis cranii are commoner and may become sarcomatous.

Osteomata may be exostoses, starting in the periosteum, or enostoses from the medullary cavity. The former are divided into *exostosis fibrosa*, in which bone forms directly from the connective tissue of the periosteum, and *exostosis cartilaginea*, in which cartilage forms first and bone from this. The tumors may be round, wedge-shaped, pointed, of large size and single, or small and multiple. They may

consist of compact or spongy bone. They are found with chronic inflammatory lesions and after injury, and occur on the bones of the skull as well as of the extremities. Cartilaginous exostosis most commonly is found at the junction of shaft and epiphysis in long bones and about joints. Independent bony tumors are called parostoses. Enostosis is unusual, but occurs in the diploe and in the jaws.

Chondroma may begin in the cartilage and is called enchondroma, or it may start in any connective tissue, and is then called ecchondroma. On bones they develop from the periosteum, the marrow, or remaining portions of cartilage, as at the epiphyseal line. They are commonest on the extremities, especially in the hand and the foot, and display a relatively marked tendency to become malignant. They may reach a large size and then or previously undergo regressive changes, such as mucoid degeneration and cystic formation. These tumors may develop in persistent cartilages after rhachitis, and sometimes are noted with arthritis deformans.

A peculiar tumor developing in the *clivus Blumenbachii*, sometimes on the vertebral column, is supposed to start in a remnant of the chorda dorsalis and is called chondroma or enchondroma physaliforme.

Myxoma and lipoma of the periosteum are unusual.

Sarcoma of bones includes a number of different tumors, among which some are distinctly endotheliomata.

A diffuse form invades the marrow of long bones, often of several, and in time of the whole skeleton, accompanied by leukemic change in the blood. This is known as diffuse sarcoma, myeloma, and myelosarcoma. The marrow presents the characters of lymphoid tissue, but the neoplasm is distinguished by its unlimited growth and its tendency to break through the bones and make metastases in other organs. It is analogous to malignant lymphoma. This condition takes its origin in the sternum, the cranial and spinal bones, and the femur. Cavernous forms are common.

Circumscribed sarcoma starts from the periosteum or the marrow, and may be small-celled, or large round-celled or fibrosarcoma.

Endothelioma may present the structure of carcinoma (true primary carcinoma does not occur in bones), the connective-tissue stroma being filled with nests of large cells. Other cases approach sarcoma, or the proliferating endothelial cells assume a high cylindrical form and resemble adenoma. Proliferation of the endothelium of vessels gives rise to perithelioma and angiosarcoma, in which the vessels are surrounded by mantles of cells. Connected with these are the

telangiectatic forms called also sarcoma telangiectoides and fungus hematodes, which may be cavernous also. They occur in the bones of the skull and the extremities. Epulis is a relatively benign giant-celled sarcoma starting in the periosteum of the jaw. Combinations of sarcoma and osteoid or bony tissue are called osteosarcoma or osteoidsarcoma. Regressive changes are common in all forms.

Disordered Development and Growth of Bone.

At birth the diaphyses of the long bones are already calcified, but the epiphyses are almost wholly cartilaginous. At various times nuclei develop in these, from which the calcification proceeds. The nucleus at the lower end of the femur measures from 2 to 5 millimetres in diameter at full term; before the thirty-seventh week it is absent. The longitudinal growth of bone occurs at the epiphyseal line. Here the cartilage develops and is steadily calcified from the diaphyseal aspect. On section two zones are found, one, about $1\frac{1}{2}$ to 2 millimetres broad, of a bluish, translucent look, is the zone of cartilaginous increase, and the other, about $\frac{1}{2}$ millimetre broad, is light yellow and hard, and is the zone of calcification. Microscopically three zones can be recognized in the cartilaginous layer. In the outer layer, near the resting cartilage, the cells are enlarged and numerous, and occur more than one in a capsule. In the next the cartilage cells are arranged in columns and are largest near the diaphysis. In the third layer lime salts are deposited between the cells and constitute the calcifying layer. The marrow spaces grow into it from the bone and remove some of the mineral matter and open the capsules of certain cartilage cells, which then become cells of the marrow (zone of primary marrow spaces). The remaining portion of the calcified tissue persists as trabeculæ, along which osteoblasts arrange themselves in a row and form bone.

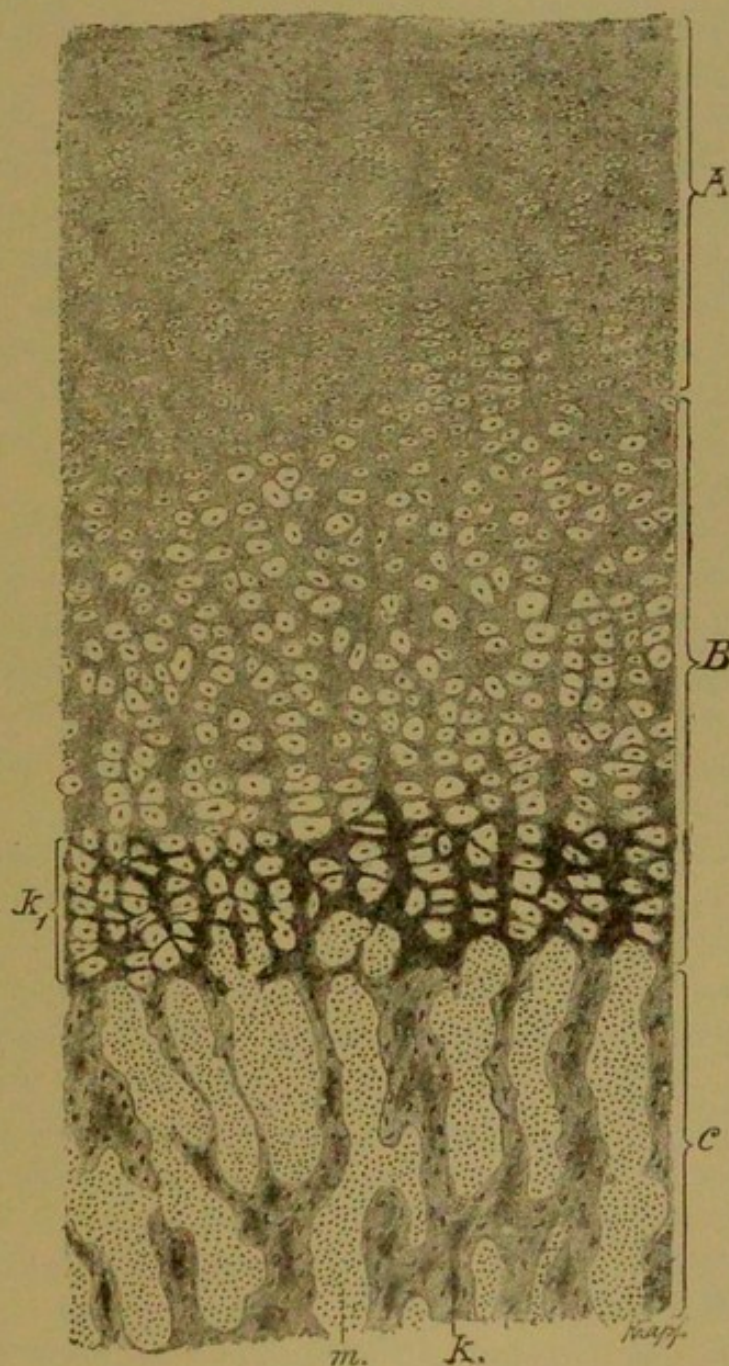
It is important pathologically that the spaces penetrate the calcified portion but remain defined from the uncalcified cartilage as a sharp line.

In a similar way the epiphysis becomes calcified and at last unites with the lengthened diaphysis.

The increase in the thickness of the bone depends upon deposits from the periosteum. From within the bone is absorbed and the medullary canal widens, and the spongy tissue forms by increase in the diameter of the Haversian canals.

The flat bones at first consist of fibrous tissue in which a centre of ossification forms and extends in all directions. On the edges an osteogenic tissue persists during the period of growth, and forms new

FIG. 323



Normal margin of an epiphysis. *A.* Resting cartilage. *B.* Zone of cartilaginous increase. *C.* Diaphysis. *k.* Trabeculae of bone. *k'.* Zone of calcification. *m.* Marrow. $\times 250$.

bone, and at last union with the neighboring bones takes place by sutures. The basis cranii consists of cartilage, and undergoes endochondral ossification.

Hypoplasia of bones depends upon disordered development of the apparatus of growth, either of single bones or of larger regions of the skeleton. Two factors especially influence the result, namely, imperfect formation of cartilage or osteogenetic tissue, so that the long bone does not increase in length or the flat bone in width; and, secondly, premature calcification of the parts, which stops the growth of the bone and leads to early synostosis.

When this occurs in the cranium generally microcephalia is the result. If certain sutures close too early, the skull is small in some diameters or asymmetrical. When the base of the skull develops imperfectly, by premature union between the basilar process and the body of the sphenoid, the basis is shortened and the root of the nose is apparently sunken or retracted, a condition characteristic of cretinism. In the extremities such malformation may occur during fetal life, and is called fetal rhachitis, micromelia, or chondrodystrophy. These conditions may develop after birth.

In the fetal cases the limbs are too short and too broad. In the later cases the general condition known as cretinism is common. This includes imperfectly developed skeleton, asymmetrical or enormous growth of the cranium, hypoplasia of genitals and teeth and other parts, sunken nose, hydrocephalus, and low intelligence. Goitre is commonly present. Cretinism is hereditary, and in certain mountainous valleys endemic.

Rhachitis is characterized by imperfect calcification and persistent softness of the bones. The development is imperfect in length, breadth, and thickness.

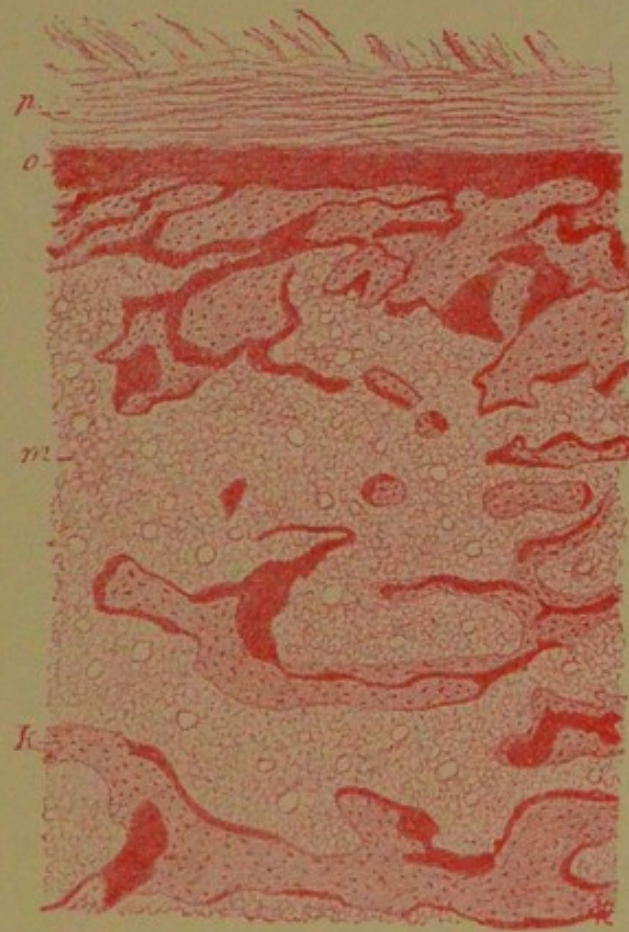
Considering the latter feature, it appears that normally the apposition of bone by the periosteum coincides with resorption within and widening of the medullary canal. In rhachitis the resorption is accelerated and the deposition externally hindered and replaced by osteoid tissue. It resembles osteoporosis and rarefaction.

Changes in length include the following:

1. Abnormally marked increase of cartilage at the ends of the bone and imperfect calcification. The cartilaginous zone is very broad, bluish, and irregular on section. The marrow spaces do not perforate the imperfectly calcified cartilage, but the capsules of the cartilage cells calcify and the cells become small and irregular, and also calcify. This is a metaplasia of cartilage to osteoid tissue. These large masses of osteoid tissue form the characteristic prominences about the ends of rhachitic bones. As a latter change these masses

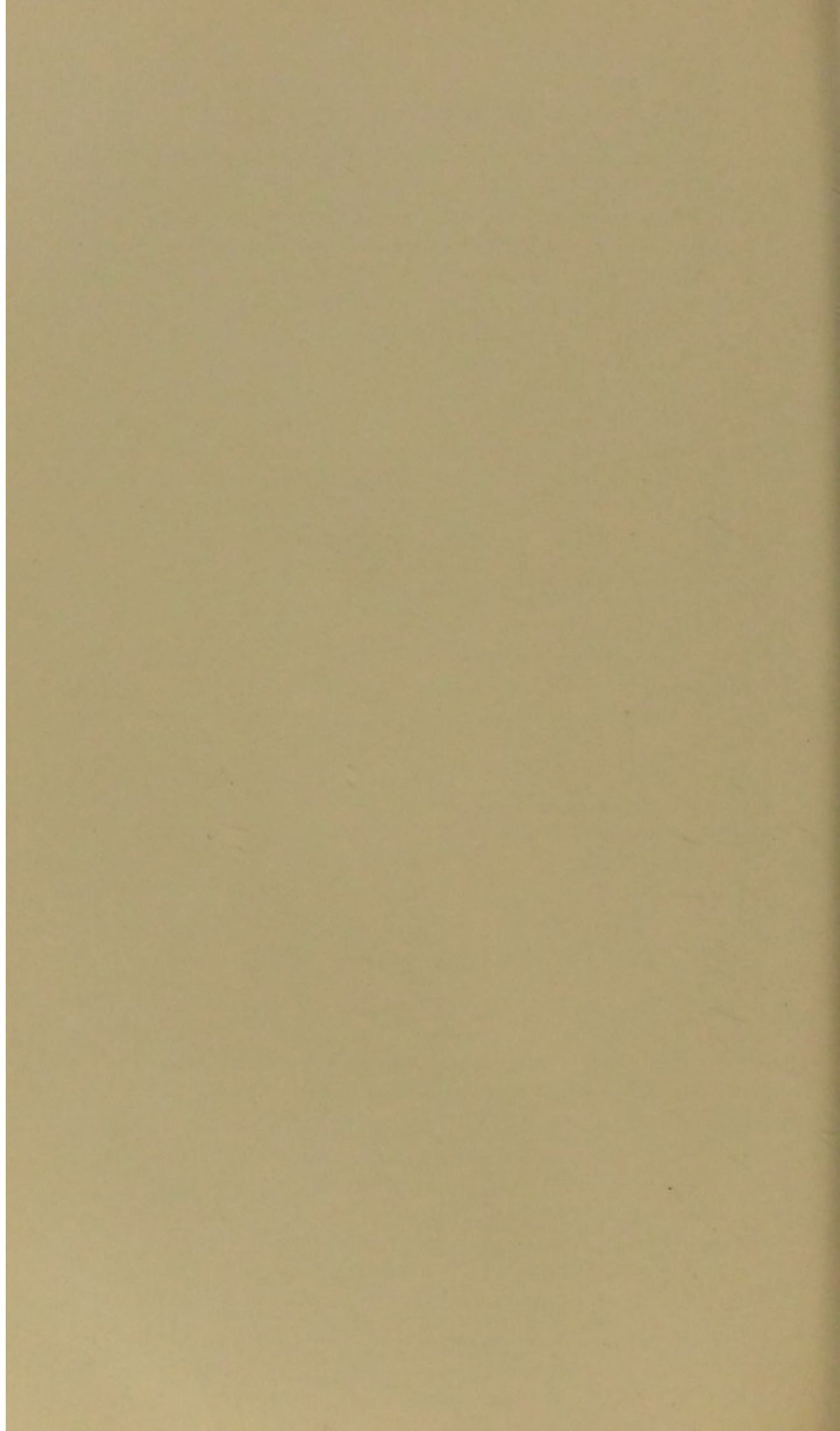
PLATE XXXV.

FIG. 824.



Transverse Section through a Rachitic Rib.

p. Periosteum. *k.* Bone. *o.* Osteoid tissue covering it. *m.* Marrow. $\times 30$.



receive a deposit of mineral matter in the centre, and osteoblasts convert them into bone.

2. Among the larger cells at the cartilaginous zone of growth calcification is imperfect, occurring as a thin line or in irregular spots. On section the normal yellow line is missed, but there are small spots in the lower layer and the columnar layer, in contrast to the normal ossification which occurs only at the margin of the epiphysis.

3. The marrow spaces form irregularly, reaching deep into the cartilage and forming there a red, hyperemic network.

In flat bones similar changes occur, and in the cranium broad defects remain between them.

Chemically the diseased bones contain less mineral matter and increased water, and their specific gravity is lowered.

Changes in Special Parts. The back of the skull is soft and flat (craniotabes). The other bones are thick. Sutures and fontanelles remain open, the large fontanelle until two to four years (normal twenty months), the sagittal suture to three years (end of first year), the coronal to the second year (four months), the lambda eighteen months (third month). The frontal and parietal eminences are prominent, and the surface between these four points is flat, giving the skull a square outline. The lower jaw is bent behind the incisors and the upper at the zygomatic junction. Dentition is delayed, irregular, and the teeth abnormally placed.

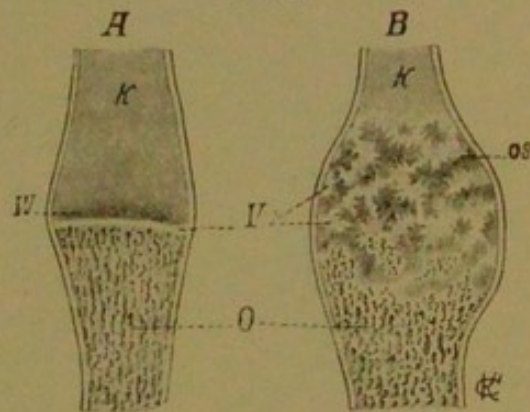
Kyphosis and scoliosis with deformity of the thorax may occur. The enlarged sternal ends of the ribs form the so-called rhachitic rosary, and the sternum is pressed forward by diaphragmatic action on the lower ribs, making the pigeon breast.

The pelvic bones are small, the sacrum is low and tilted forward, so that the true conjugate diameter is very small, the whole pelvis is flat and may be generally small and asymmetrical.

The legs are bowed, and infractions may occur.

The disease usually develops during the second year of life, but a congenital form is seen, and it may also appear about puberty. Heal-

FIG. 325.



Section through a normal and a rhachitic rib. A. Normal rib. B. Rhachitic rib. K. Resting cartilage. W. Zone of proliferation of cartilage. V. Zone of calcification. os. Osteoid tissue. $\times 6$.

FIG. 326.



ing occurs, with general ossification of the osteoid tissues, but the deformities remain, even though good bone replace the osteoid.

The nature of the disease has been much discussed, and insufficient supply of mineral matter, abnormal formation of lactic acid in the bones, and nervous influences, have been advanced to explain it. Dyspepsia is certainly an important factor and also unsanitary and depressing surroundings. Heredity also plays a part.

Barlow's disease resembles rhachitis, but lymphoid marrow is lacking in the bones, and calcification is imperfect and irregular. Hence the skeleton suffers fractures, epiphyses separate, and hemorrhages occur in the medulla and under the periosteum.

Summary of Changes of Form in Various Parts of the Skeleton.

Skull. 1. Large and hydrocephalic skulls. Increase of the ventricular contents during the period of growth makes the flat bones thin, the parietal and frontal bosses prominent, and the whole cranium disproportionately larger than the face. The orbits are decreased by downward pressure, and the eyes are prominent, the supra-orbital ridge is lost, the external auditory meatus is deep and directed downward, all bones are thin and transparent. The fontanelles and sutures are wide and closed by membrane.

2. Abnormally small skulls may be due to premature synostosis. All sutures being closed, the generally small skull is termed *nanocephalia*, but if only single sutures close the following forms arise: *Plagiocephalic*, or obliquely narrowed crania, when half of the coronal or lambdoid suture closes; *dolichocephalic*, when the sagittal, sphenoparietal, or sphenofrontal suture closes; the former gives a simple form, the second is called *clinocephalic*, and the third *leptocephalic*. Entire closure of the coronal or lambdoid suture shortens the head and is termed *brachycephalic*. Compensating increase of the forward part of the dome makes *oxycephalic*, and partial closure of the coronal makes round forms or *trochocephalic* crania.

Pelvis. The normal form is due to the primary disposition of the parts and their further development, pressure from above transmitted

DESCRIPTION OF FIG. 326.

Longitudinal section through the epiphyseal margin of a rhachitic rib. *A*. Growing cartilage. *B*. Zone of large cells. *C*. Diaphysis. *E*. Cartilage. *k¹, o*. Osteoid tissue. *o¹*. Osteoid with calcified cartilage cells and capsules. *o²*. Osteoid in the trabeculae of the diaphysis. *k₂*. Completed bone. *m*. Marrow cavities. *g*. Vessels. $\times 30$.

through the sacrum and from below through the femora, the weight of the contained organs, the tension of attached muscles, and the normal resistance of the bones. Pathological forms depend upon increase of weight and tension and loss of resistance. They include the following:

(a) Narrow pelvis without alteration of form:

1. Uniformly smaller in all diameters; found in persons otherwise large.

2. Dwarf pelvis, in actual dwarfs.

(b) Narrow pelvis with altered form:

3. Simple flat pelvis, short conjugate vera, transverse diameter normal or long. This may be:

I. Simple flat non-rhachitic pelvis with normal bones, sacrum slants but is not twisted.

II. Rhachitic pelvis, bones small, light, with thickenings and exostoses, iliac wings horizontal, sacrum convex or angular, lies deep, its bodies prominently convex, so narrowing the cavity, the anterior superior spinous processes as far apart as the crests of the iliacs, pelvic outlet rather large.

III. Generally narrowed flat pelvis, rhachitic or not, all diameters short.

4. Obliquely deformed pelvis:

I. Kyphoscoliotic, sacrum twisted about its vertical axis toward the other side, and its wing shortened on that side, ischium forced up and in, symphysis to the other side, inlet and entire pelvis obliquely narrowed.

II. Coxalgic pelvis, caused by caries and other diseases at the hip-joint. The affected side is thin and small and pressed inward. Amputation and fracture and old luxation on one side have the same effects from inactivity.

III. Synostosis pelvis, from early closure of a sacro-iliac suture, the sacrum there remains undeveloped, the pubic bone is pushed to the other side and the pelvis is obliquely narrowed.

5. Transversely narrow pelvis, with synostosis of both sacro-iliac joints.

6. Funnel-shaped pelvis, inlet normal or larger, outlet narrow in one or both diameters. Occurs with spinal curvature.

7. Beaked pelvis, from pressure transmitted through the femora to soft bones as in osteomalacia and sometimes in rhachitis, noticed especially in the anterior arch, the symphysis forward and prominent, the remaining pubic portions approximated.

8. Spondylolisthetic pelvis, gliding of the body of the fifth lumbar vertebra over the sacrum forward, so that it forms the promontory, or in severe cases the fourth or even the second lumbar forms the promontory.

9. Narrow pelvis from fracture, tumor, and exostosis.

10. Split pelvis, from imperfect symphysis.

Spinal Curvature. 1. Scoliosis, lateral curvature, from lesions of the vertebræ or bad position of the body, called "habitual" in the latter case. This may be due to contracture at the hip-joint, osteomalacia, rhachitis, or muscular weakness. The intervertebral disks on the affected side are compressed and become wedge-shaped. With a marked curve in one region, compensatory curvature in another is common. The vertebræ also suffer a twisting to the affected side about a vertical axis. The severest grades are combined with kyphosis.

2. Kyphosis may be senile, or due to rhachitis and osteomalacia, and combined with scoliosis. The entire spine is more or less affected. If it follows caries (Pott's disease) the body of one or more vertebræ will be destroyed, angular deformity results on the anterior aspect, the corresponding arches are separated. Similar effects occur with arthritis deformans and fractures.

3. Lordosis is an increased curve of the lumbar spine forward and compensates for kyphosis in the thoracic region and slanting positions of the pelvis with coxitis and ankylosis of the hip, to assist in walking.

B. DISEASES OF THE JOINTS.

The articulations are divided into the synarthroses and the diarthroses. In the former the bones are united by fibrous or cartilaginous tissue or bone, and these are called syndesmosis, synchondrosis, and synostosis. In a diarthrosis four parts are to be distinguished, the two bones, covered with hyaline cartilage, the capsule of the joint, outwardly strengthened by ligaments, and the synovial membrane, a vascular layer of connective tissue invested with endothelium.

Pathologically the most important parts are the cartilages and the synovial membrane. The latter covers the capsule, but not the cartilages, and from it project certain synovial fringes, made of connective tissue with or without vessels, containing also fat, and mucous or cartilaginous tissue. These structures may become hyperplastic.

Regressive Processes.

Fatty degeneration of cartilage cells may be senile or accompany inflammations. Fibrillation is relatively common and consists of a solution of the cement substance and proliferation with fatty changes in the cartilage cells. The surface is soft and satiny, with little papillæ, or finely fibrous. Chondromalacia, or softening of the cartilage, often coexists and is part of senile or inflammatory change. The softened parts are whitish and glistening, or, in marked degrees, transparent and yellow or brown. At last a focus of softening forms and defects and fissures develop or the part is cystic. Connective tissue may grow into the lesion or calcium salts be deposited there, or actual ossification may occur. Amyloid degeneration affects all parts of the cartilage, the cells, their capsules, and the ground substance, and converts it into a homogeneous mass. This occurs in old age.

Lime salts, urates, and pigment may be deposited in cartilage, the former occurring especially along the edges in senility. Urates occur in gout. Brown or black pigment at times invades the tissue and neighboring fibrous structures, as tendinous insertions and ligaments, and is known as *ochronosis*.

Metaplasia of cartilage is common and converts it into mucoid or fibrous or osseous tissue, and one kind of cartilage may change into another, as hyaline to fibrocartilage.

Caries, erosion, and necrosis are caused by factors similar to those affecting bone, and necrotic portions may form sequestra.

Disorders of Circulation. Inflammation.

Congestion and serous exudates (*hydrarthros*) occur in joint cavities. Small hemorrhages are found with inflammations, and hemorrhagic conditions of the system. Large collections of blood (*hemarthros*) may be the result of injury or occur with inflammation. The blood usually remains fluid and is absorbed quickly, but a certain pigmentation of the synovial tissue remains. With severe bleeding a serous transudate occurs afterward. The clots undergo fatty changes and are absorbed, or become organized. Adhesions in the joint after hemorrhage are uncommon.

Exudative inflammation affects the synovial membrane especially, and is hence a *synovitis*, and on the cartilages *synovitis pannosa* and regressive lesions are observed. All varieties of inflammation occur in joints, serous, serofibrinous, seropurulent, etc.

Serous fluid in the joint, *acute hyarthros*, fills it with serous transudate which is clear and thinner than the normal fluid. The synovial surface is red and edematous, and the entire joint consequently is swollen. This condition is never the result of stasis. Healing follows resorption of the exudate, or the condition becomes chronic.

Serofibrinous and pure fibrinous inflammation lead to adhesive arthritis and ankylosis, on account of the difficulty with which the fibrin is absorbed and its tendency to become organized. Synovitis pannosa occurs when the synovial membrane grows over the cartilages and covers them with a vascular layer of connective tissue, like pannus of the eye.

Purulent arthritis may be superficial or deep, and in both cases the synovial membrane is reddened, swollen, and infiltrated or covered with yellow masses of pus. When all parts of the joint are included in the lesion it is called panarthritis. The cartilages undergo fatty degeneration, softening, caries, or necrosis, and the same is true of the ends of the bones. The pus may rupture the capsule and cause peri-articular phlegmon. In mild grades of this disease complete cure is possible, but the more severe cases form granulation tissue in the joint and consequent ankylosis, or end fatally from pyemia.

Acute arthritis may follow injuries or extension from similar lesions in the vicinity, or infection through the blood. In hematogenic infection the lesion accompanies acute exanthemata, typhoid and puerperal fevers, gonorrhea and syphilis, and is almost always purulent.

Polyarthritis acuta, or articular rheumatism, is usually serous, seldom purulent, and is an infectious disease in which many joints, at different stages, may be affected, and the heart may be the seat of verrucous endocarditis.

Chronic serous and *serofibrinous arthritis* may follow the acute forms or develop by itself. The fluid may be thin, or thick and colloid, and its pressure may distend the joint. Proliferation of the synovia and its fringes and synovitis pannosa occur, and free bodies in the joint may be formed from fibrinous masses or broken fringes. Regressive lesions affect the cartilages, and adhesions form which may stiffen the joint permanently. Chronic purulent arthritis may follow acute pyarthros or accompany tuberculosis, and leads to similar ankylosis.

Arthritis uratica, or *gout*, begins acutely with serous exudation into the joint, but then becomes chronic and relapsing. The joint becomes red and swollen and acutely edematous, including the

adjacent soft parts, and with this there is a deposit of urates in the cartilages, ligaments, and capsule of the joint. Repeated attacks cause alterations in the joint similar to those of chronic arthritis, including fibrillation of cartilage, thickening of synovial structures, and many deformities in the bones. *Tophi* are precipitates of urates in the tissues, and appear as small, round nodules of chalky look, consisting of needles of sodium urate and a little fibrin. They occur about joints and in them, in the skin, and the external ears. The ends of the bones may present foci of softening which form fistulae and ulcers when they break through the skin, and from these, often with much suppuration, there is a discharge of softened tissue and urates. Gout commonly affects one joint at a time and most frequently the metatarsophalangeal of the great toe (*podagra*) or small joints of the hand and fingers (*chiragra*).

Chronic arthritis includes a series of lesions in which exudation is relatively unimportant and regressive lesions more pronounced, with productive changes in the synovial membrane. The cartilages soften or become fibrillated, and the ends of the bones may be laid bare. At other times the cartilages thicken and enlarge and break down later, or become calcified. The denuded bones become eroded or porous, and with destruction in one place new bone forms elsewhere as osteophytes. The synovia becomes thickened and forms more or less fungous granulation tissue, and this may become fatty or cartilaginous or even bony. When such proliferations occur at the margins of the joint they destroy its form and function, produce large exostoses and ecchondroses, and lead to spontaneous luxation. The ends of the bones may become rounded and form a false joint in the new position.

1. Arthritis deformans is common in the knee, hip, and fingers, but affects the vertebral articulations also, causing curvatures and ankyloses. It is accompanied with productive and destructive lesions in the articular ends of the bones, proliferation of synovial structures and great deformities.

2. Other forms of chronic arthritis are characterized by regressive changes in the bones and cartilages, without hyperplasia, and lead to severe destruction of the articular tissues. They occur in old age at the hip (*malum coxae senile*), elbow, shoulder, and vertebrae, and are grouped under the name arthritis ulcerosa sicca.

3. Arthritis adhesiva includes those cases where there are adhesion and ankylosis, as the result of preceding serous and purulent inflam-

mation, or which begin independently with synovitis pannosa. This condition is also known as chronic rheumatoid arthritis (*pauperum*), and affects the single joint, or several at a time, in early and middle life. The motion of the joint may be limited, or, by contraction of the capsule, lost altogether.

The etiology of chronic arthritis without exudation is still for the most part unknown. Old age, injury, rheumatic inflammations, and diseases of the nervous system, by trophic changes and impaired sensibility, all play a part in its production. In tabes and syringomyelia such neurotic arthritis is common.

Infectious Granulomata.

Miliary tubercles in the synovial membrane occur in general infection.

Arthritis Tuberculosa. Fungus of joints is one of the commonest and most important articular lesions. It may begin as a pri-

mary tuberculous synovitis or follow similar lesions of the bones which extend to the synovia. In either case grayish-red, spongy masses of tuberculous granulations form in the synovial membrane, and on gross inspection tubercles and caseous masses may be discovered. The tendency to extensive caseation and to fibrous transformation are noted as elsewhere. The cartilages are involved by extension from adjacent bones or directly from the synovia, being softened and fibrillated, permeated by the granulations and rarefied, so that they are destroyed by caries. Portions of the cartilages or the entire investment of the bones may be cast off as necrotic masses. In the primary synovitis the cartilages are secondarily invaded by granulations, their cells multiply, and canals filled with leucocytes pierce them in all directions.

FIG. 327.



Femur from a case of arthritis deformans.

Various forms of articular tuberculosis are distinguished. Large masses of granulation tissue with but little caseation constitute the fungous form. In this the so-called rice bodies are common. When the synovial membrane presents many large gray tubercles and is but little thickened, it is called synovitis granulosa. Ulcerating forms are accompanied by severe and rapid caseation, and lead to marked destruction of the parts.

The cavity of the joint is filled in part by granulations and in part by exuded fluid and softened tissue. In the ulcerating forms this may be puriform or actual pus, containing necrotic pieces of bone and cartilage.

In the vicinity of the joint the soft parts become swollen with edema and peculiarly smooth and glistening, a condition known as white swelling (tumor albus). Beside the edema there is inflammatory proliferation of the cells, and the granulations from the joint may enter the tissues and perforate externally. Fistulæ and abscesses may result.

In the remaining portions of the affected bones there are sclerotic and hyperplastic lesions, or osteoporosis, or a condition termed caries sicca, without much exudation.

The course of the disease is chronic and variable. Healing after evacuation of the contents of the joint is possible, but usually accompanied by adhesions, with atrophy and contraction of muscles, and more or less ankylosis. Spontaneous luxations and subluxations are common. Foci with bacilli may persist and lead to later renewals of the lesion. The joints most affected are the hip, knee, hand, and foot.

Syphilis causes serous and serofibrinous arthritis in the early stages, and gummatous infiltration in the later stage. Irregular scars of fibrous tissue may be left after the erosions heal.

Tumors are uncommon in the joints. *Lipoma arborescens* occurs as branching fatty growths in the synovia.

Floating bodies in the joints may be free or pedicled, and consist of fibrin with enclosed cells from inflammatory exudates, usually round or flat, and at times in great numbers. These are known as *corpora oryzae* or "rice bodies." Other forms are pieces of cartilage and bone mechanically broken off, or fragments of synovial tissue, or foreign bodies which have entered the joint.

Ganglion is the name given to hernial projections of synovial membrane filled with thickened fluid.

Ankylosis indicates a loss of motion in a joint and may be due to fibrous, cartilaginous or bony adhesions between joint surfaces, and hence its varieties include ankylosis fibrosa, cartilaginea and ossea. Contraction of the tissues about a joint and bony growth may fix a joint in abnormal positions, as is common in arthritis deformans.

Contracture of a joint lessens its mobility by shortening of the various structures about it, and may be arthrogenous, cicatricial, myogenous, tendogenous, or neurogenous, according as its cause is articular or depends on other tissues.

Arthrogenous contraction is usually due to chronic inflammatory lesions. Scars of the skin and subcutaneous tissue may contract and fix the position of the joint, especially after severe burns. Muscles and tendons shorten from scars after injury or nervous lesions, as poliomyelitis anterior. If all the muscles about a joint are paralyzed, it retains any position in which it is placed or which gravity compels. Thus the foot assumes the position of varo-equinus when its muscles lose their function. Contracture of the foot in plantar flexion is called *pes equinus*, in supination is called *pes varus*, in dorsal flexion *pes calcaneus*, and in pronation *pes valgus* or flat foot. Paralysis of certain muscles allows contracture of their opponents.

When a freely movable joint is held permanently in one position, as with paralysis of the muscles, the surfaces of the joint adapt themselves to the new position and lose their motility. This is especially noted when the subject is young and certain parts of the joint have to bear any degree of pressure; these remain undeveloped, other parts develop in excess, and the abnormal conditions lead to much deformity, as is commonly observed with the various kinds of club foot.

When the bones are soft they are liable to deformity from the effects of pressure. Thus in the rachitic subject pressure on the external condyle of the femur prevents its growth, and the internal increases so that the knees are in apposition, giving the condition called *genu valgum*, with which *pes valgus* often exists. The contrary of this is due to excessive growth of the outer condyle, and is called *genu varum*.

Certain forms of these lesions are congenital. *Pes varus* may be due to uterine pressure when the liquor amnii is deficient in amount.

Distortion of a joint is a momentary stretching of the tissues, often with some tearing of the capsule, due to violence. Luxation is a persistent complete shifting of the bony surfaces, subluxation an

incomplete degree of the same condition. The causes of luxation may be traumatic, inflammatory, or congenital.

C. DISEASES OF THE TENDONS AND BURSÆ.

Tendosynovitis may be serous, serofibrinous, or purulent. In purely fibrinous inflammation, *tendovaginitis sicca*, there is a peculiar crepitation on movement. *Tendosynovitis purulenta* is usually secondary to infected wounds, *panaritium*, or *phlegmon*, and can heal or lead to adhesions between the tendon and its sheath, or to fibrillation and necrosis.

Chronic inflammation leads to swelling of the sheath (*hydrops tendovaginalis*, *hygroma*), as a circumscribed cystic formation, or to adhesions. The tendons of the palm are most often involved. Rice bodies occur in the hygromas.

Mucous bursæ present about the same lesions. *Bursitis* may be of any variety, with thickening of the walls of the bursa and formation of rice bodies. Hernial protrusions occur as in joints, and are called *ganglions*. Tuberculosis of the tendinous sheaths may be primary or accompany disease of bones and joints. It may spread for long distances as miliary nodules or diffuse caseous lesions. Rice bodies are large and numerous.

D. DISEASES OF THE MUSCLES.

The single muscle fibres have a length up to 5 centimetres, and a breadth of 15 to 55 μ , and consist of alternate refractile disks, some of which are doubly contoured and called anisotropic, and others which are singly contoured and are called isotropic. In the middle of the latter are intermediate disks. Contraction of a muscle makes the single fibres shorter and thicker at the expense of the isotropic portions. Each fibril is surrounded by the sarcolemma, and within it are the muscle corpuscles, appearing as nuclei arranged longitudinally and having a small amount of protoplasm at their poles. The fibrils are grouped in bundles, each of which is enclosed in the perimysium internum, at times with a small collection of fat. From this sheath processes reach into the bundle. The perimysium externum (epimysium) is the connective tissue which encloses the entire muscle.

The finest elements are not the fibrils mentioned, but primitive fibrillæ, which are made up of disks and separated by homogeneous or granular sarcoplasm. These fibrillæ arranged in bundles and with sarcoplasm about them give peculiar cross-sections termed Cohnheim's fields.

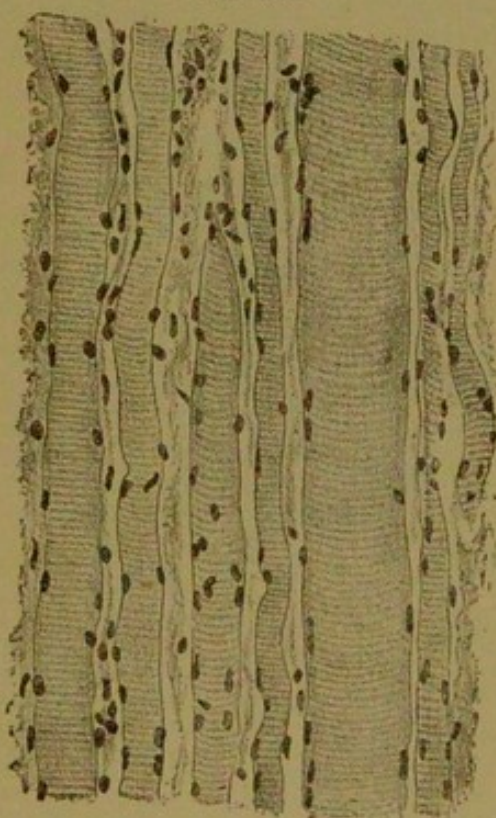
Atrophy leads to shortening and narrowing of the fibres and alteration of the striation. If general the muscle is pale and its hemoglobin is diminished. When the muscle is dark from deposits of pigment (hemofuscin), as in certain cardiac atrophies, it is called brown atrophy.

FIG. 328.



Teased preparation of muscle. Q. Transverse disk. h. Median disk. z. Intermediate disk with isotropous layer on each side. $\times 1200$. (After BÖHM-DAVIDOFF.)

FIG. 329.



Muscle fibres in simple atrophy.

Cloudy swelling is accompanied by the formation within the sarcoplasm of minute granular bodies which dissolve with acetic acid and potassium hydrate solution. These hide the striæ and give the muscle a dusty look. Fatty degeneration presents droplets of fat in the sarcoplasm which do not dissolve with the reagents mentioned. In cloudy swelling the muscle appears opaque and pale red; in fatty changes it is pale yellow in the gross, with perhaps a fatty lustre.

Frequently a degenerated muscle presents homogeneous hyaline changes at one part, and is breaking down at another. Amyloid

lesions are not very important, but hyaline and waxy degenerations are common in the course of many diseases.

When muscle is breaking down the process begins by the striæ becoming very thin and indistinct, simultaneously over large sections of many fibres, and this condition, which resembles physiological contraction, is called nodular thickening. Loss of the striæ gives the part a peculiar homogeneous and glassy appearance. Then the contractile substance splits up into smaller and larger fragments and leaves parts of the sarcolemma as an empty tube. The fragments undergo granular solution or persist as large masses (sarcolytes) which gradually crumble along their edges and are absorbed.

FIG. 330.

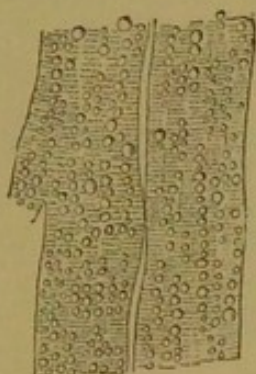


FIG. 331.

FIG. 330.—Fatty degeneration of cardiac muscle. $\times 350$.

FIG. 331.—Necrosis of muscular tissue with hyaline and granular changes. Below, to the left, the striæ persist, but the fibrillæ are split lengthwise. In the middle the fibres are transversely divided. $\times 350$.

Waxy degeneration may vary in its significance according to the case. Nodular thickening occurs in tetanized muscle and also in normal muscles when taken fresh and living and put into fixing fluids, and this fact renders its pathological importance questionable.

Still, in many cases, it surely occurs during life. Necrosis occurs often with accompanying hyaline and waxy degeneration under various conditions. Local causes, like injury, freezing, and burns, and local anemia, inflammation and hemorrhages, and neighboring tumors, determine the lesion at times. In other cases there is a general infection, and a good example is furnished by the degeneration of the recti abdominis and the adductors of the thigh in typhoid

fever. In waxy degeneration the muscle is opaque, dull, pale, and resembles fish flesh. Calcification is occasionally noticed in muscles.

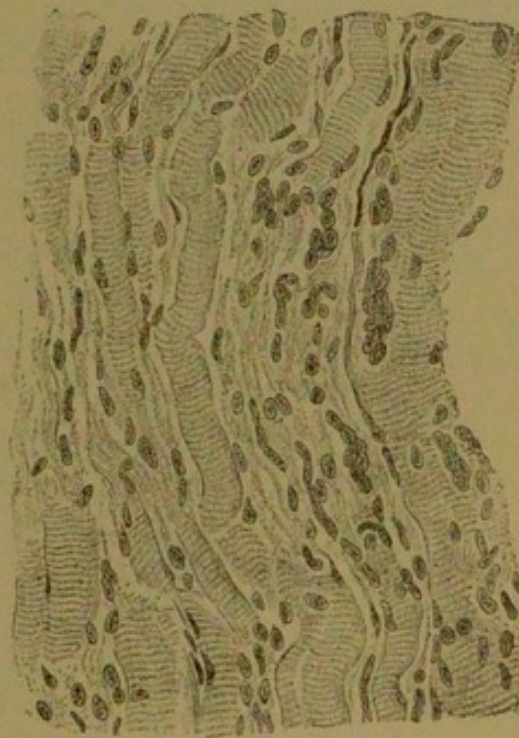
Apart from hyaline changes the muscles may present fissures and transverse tears in atrophic conditions, and the fibrils may separate longitudinally, dichotomously, and otherwise, and vacuoles may form as with edema. A tubular degeneration converts the fibre into an empty tube of sarcolemma, which may be striated or homogeneous and present many nuclei. The fibres apparently return to an embryonal condition. Large vacuoles and projections often occur from the fibres, and within the spaces giant cells may be found. In atrophic muscles a few of the fibres may be unusually broad, probably from contraction.

Proliferation of the nuclei in atrophy is common, and this may produce large giant cells, called myoblasts, or the muscle corpuscles with a good deal of protoplasm lie in series along the sarcolemma. The perimysium may remain unchanged or become thickened by fibrous hyperplasia, and lipomatosis may

be associated, as in the muscle of the heart. This increase of the fatty tissue, which must not be confounded with fatty degeneration, may be so large that the decreasing volume of the atrophic muscle is more than replaced, and pseudohypertrophy results. In many cases there is only a replacement or fatty hyperplasia *ex vacuo*. In fatty subjects and overfed animals the fatty growth may begin before the atrophic changes, and pressure of the fat between the vascular bundles causes them to disappear. Such a progressive lipomatosis occurs in the heart and perhaps also in the bodily muscles.

Longitudinal atrophy of a muscle depends upon apparent increase of the interstitial connective tissue, but actually it is due to the loss of terminal fibres and compensating growth of the tendinous connec-

FIG. 332.



Atrophy of muscle with proliferation of nuclei.
× 250.

tive tissue into the muscle to take the place of the lost tissue. There is then a progressive shortening of the muscle fibres.

Lesions in the central nervous system are responsible for many muscular atrophies. Any degeneration within the peripheral motor

FIG. 333.



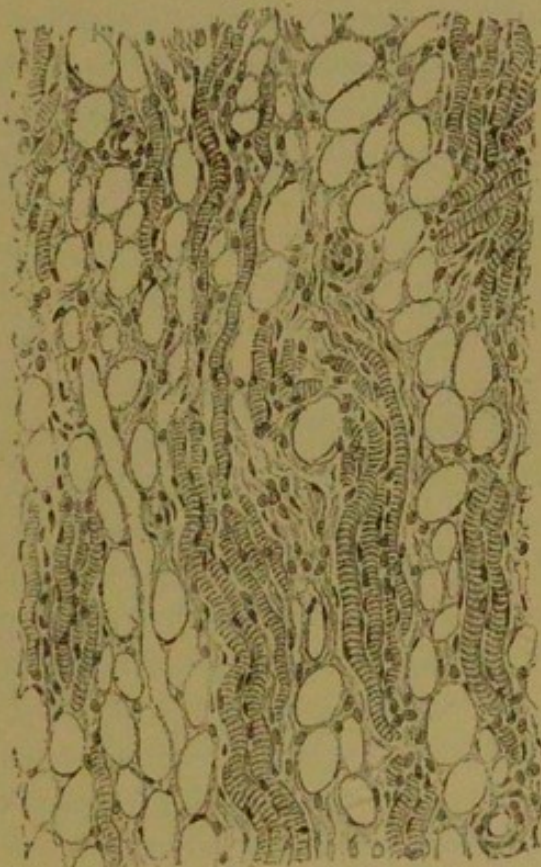
Regenerative growth of muscle corpuscles after waxy degeneration in a case of typhoid fever; myoblasts and giant cells. $\times 250$.

neuron may cause Wallerian degeneration of the distal nerves down to the end plates, and to this is regularly added atrophy of the muscle supplied by the nerve. The fibres grow narrow, though for a time they are striated, some fibres are hyaline or waxy, and free hyper-

plasia of fibrous and fatty tissue is liable to follow. The further course of the lesion depends in great measure upon its site.

After division of a nerve the peripheral section may degenerate and be restored. In this case the muscular changes may also be repaired by the development of myoblasts and new fibres. If the stumps of the nerve are too far retracted or fibrous tissue intervenes and the nerve does not heal, the muscular degeneration resembles that dependent upon disease of the anterior horns. In a similar way

FIG. 334.



Atrophy and lipomatosis of a muscle. Fibres very slender, much fat between them, but as the technical methods have removed the fat the cells appear as empty spaces. $\times 250$.

when the cerebral nuclei are degenerated the muscles supplied by the corresponding nerves degenerate. But with general paralysis due to central lesions, as a rule, there is no muscular atrophy or degeneration other than that connected with inactivity.

Atrophy of muscles is observed in the following:

1. Degeneration of peripheral nerves, with infectious diseases, polyneuritis, lead and other poisoning, injuries and divisions. Regeneration of both nerve and muscle possible.
2. Transverse lesions of the cord or degeneration of the anterior horns and large motor ganglion cells. Myelitis, poliomyelitis ante-

rior, both acute and chronic, progressive spinal muscular atrophy, amyotrophic lateral sclerosis, myelitis from compression, tubercular and syphilitic spinal pachymeningitis, and injuries of the cord.

3. Lesions of the anterior roots.

4. Progressive bulbar paralysis.

Primary myopathic atrophy, in contrast to the forms mentioned, is due to causes in the muscles themselves. Inactivity leads to atrophy of muscles because of the reduced demand upon their function, and occurs with various diseases of the bones and joints, diseases of the nervous system, in old age and marasmus, and as a progressive dystrophy. Myopathic progressive muscular atrophy may begin in early childhood in the muscles of the shoulder and arms, the hips and buttocks, and gradually affects most of the voluntary muscles. It shows a hereditary character in some families. Marked lipomatosis may be associated with the lesion, and the name pseudohypertrophy is given to those cases which affect certain groups of muscles, as the calves, thighs, and deltoids.

Regeneration of muscular tissue starts in the nuclei of the old fibres which proliferate and form myoblasts, at times mononuclear, but often polynuclear, and these both remove remnants of old fibres and build new ones. Where there is a solution of continuity a scar may form, and muscular tissue may penetrate this later.

Hypertrophy of muscles is usually functional and affects single muscles and special groups. A pathological hypertrophy is known as Thomsen's disease, in which large size does not correspond with the functional power of the muscle (*myotonia congenita*).

Edematous infiltration of muscles may be inflammatory or follow injury and occur with hemorrhages. In acute muscular rheumatism there is probably such an infiltration of serocellular fluid, and the same is found with trichinosis. Large hemorrhages may occur in scurvy.

Primary inflammation of muscles is rare. *Polymyositis* with fever and doughy swelling of the muscles, which later becomes hard, and similar changes in the skin, is an infectious or toxic disease which may end fatally. Anatomically the muscles are discolored a grayish or whitish tinge, resemble the muscle of fish, and are hard or may be dark from hemorrhages (*polymyositis hæmorrhagica*). Microscopically the fibres are in cloudy or fatty degeneration with rupture of the fibres, and the interstitial tissue is filled with red and white blood cells and fibrin. A suppurative form of this disease leads to phlegmonous necrosis of the muscular tissues.

Almost all inflammations of muscles, especially of purulent type, are secondary to lesions of bones and joints. Abscesses may become encapsuled, or heal with fibrous scars after the pus is voided. Slight degrees of inflammation are not accompanied by much degeneration.

Myositis fibrosa consists of fibrous hyperplasia throughout the muscle and follows acute inflammation or develops gradually in muscles which lie in the vicinity of inflamed bones and joints, or those in neurotic atrophy.

Myositis ossificans indicates the formation of osseous tissue in the muscles, and in circumscribed form this is associated with long-continued irritation, especially mechanical. "Exercise bones" thus develop in infantry soldiers in the deltoids, and "rider's bones" in the adductors of the thighs of cavalry soldiers. Near chronically inflamed joints, parosteal exostoses may form in muscles, and usually the tendons and ligaments are also involved.

Myositis ossificans progressiva is a chronic process beginning in the muscles of the neck and back and slowly extending to others. It begins as a doughy swelling which then becomes fibrous and forms osseous tissue. The muscular elements passively disappear. In the end the bony hyperplasia may fix the body rigidly. The muscles may be brittle. The bony matter may be in rods, plates, and sickle shapes, or irregular masses, and unite the bones of the skeleton. The disease occurs in young subjects.

Tuberculosis may extend from carious bones to the intermuscular tissue and cause caseous and fibrous lesions with degeneration of the muscular fibres. Syphilitic gummata sometimes produce caseous lesions and fibrous scars in the muscles.

Among the tumors sarcoma is the commonest, usually starting in the intermuscular tissue or else metastatic. Carcinoma may be secondary to distant tumors.

The commonest parasites of muscles are trichinæ and cysticercus cellulosa.

CHAPTER XIV.

DISEASES OF THE GENITAL ORGANS.

A. DISEASES OF THE FEMALE GENITALS.

THE tubes, the uterus, and the vagina develop from the Müllerian ducts; the upper section remaining separate and forming the tubes, the middle and lower segments uniting to form the uterus and vagina. At the point where union ceases, at the line between the upper and lower segments, about at the fundus uteri, there remains a depression for a time which is built out later. For some time after the external union of the lower segments there remains a septum in the interior,

dividing the lumen into two chambers; this disappears in the course of development.

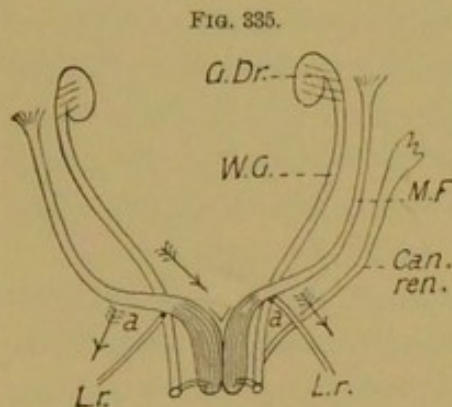


Diagram of primitive genital organs.
G. Dr. Genital gland. W. G. Wolffian duct. M. F. Müllerian duct. Can. ren. Canalis reuniens. L. r. Round ligament.
(After V. WINCKEL.)

Congenital Anomalies. The uterus may be absent from disorders of development during the first months, or it may be rudimentary (*uterus rudimentarius solidus*, *u. partim excavatus*) with atresia. If the Müllerian ducts do not fuse the uterus and vagina may be partly or completely double. Among such forms there are *uterus didelphys* (uterus and vagina double), *u. bipartitus* (cervix simple with two

cornua), and *u. bicornis* (only the upper portion of the uterus double). Imperfect development of one Müllerian duct makes *u. unicornis*.

Anomalies which arise later include *u. septus* and *bicameratus*, and with marked inversion of the fundus, *u. introrsum arcuatus*. Or the organ may remain on the plane of fetal, infantile, or virginal development, or, with lateral hypoplasia, form the *uterus inequalis seu obliquus*. The *uterus membranaceus* probably depends on pressure from a hypertrophied bladder.

Anomalies of the tubes are atresia, accessory openings, and hypoplasia, and usually accompany uterine malformation.

The ovaries may be lacking on one or both sides, rudimentary or partially formed, and a third ovary may be found.

The vagina may be partly or wholly double, narrow and atresic, rudimentary or hypoplastic. *Atresia vaginalis* means that the cavity ends blindly below, *atresia vaginae hymenalis* means that the hymen completely closes the canal, *atresia ani vaginalis* occurs when the cloaca persists and both rectum and vagina open into it high up.

Diseases of the Ovaries.

The ovary consists of a medullary portion into which the vessels and nerves enter at the hilum, and a cortical layer which is interrupted at the hilum, and surrounding this a tunica albuginea. Externally the organ is covered with cylindrical epithelium, and in the cortical or parenchymatous layer are the follicles, bedded in connective tissue, many of which are microscopic, but some visible vesicles. Of these primordial follicles we distinguish the maturing and the ripe or Graafian. The former develop during embryonic life by inversions of the germinal epithelium and vary in size from 54 to 58 μ . They consist of the ovule and a single layer of flat epithelia, persist in the ovary throughout sexual life, and are estimated in the human subject as 36,000 in number.

In the maturing follicle the epithelium grows to a manifold layer of round cells enclosing the ovum, and then at one part there is a division of these cells into two portions, and the space is filled with the *liquor folliculi*. The inner group of cells is called the *discus proligerus* and the outer lying on the theca, called the *membrana granulosa*. The *theca* is a double layer of connective tissue surrounding the ovum. One follicle holds but one ovum as a rule, but two or three may be present. Twin ova with a double yolk have not been observed. The Graafian follicle forms by widening of the fissure and increase of the fluid, and only a few are present at one time. After they form in the depth of the organ they reach the surface and measure 1 to 1½ centimetres in diameter.

Rupture occurs, as a rule, at the time of menstruation. On the deepest part of the follicle there is a vascular proliferation of the theca in which large epithelioid lutein cells form and compress the ovule, and as the investing epithelia soften the follicle bursts and the ovum is free in the abdominal cavity, from which it usually reaches the tube and the uterine cavity.

After rupture a *corpus luteum* forms in the follicle, after bleeding into its cavity and distention to 1 to 2 centimetres. The blood coagulates as a dark-red, and later, brownish-red mass, containing much pigment. Organization follows from the theca, the lutein cells enclose the clot as a broad, yellow, wrinkled membrane, in which papillary projections are formed by the vessels from the theca. After resorption of the blood the luteal margin is more wrinkled, and only a spot of pigment may remain. Apart from pregnancy, the corpus luteum has become a corpus albicans in about four weeks, by the disappearance of the luteal cells and formation of hyaline material, and, after a time, a fibrous scar closes the process and dimples the surface.

The corpus luteum of pregnancy begins with a larger hemorrhage, and does not begin to disappear until the middle of pregnancy, and may still be recognized several months afterward. Many follicles never rupture on account of so-called atresia, the follicle and the ovum undergoing fatty degeneration and collapsing, with a final scar formation.

The ovary presents different proportions between its stroma and follicles, and variations in size and form, according to the period of life when it is examined. In the child it is smooth, but with puberty it begins to present scars on the surface, and these multiply until the climacteric, when all follicles disappear. In their place certain corpora fibrosa may be found, due to imperfect formation of follicles in late years and conversion into hyaline fibrous tissue. In old age the albuginea is very thick and may be calcified, the organ is atrophic and granular, with many scars on the surface.

Malpositions of the ovary are commonly secondary to inflammatory adhesions, tumors, and displacements of the uterus. If the organ is large and heavy, or its ligaments are loose, as after pregnancy, it may suffer a prolapse. It has been found in hernial sacs, usually inguinal, and this may be congenital or acquired, and the tube usually accompanies it. Stasis and edema are caused by displacement.

Disorders of Circulation. Physiological *congestion* occurs with menstruation and renders the ovary large, reddish, edematous, and soft. Pathologically it accompanies inflammation, and a passive form may be due to twisting of its vessels and pressure on them.

Hemorrhage into follicles occurs with inflammation, infectious diseases, poisoning with arsenic or phosphorus, severe burns, and

marked stasis. In the follicles the blood undergoes changes similar to those after ovulation. In the stroma large hematoma may form. If the theca is ruptured the blood enters the peritoneal cavity and may be fatal. Edema occurs with stasis and inflammation.

Acute Inflammation. Parenchymatous Degeneration.

Acute oophoritis follows extension of an inflammation through the lymphatics, from the uterus or tubes or peritoneum, or is a hematogenic lesion. It is frequently bilateral, and may be serous, hemorrhagic, or purulent and necrotic. The organ at first is swollen and red, succulent, and perhaps hemorrhagic, and lies deeper in the pelvis. Microscopically there are foci of cellular infiltration in the stroma, and the follicles suffer albuminous or fatty degeneration. Phlegmonous inflammation may be diffuse or form single abscesses, some of which are follicular. The etiology is usually septic or gonorrheal infection.

Septic oophoritis is commonly puerperal, or follows operation with infection of the wound, and the lesion may extend from the cervix or the parametral connective tissue or pelvic peritonitis. Typhoid fever, cholera, pneumonia, and certain poisons may cause the disease, and while often a parenchymatous lesion with degeneration in the follicles and destruction of the ova, it may be hemorrhagic and purulent.

The disease may terminate in atrophy (presenile), or pass into a chronic form with enlargement of the organ. If purulent the lesion may excite general or local peritonitis, or the pus may be enclosed by fibrous adhesions for a time. Adhesion of the ovary to other organs is common, and if pus escapes in this way fistulae may remain. Single abscesses in the organ may be encapsuled and their contents thickened and calcified, but new inflammation may arise from them.

Acute or chronic peri-oophoritis and pelvic peritonitis very frequently accompany inflammation of the ovary, and, while these lesions may be of any type, they frequently are adhesive and fasten the organ to other structures by fibrous bands.

Chronic Inflammation and Atrophy.

In old age atrophy is physiological and is due to the gradual rupture and loss of follicles and consequent scarring. A similar condition may follow inflammation, and is known as presenile atrophy.

The surface is rough and irregular, especially after suppurative processes.

Chronic inflammation leads to cellular infiltration of the ovary and fibrous hyperplasia, and results in destruction of remaining follicles, and induration. It is often associated with chronic inflammation in the adjacent tissues. Presenile atrophy may be found with any disease which causes general inanition, as diabetes, pulmonary tuberculosis, chronic nephritis, myxedema, severe anemia, etc. Pressure of scars and tumors leads to similar effects.

Infectious Granulomata.

Tuberculosis of the ovaries seldom occurs. Commonly it develops with tubal lesions, and the disease is transported along the peritoneum. Hematogenous infection seldom happens. It appears as miliary tubercles or larger caseous nodules. Miliary tubercles have been found microscopically in organs which appeared normal in the gross.

Actinomyces of the ovary has been observed.

Hypertrophy. Tumors. Cysts.

Hypertrophy of the ovary may be congenital, or develop at puberty, or with premature ovulation and menstruation.

Cysts may be either retention forms or true neoplasms.

Hydrops of the Graafian follicle is a cystic distention of these structures which causes destruction of the ovum, but does not rupture. Such a cyst is often single and has smooth walls, or adjoining cysts may fuse. At times they may be due to unusual thickness of the theca which prevents rupture and collects quantities of serous fluid. Pressure on the rest of the ovary leads to atrophy, and the cyst grows no larger. Its size very seldom exceeds that of a walnut. Cysts of this kind often are found in chronic oophoritis and may form transitions to the so-called small cystic degeneration.

Other cysts are due to active growth and exudation on the part of the epithelium, and the size of this variety is not limited. On the inner surface there is a layer of low epithelia which have been derived from the original cylindrical cells, but these may degenerate and be lost. Cysts of the corpus luteum are retention forms, lined with lutein cells, which may be stripped up as a membrane, and contain transudate from the vessels of the theca.

Degeneration with small cysts yields an organ which is filled with small cavities holding fluid, about the size of follicles. It may occur

in the newborn, at puberty, and other times, and is probably due to premature ripening of an enormous number of follicles, or follicular hypertrophy, or in other cases to chronic inflammation and cystic distention of the follicles. The latter may contain ova.

Large cysts of the ovary are most frequently *cystadenomata*. These tumors are due to proliferation of the epithelia and cystic dilatation of the new glandular acini by secretion from the epithelia, and serous or seromucous transudation, or colloid material. They may be due to inversion of the germinal epithelium or to proliferation in the follicles. In the former case the inverted process closes and dilates by its own secretion. Daughter cysts form on the walls, which at first are attached but gradually become more independent. In these other parietal cysts form, and thus a multilocular tumor results. Where inversions occur to prepare for new cysts the inner surface presents depressions. In hydrops of the follicles there are no secondary cysts formed in the wall, but, if two or more fuse, remnants of the septa may remain on the inner surface.

Cystadenoma (myxoid cystoma) of the ovary is usually round, with a glistening smooth surface, often transparent and opalescent. Commonly there is one cyst which is very large and a number of smaller ones, and thus the surface presents many prominences of varying size.

Such tumors have been observed which exceeded in weight that of the subject afflicted. They grow freely into the peritoneum or between those folds of the peritoneum which form the ligaments of the pelvis, and are then called interligamentous. The ovary atrophies and may not be discovered. If the tumor has a pedicle this is formed by the ovarian ligament, the suspensory ligament of the ovary, the broad ligament, and the tube, and they are all more or less stretched and distorted. When the pelvis can no longer contain the tumor it rises above the brim and then may suffer torsion of the pedicle, compression of its veins and arteries, and various degrees of necrosis. Even then its nutrition may be provided by vessels in adhesions between the tumor and other parts.

Fatty degeneration is common in these tumors, and calcification may form large bony plates and masses. At times such a tumor may suppurate, as after puncture. The interligamentous forms are especially apt to cause displacement and atrophy of the other pelvic organs.

The adhesions mentioned between the tumor and the abdominal wall and organs are partly due to friction and removal of endothelial

cells, and partly to inflammation from torsion of the pedicle and superficial hemorrhages, and they may be so large and firm that separation is almost impossible. When the intestine is adherent and the pedicle becomes twisted, symptoms of intestinal strangulation may occur. Spontaneous and traumatic causes may lead to opening of some cystic cavities.

Ascites may complicate the case from continual irritation of the peritoneum or exit of the contents of the cyst, perhaps also from irritating products which enter the cavity from the cyst.

While these cysts are not in themselves malignant they are injurious mechanically, especially from their size. At times they become carcinomatous. At other times portions of the tumor become separated and affix themselves to different sites in the peritoneum, and by their activity of growth take on an added development. The entire serous surface may be sown with them in this *metastasis by implantation*, and other organs may be invaded by the vessels and lymphatics.

Two varieties of these cysts are found: (1) The glandular, and (2) the papillary.

The glandular form is usually multilocular, with smooth internal surface except where there are shallow depressions, and, while remnants of septa may be found, there are no papillary outgrowths. The inner surface is covered by a single layer of rather light and high epithelia, among which are many beaker cells; these may entirely undergo mucoid degeneration. The contents of the cyst are slimy, viscous, or thick and colloid, or rarely serous, and always contain pseudomucin. The tumor shows neither destructive nor metastatic growth. The pseudomucin is mucoid, does not precipitate with acetic acid nor on boiling, but on boiling with acid gives a reducing substance. Paralbumin is a mixture of albumin and pseudomucin.

The papillary form develops like the other, but on its inner surface the proliferating epithelium lifts itself into papillary projections, into which the stroma grows as a core, and these papillæ may fill the entire cavity and even perforate the wall. Transitional forms between the two varieties occur. The papillary are usually smaller than the other tumors, and may be bilateral. Their contained fluid is thin and serous, and has no pseudomucin, or but a trace of it. Psammoma bodies and deposits of lime salts are common. The epithelia may be partly ciliated, which has been ascribed to an origin from the parovarium, but these cells are derived from the germinal layer, which

also presents cilia at times. In about 13 per cent. these tumors are malignant by implantation and metastasis. Carcinomatous and sarcomatous transformations may occur. Their prognosis is bad because of their interligamentous position and the difficulty of extirpation (p. 154).

Superficial papillomata of the ovary are due to proliferation of the germinal epithelium and the fibrous tissue beneath it, and from cauliflower masses of some size, with enclosed cysts. They may cause ascites and implantation.

Parovarial Cysts. The parovarium is a small comb-shaped body in the broad ligament, made up of canals with ciliated epithelium. Cysts of small size may develop in these, and are usually smooth and partly filled with clear fluid. They may rupture without severe results, and are generally benign.

Pseudomyxoma of the peritoneum is the name given to peculiar gelatinous masses which lie upon the serous membrane of the wall or abdominal organs. They are probably due to escape of colloid material from cysts, and as this is difficult of absorption the serous membrane encloses it in false membranes; or they may be portions of a colloid cystadenoma which have separated from the main tumor.

Dermoid tumors and teratomata of the ovary may be cystic, and are congenital, but may develop only after puberty. They are commonly unilateral, and the ovary is a favorite site for their location. They undergo torsion of their pedicles and other changes as the larger cystic forms, and may become sarcomatous or carcinomatous.

Solid tumors of the ovary are less frequent than the cystic. They increase the size of the organ as a whole, or are pedicled. Small fibromata are common, and like fibromyoma may be pedicled or diffuse. Spindle-celled sarcoma and mixed forms occur. Angioma, chondroma, myxoma, and adenoma are unusual. Endothelioma and carcinoma may be found, the latter starting in the germinal epithelium or the follicles, as adenocarcinoma. Cysts which may be papillary may occur in these tumors. Often a carcinoma develops from a cystadenoma. Medullary and scirrhous types occur, and metastatic invasion infrequently.

Diseases of the Fallopian Tubes.

Congestive hyperemia occurs with menstruation and inflammation.

Hemorrhage may be due to infectious disease, stasis, or poisons. With tubal pregnancy the hemorrhage may be copious and pass into

the uterus or the abdomen. If the outer end of the tube is closed the blood distends the part; this is called hematosalpinx.

Inflammation may pass to the tube from the uterus, or less often from the ligaments and through the blood, and the salpingitis is usually bilateral. It may be catarrhal, purulent, diphtheritic, necrotic, or caseous. Salpingitis, if chronic, commonly involves the wall as well as the mucosa, and also the adjoining tissues as a perisalpingitis, especially when the fimbriated end is closed and the tube much dilated. Chronic catarrhal and purulent salpingitis cause marked thickening of the mucous folds and adhesions between their edges, and in the spaces so formed cystic collections may develop. In the severest cases the mucosa may become necrotic, and also the muscular tissue in part, and the deep scars which result may obliterate either the ostium or the whole lumen of the tube. The most important cause of salpingitis is gonorrhea.

**Closure of the Ostia. Hydrosalpinx. Hematosalpinx.
Pyosalpinx.**

Closure of the fimbriated end of a tube may be due to inflammations within or about it, and adhesion of the fimbriæ to some other organ, or to pressure from without. Although the uterine opening may be permeable, fluids and pathological exudates collect in the tube.

Hydrosalpinx, or *hydrops tubæ*, is an accumulation of serous fluid in the tube, and may occur in the part without other lesion than closure of the outer ostium or with catarrhal salpingitis. The fluid may be thin and without included cells, or turbid, or reddish from diapedesis of red cells. The ampulla is especially distended, while the median portion may be of normal size and stretched or tortuous. The wall presents folds and septa. In size the collection may vary from that of a fist to as large as the head. The mucosa atrophies and becomes smooth and anemic. Perforation may occur, and occasional escape of the fluid is common (*hydrops tubæ profluens*).

With purulent catarrh the collection receives the name *pyosalpinx*, and in this case perforation is liable to occur, with subsequent peritonitis, unless the part is shut off by adhesions. The pus may also thicken and calcify.

Hematosalpinx may be of large size with repeated hemorrhages in the tube. Usually the blood does not coagulate, but slowly thickens to a dirty brown, dry mass. The wall is at first thickened, but after

a time becomes thin, and may burst with a new hemorrhage, or when a coexisting hematometra suddenly empties, or after traumatism. The loss of blood into the abdominal cavity may be so large as to be fatal, or, in slighter degrees, it makes a retro-uterine or an ante-uterine hematocele.

Atresia of the uterine ostium may be congenital and one cause of sterility, or, if unilateral, may permit extra-uterine pregnancy. Later in life inflammatory and other causes may close this opening and lead to retention of fluid in the tube.

Infectious Granulomata. The tubes are the commonest seat of *tuberculosis* in the female genital organs, and usually are first and most severely involved. The diseased tube is dilated and distended, and its walls are thickened, and on opening it the lumen is found filled with caseous pus or dryer masses. Diffuse infiltration of the mucosa, caseous nodules, and ulcers are found. Chronic adhesive inflammation in the adjacent structures leads to fixation of the ovary to the uterus, rectum, appendix vermiformis, and other parts. Pyosalpinx is commonly associated with the lesion, and may lead to perforation.

The disease may occur at any time of life, and has been observed in childhood. The supposition that infection may occur during coitus, from genital tuberculosis in the male, is thus seen to be improbable. The lesion may be due to extension of peritoneal tuberculosis.

Tumors. Primary neoplasms are not common in the tubes. Fibroma, myoma, and lipoma have been observed, and a papillary growth in the mucosa may be the starting point for carcinoma. Secondary invasion from neighboring organs is common, and may destroy the tubes.

The cysts of the Müllerian duct known as hydatids of Morgagni are common, usually about the size of a pea, and found in the fimbriae. Other small cysts occasionally form on the outer surface of the tube. Tubo-ovarian cysts are due to inflammatory adhesion of the fimbriae to the ovary, with salpingitis, inversion of the fimbriae and formation of a cyst lined by them. Free ova may enter the cyst.

Diseases of the Uterus. Puerperal Lesions of the Parametrium and Perimetrium.

The normal uterine mucosa lies directly upon the muscular tissue, without any submucosa, and has a different formation in the cervix and the fundus. The mucosa of the body of the uterus is made of

loose meshes of connective tissue, containing many round cells and covered by ciliated epithelium and pierced by glands whose cells are ciliated. The glands are tubular and forked and about 1 mm. in diameter. The mucosa of the cervix has a denser connective tissue and acinous glands which furnish transparent mucus. The outer side of the portio vaginalis is covered by squamous epithelium.

The fetal uterus at term is round, and measures about 2.5 cm. in length; there is but little distinction between cervix and body, and the latter is but half as long as the former; the plicæ palmatæ reach to the fundus.

Approaching puberty the body of the uterus increases in length and its cavity becomes triangular; the plicæ are found only in the cervix. This is termed the uterus infantilis.

FIG. 336.



The uterine mucosa. Z. a. Zone of tubular glands. Z. b. Zone of tortuous glands at the base of the mucosa. (After AMANN.)

With menstruation the cervix is half the length of the body; the cervical canal is marked off from the uterine cavity by the os internum; the os externum is a smooth transverse fissure; the organ measures 6 to 9 cm. long, 4 to 5 cm. between the tubes, and 1 to 1.5 cm. in thickness of walls.

The menstruating uterus is large, succulent, with swollen mucosa, extravasations of blood in the cavity, and free secretion of mucus from the cervix. The increase of the gravid organ depends upon enlargement of the single fibres, about five times in breadth and seven to eleven times in length, with multiplication of these fibres and formation of new vessels.

After parturition the uterus becomes smaller by contraction, and then by fatty degeneration of the muscle fibres. The os remains open until the tenth or eleventh day, and may present lacerations. On section the uterus presents wide vessels in its walls, fragments of decidua on its internal wall, and thrombosed vessels at the site of the placenta. Involution lasts six to eight weeks, and during this time the organ is soft and relaxed. The lochia are bloodless after the tenth day.

The uterus does not return to virginal dimensions, but remains permanently larger and rounder; the cervix is smaller in proportion to the body, and the external os is round and irregularly indented by scars. The vessels in the wall are thicker and more prominent on section. All these changes are marked according to the number of pregnancies experienced. The uterine dimensions are: length, 9 to 10 cm.; breadth, 5.5 to 6.5 cm.; thickness, 2 cm.

After the menopause senile atrophy diminishes the cervix especially, but also the body of the uterus; the cavity is narrow, the walls are dense but relaxed, the vessels thickened, and the mucosa thin and smooth.

Atrophy and involution may be presenile and due to loss of the sexual glands or their function, as after double oophorectomy, with diabetes, Addison's disease, Basedow's disease, and hyperinvolution after parturition, especially with too long-continued lactation.

Circulatory Disorders. *Hyperemia* with hemorrhages is normal during menstruation. In subjects dying at this period the uterine mucosa is infiltrated with serum and blood, and as much as 7 millimetres thick, and the cavity contains mucus and blood; the hemorrhages are scattered through the mucosa and cause it to project over them and rupture, but there is no marked general loss of epithelium.

After the blood has escaped the mucosa reappplies itself to the wall. A few days afterward there are regenerative changes in the epithelium, and some of its cells are lost. Blood remaining in it is absorbed or converted to pigment. The cervix shares in the process by increased excretion of mucus. Other physiological hemorrhages occur with abortion and parturition.

Menorrhagia is the name given to excessive escape of blood during the menses, and is due to anemia, chlorosis, metritis, and endometritis, and uterine tumors. At other times than menstruation the uterus may be congested, and blood may be lost, from certain poisons (phosphorus), infectious diseases, hemorrhagic diathesis, inflammation,

ulceration, and tumors of the organ, and in these conditions the hemorrhage is called metrorrhagia.

Stasis in the uterus is common with general or local causes, especially with displacements of the organ, flexion, and prolapse. The body, or the cervix, or both may be thus congested. The organ is somewhat enlarged, livid, dense, and its mucosa is dark and marked by varices. Hemorrhages into the mucous membrane and the cavity are frequent, and varicose enlargements in and about the portio vaginalis are observed. Other hemorrhages are due to arrosion of vessels by tumors and traumatism, or to operations.

Apoplexy of the uterus occurs in the aged and atrophic organ, as necrosis of the mucous membrane and hemorrhages into it as well as into the muscular tissue. Arterio-sclerosis and infarction are the usual causes.

Edema of the uterine wall and lining accompanies stasis and inflammation, and renders the organ soft and doughy.

Inflammation. Affecting the uterine wall, an inflammation is called *metritis*, and involving mucous membrane, *endometritis*; they commonly occur together or extend from one to the other. Inflammations of the cervix differ from those of the corpus, and the non-puerperal from the puerperal.

(a) **Non-puerperal Inflammation of the Uterus.** *Acute endometritis corporis* begins with swelling and edema of the mucous membrane, which may be stripped from its attachment and is infiltrated with hemorrhages. Increased and perhaps bloody excretion follows. Microscopically the membrane is infiltrated with small cells and blood, the superficial and glandular epithelia are cloudy, swollen, and desquamating, and in the glands and cavity there are masses of thickened mucus, leucocytes, and red cells. In some cases one of these elements predominates, and hence the findings vary.

Acute endometritis frequently follows menstruation. The distinction between physiological and inflammatory congestion is not always easily made. The lesion is often due to gonorrhea, and is then usually a profuse catarrh of purulent type. Similar conditions occur with various infectious diseases.

Metritis is a frequent complication of gonorrheal endometritis, and occurs as diffuse, or localized, edematous and cellular infiltration of the muscular tissue, which may involve its entire thickness and lead to formation of abscesses. The lesion may be due to the gonococcus or to mixed infection.

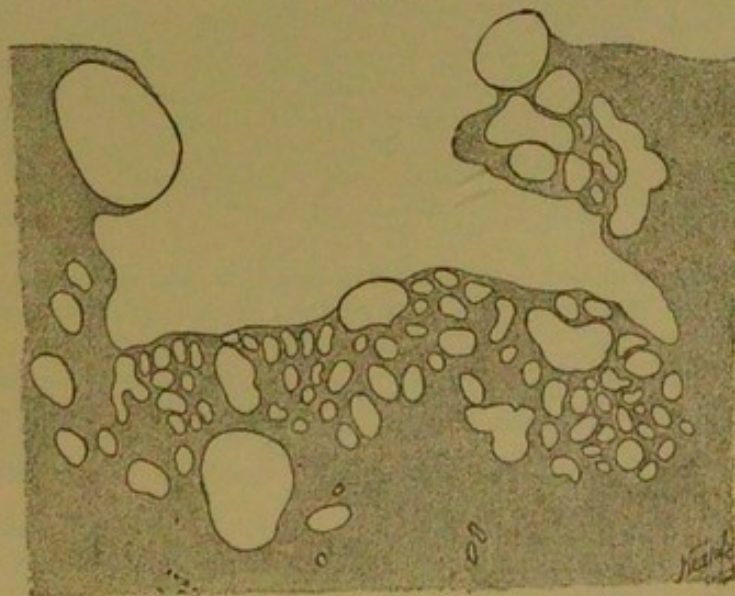
Chronic endometritis follows acute inflammations or develops *de novo*. Gonorrhea is the most common cause, but stasis and sub-

FIG. 337.

Endometritis corporis with hypertrophied glands. $\times 40$. (After AMANN.)

mucous tumors are capable of producing it. The mucosa is usually spotted with pigment from small hemorrhages, but the most marked

FIG. 338.



Cystic degeneration of the uterine glands. Transverse section. (After AMANN.)

change is proliferation of both stroma and glands. According to the proportion of these lesions, glandular, interstitial, and mixed forms of the disease occur.

In the glandular type enlargement of the glands (hypertrophic form), or multiplication of them (hyperplastic form), may occur, and in the latter they are spirally twisted and increased by lateral branches, and often cystic. Both glandular and interstitial forms produce a thickening of the mucous membrane, either diffusely or in areas, and with the latter, nodular, polypoid, and fungous projections develop. In extreme cases the thickened mucosa entirely fills the uterine cavity.

As in other catarrhal inflammations, the last stage of the process may be atrophy of the uterine mucosa. It then presents, instead of the usual round cells, spindle cells in a fibrous stroma and loss of the

FIG. 339.



Hyperplasia of the uterine mucous membrane. The epithelium of the glands and of the surface strongly folded, the glands dilated in places. Magnifying glass. (After AMANN.)

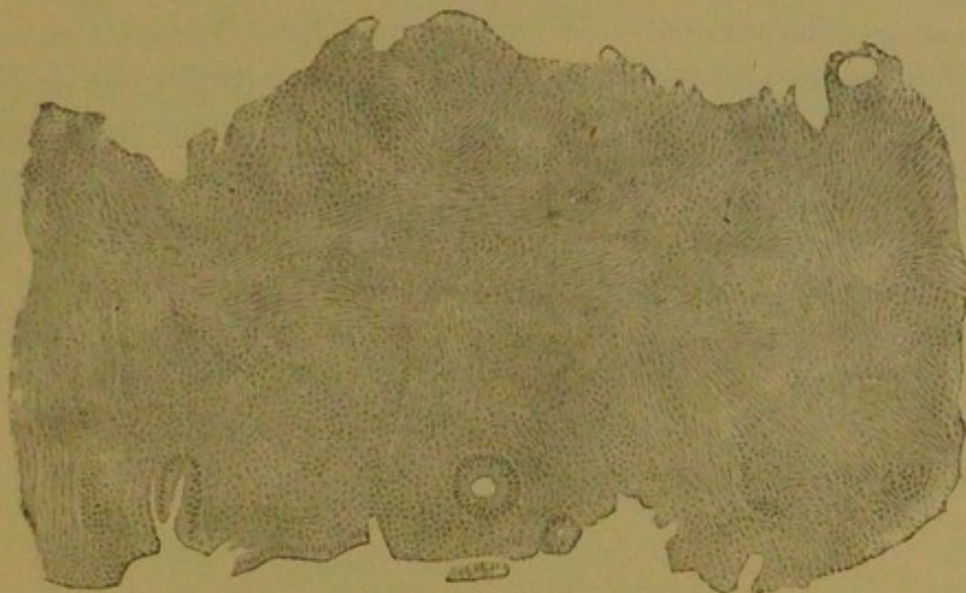
glands and superficial epithelium. Hence the membrane is thin and smooth, and previous hemorrhages may have left spots of pigment.

Less frequently there is a large-celled transformation of the mucous stroma, or a change known as psoriasis uteri, which consists in partial or complete conversion of the epithelia into squamous or horny cells.

Endometritis exfoliativa, or *dysmenorrhea membranacea*, is a special form of uterine inflammation in which there are desquamation of the membrane and its extrusion in flakes, or even complete, as a triangular sac in which the tubal ostia may be seen. The lesion is an interstitial endometritis with small-celled infiltration of the mucous membrane,

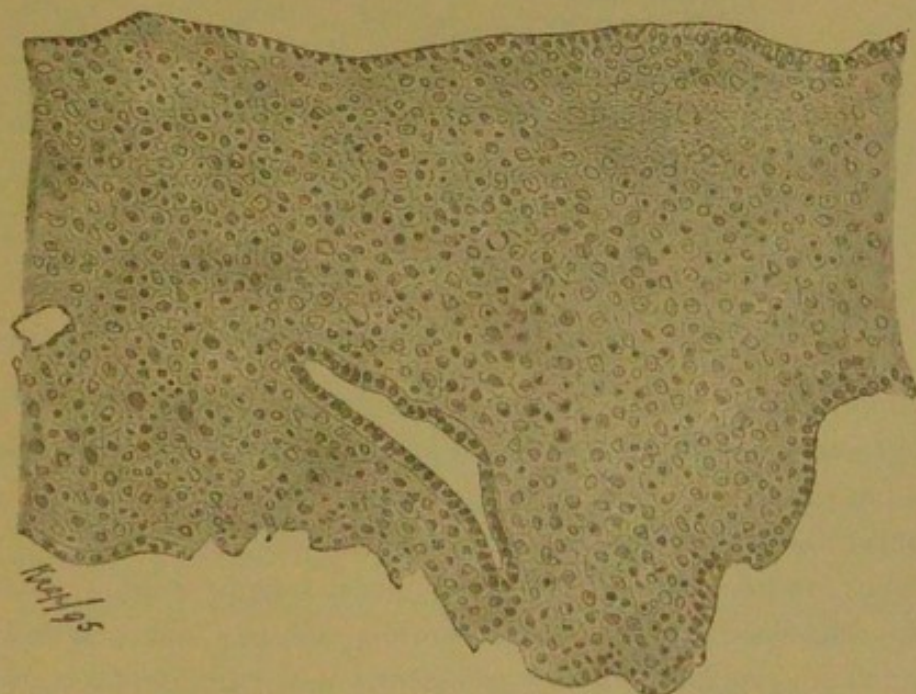
and in the cast there are glandular tubes irregularly dilated. The cells of the stroma may be so large that they resemble those of the

FIG. 340.



Atrophic endometritis. Indurating increase of connective tissue, loss of glands and epithelium. (After DÖDERLEIN, in Veit's Handbuch.)

FIG. 341.



Cast from a case of membranous dysmenorrhea. Composed of investing epithelium and glands, the stratum proprium containing large cells which enclose leucocytes. (After AMANN.)

decidua, but are not so numerous as with pregnancy. Masses of fibrin may be passed during menstruation.

Cervical endometritis may accompany inflammation of the body or be the first and only lesion. Gonorrheal and puerperal cases often begin in the cervix. Acute and chronic types are seen which resemble those of the corpus, but the secretion is more copious and either mucous or mucopurulent. In the chronic form thickened secretion is a frequent symptom, together with redness and swelling of the mucosa, especially marked in the plicæ. Glandular proliferation causes cystic formations with a single layer of epithelium on the inner surface. The hyperplastic glands may penetrate farther than normally

FIG. 342.



The cervical mucosa. C. Dr. Acinous glands. (After AMANN.)

into the muscular tissue. Laceration of the cervix and eversion of the lips (ectropion) permit a view of the thickened cystic membrane and its increased secretion. Papillary and follicular erosions, ovules of Naboth, and polypoid outgrowths accompany this lesion.

Erosions occur with the loss of the investing epithelium of the cervix, either of the squamous covering of the outer side of the portio, and its replacement by cylindrical cells, which constitutes the erosion of the gynecologist, or in follicular form on the inner side. The former lesion is due to the growth of cylindrical epithelium beyond the normal boundary of the external os, or to loss of the squamous covering of the part and exposure of the lower cylindrical

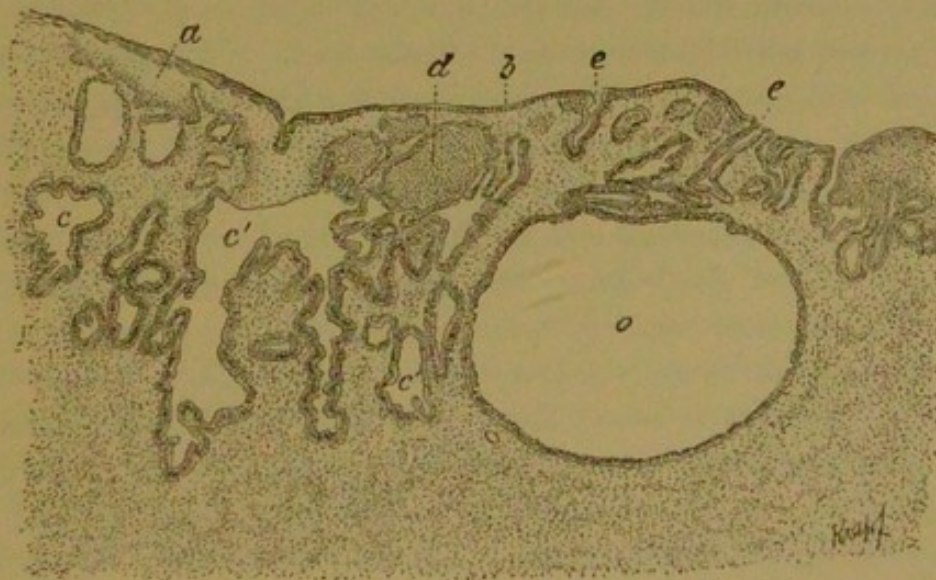
cells. As such areas have a dark-red color, in contrast to the pale portio, they have been called erosions. The papillary type is caused by deep proliferation of glands and papillary outgrowths between the

FIG. 343.



Ectropion and erosion of the cervix. *C. Dr.* Cervical gland. *Er. B.* Depressions from the surface clothed with cylindrical epithelium. *Er. Dr.* Large gland. *Pl.* Flat epithelia. (After AMANN.)

FIG. 344.



Cervical endometritis; erosion healing. Flat-celled epithelium replacing cylindrical. *b.* Cylindrical cells. *a.* Erosion. *e.* Glands. *c, c'.* Proliferating glands. *o.* Cystic glands. $\times 40$. (After AMANN.)

glands, so that the surface has a fissured appearance. With cystic changes in the glands the follicular type occurs. The ovules of Naboth are such retention cysts of the glands and may be as large as peas, with serous or colloid contents.

The cervical mucosa has a special tendency to form polyps. The mucous forms are pedicled and are made of circumscribed proliferation of glands, and contain all the elements of the mucosa. The glandular are groups of a few dilated projecting follicles.

(b) **Puerperal Inflammations of the Uterus.** *Etiology.* Wounds of the vagina and cervical lacerations, rupture of the perineal body, and traumatism of the uterine cavity, together with the placental site, present an immense surface through which infection is possible after parturition. The streptococcus pyogenes is frequently found, and general septic infection as well as local lesions may be due to this organism. Putrefaction of material retained in the uterus is followed by absorption of ptomains and toxins. The pyogenic organisms may be introduced by the fingers in examination, by instruments, or from the cocci which usually are to be found in the vaginal secretion and lochia (not in the lochia from the uterus). Areas which have suffered great pressure and become necrotic may also permit infection, placental fragments which putrefy are another source, and organisms may be carried up from the vagina. Previous gonorrheal inflammation of the uterus and tubes, which may have become latent, may break out again with added infection.

The wounds which become infected develop into ulcers with necrotic grayish-yellow exudate on the surface. They spread rapidly in depth and laterally. The lesion remains local or becomes general.

1. Primary puerperal endometritis may be purulent or also necrotic. The inner surface is covered with pus and fibrin and shreds of dead tissue, and the placental site and lacerations of the cervix are especially the seat of the lesion. The entire mucosa may die, bleeding is common, and severe cases become gangrenous.

2. Injuries of the cervix and vaginal dome permit the infection of the connective tissue about the cervix and in the broad ligaments. This is called parametritis. The serocellular exudate may be absorbed or converted into a purulent fluid, and putrefactive organisms may lead to gangrene of the parts. Thrombophlebitis of the uterine plexus often coexists. In mild cases there are firm, fibrous, and nodular lesions remaining after the acute inflammation subsides. Such indurative parametritis may be present from the first.

3. The muscular tissue of the uterus is almost always involved in these inflammations, and on section the lymphatics may be found distended with pus, and perhaps dilated to cysts. Such metro-lymphangitis is especially marked about the insertions of the tubes,

where the lymphatic vessels are grouped. Diffuse phlegmonous inflammation of the muscle gives it a uniformly swollen yellowish appearance, or circumscribed abscesses are found, which differ from the lymphatic form in having irregular walls. Gangrenous softening and perforation may occur.

4. Pelvic peritonitis and perimetritis may be due to the extension from the tubes, the ovaries, or the cavity of the uterus. Its nature resembles that of the primary lesion, and its course is that of any localized peritonitis. It may also become general and fatal.

5. The vessels of the internal uterine surface are closed after parturition by contraction of the tissues and by thrombi, which form in them and become organized. Infection of the thrombosed vessels is particularly liable to happen at the site of placental attachment. The consequent purulent softening and inflammation in the veins is called thrombophlebitis and periphlebitis. The thrombus extends to the hypogastric and spermatic vessels, or even to the vena cava inferior, and the danger of general infection from the softening purulent thrombi is always very great and at times rapid.

6. Salpingitis and oophoritis of puerperal origin have been cited.

The inflammation in any of these cases may extend to the veins of the lower extremity, as phlebitis and periphlebitis of the great saphenous vein, with secondary phlegmonous inflammation, or the latter feature may develop first (*phlegmasia alba dolens*). Puerperal erysipelas of the external genitals and adjacent parts is due to infection by the streptococcus, which is identical with the organism of erysipelas.

Puerperal fever may accompany any of these forms of puerperal infection, and at times the local lesion is relatively unimportant, as a small tear in the vagina, and hence may be overlooked. Pyemic conditions with pleuritis, pericarditis, and ulcerative endocarditis, infarctions and abscesses in the organs, etc., are due to infected emboli from the genital lesion and also from the cardiac suppuration.

A form of chronic metritis, sometimes called infarct of the uterus, follows puerperal, gonorrheal, and other inflammations. The organ is enlarged, and in the early stages is edematous and succulent. In time it becomes firmer, with venous stasis and dilatation of the lymphatics. The wall of the uterus may measure as much as 2 to 3 centimetres in thickness. In the end there is great increase of the stroma, and, according to some authors, a hyperplasia of the muscle also. This lesion, which resembles induration with stasis in other organs, may follow chronic inflammation or subinvolution, or occur with

tumors and diseases of the adnexa, or as a hyperplasia, and lastly, with diseases of the heart.

Decidual endometritis, or *deciduoma*, is due to imperfect involution of the uterine mucosa and proliferation of large cells in the retained fragments of decidua, which leads to insular thickening of the mucous membrane. It is commonest after abortion. Necrosis and demarcation of the uterine mucous membrane may occur after abortions, and large decidual cells are a marked feature of such lesions.

Infectious Granulomata. Miliary *tubercles* in the uterine mucosa are found with general infection. Chronic tuberculosis of the organ is often an interstitial lesion in which the thickened mucous lining contains microscopic tubercles. Later stages are marked by ulceration, and this may involve the muscular elements (*phthisis uteri*). The disease is more common in the body than the cervix, for it commonly starts by invasion from the tubes.

Syphilis may occur as a primary lesion on the cervix.

Changes in the Lumen of the Uterus. Abnormal Contents. Stenosis and atresia of the uterus may be congenital or acquired. In the latter case it is due to tumors or displacement with flexion. The effects of atresia are noticed usually only after puberty, by the accumulation of blood in the cavity (hematometra).

After the menopause hydrometra is not uncommon. Pyometra is the name given to purulent collections in the uterus, and when its contents putrefy and gas forms, the name physometra is applicable. Closure of the vagina leads to similar results which include this canal, making hematocolpos, etc.

Increase of the cavity of the uterus may be due to hypertrophy or to atrophic thinning of the walls.

Malpositions of the Uterus. Normally the position varies with the fulness of the rectum and of the bladder, and the intra-abdominal pressure. Physiological anteversion occurs with an empty bladder. Pathological displacements are distinguished by fixation of the uterus in abnormal positions. With total displacements there may also be a bending of the organ, termed flexion. The cause of the condition is frequently extra-uterine. Tumors in the pelvis, exudates in the parametrium, and contracting scars are common factors. Abnormal rigidity of the uterine walls, relaxation, and uterine tumors are other causes of displacement.

Elevation of the uterus may be due to pelvic tumors, or attachments formed during pregnancy which do not permit return to normal rela-

tions. Uterine descent, prolapsus, is caused by loss of support in the pelvic floor and the uterine ligaments, together with excessive pressure from above, and is described as simple descent, partial and total prolapse. In the latter condition the uterus is wholly outside the pelvis. Prolapse without descent is the name given to great hypertrophy of the portio vaginalis, so that it presents at the vulva, without necessarily any descent of the uterus as a whole.

Displacement forward is either *anteversion*, when the form of the uterus is unchanged, or *anteflexion*, with bending of the organ. It is caused by adhesions on the anterior surface, contraction of the round ligaments, and cicatricial contraction of the posterior parametrium and recto-uterine ligaments which drag the cervix backward. Flexion brings the anterior surface of the fundus nearer to the cervix and the organ either cannot be straightened or resumes its bend; it may be due to the subinvolution of the posterior wall of the uterus.

Retroversion and **retroflexion** are the opposite conditions and arise from relaxation of the round ligaments, anterior parametritis, lengthening of the sacro-uterine ligaments, and displacement of the cervix forward. Abdominal pressure increases the displacement, and contracting scars on the posterior uterine surfaces have the same result.

Lateral version and **flexion** are usually associated with backward displacement and shortening, or adhesions of the ligamentum latum.

Torsion of the uterus may be due to contracting adhesions, tumors of the uterus or ovary, and other displacements.

Inversion of the organ consists of a sinking of the fundus into the cavity, and is possible with a very wide cavity and relaxed walls. These conditions occur almost exclusively in pregnancy. Traction on the placenta or an internal tumor may be the immediate cause of the displacement. If complete, the inverted uterus lies outside the pelvis, and prolapse usually occurs at the same time.

Uterine Tumors. A sharp line cannot be drawn between inflammatory hyperplasia and epithelial neoplasms of the uterine mucous membrane, on account of many transitions between them. Adenoma, with more or less typical arrangement of its glands, differs from simple hyperplasia only in the larger proportion of the glands and their slighter proportion of stroma, and the occurrence of more than one layer of epithelial cells. Adenoma may be broad, nodular, or polypoid. Follicular hypertrophy of the portio vaginalis is accompanied by such polypoid growths, and they occur in the mucosa of the body. Transitions to adenocarcinoma are common.

Malignant tumors of the uterus are among the commonest examples of their class. About 25 per cent. of all carcinomas occur in the uterus. Tumors of the cervix may be squamous-celled epithelioma or carcinoma, beginning in the cylindrical epithelium.

The squamous-celled variety starts on the outer surface of the portio vaginalis, and forms papillary, so-called cauliflower, tumors, attached to the lips of the external os, with little tendency to invade the cervical mucosa, but rapid invasion of the vagina. Or a more malignant form occurs by carcinomatous development in the depth of the cervix, and gradual external perforation. Extension to the body of the uterus is not common with either variety.

Carcinoma of the cervix causes ulceration of the cervical mucous membrane and often extends to the corpus uteri.

All forms of this neoplasm tend to break down rapidly and form ulcers, with necrosis and severe local destruction. They usually come late to autopsy, and the various forms may then be indistinguishable. The bladder, parametrium, and ureters are frequently attacked early in the disease, and with the latter condition hydro-nephrosis and uremia may lead to death. Ulceration and fistulae between the pelvic organs very frequently develop.

Carcinoma of the body of the uterus is histologically a carcinoma simplex, or an adenocarcinoma, and the latter form often starts in hyperplastic areas of the mucosa. The tumor is malignant and invades the muscular tissue.

Among the other tumors of the uterus myoma is very common. It may appear as submucous or subperitoneal polyps or be intraparietal. The polypoid forms in time become pedicled, and if submucous may reach into the vagina or even be cast off by destruction of the pedicle. Several myomata may occur in the same uterus. In the cervix they are very uncommon. Transition to malignant myosarcoma is rare. Complicating conditions are catarrhal metritis, displacement, etc.

A rather infrequent tumor of the uterus is sarcoma, which is found in both the cervix and the corpus. It occurs in two forms, either as a tumor of the parenchyma, making nodules and diffuse growths in the wall, or sarcoma of the mucosa, appearing as diffuse or broad nodular tumors in the internal surface. Adenoma sometimes becomes sarcomatous by changes in its stroma.

Diseases of the Placenta, the Fetal Envelopes, and the Umbilical Cord. Extra-uterine Pregnancy.

The amnion is a delicate membrane of connective tissue, clothed with epithelium and filled with water (*liquor amnii*), which immediately surrounds the embryo. The chorion originally has many villi on its outer surface, but the major part of these are lost later. The decidua vera arises from hyperplasia of the uterine mucous membrane; the decidua reflexa arises from the site of attachment of the fetus and surrounds it; these two become fused at the fifth month. The decidua serotina forms at the place where the ovum comes to rest. From this and the chorion the placenta develops, consisting of a fetal and a maternal portion. Here the chorionic villi develop very strongly. They consist of a delicate mucoid tissue containing vessels and covered by a double layer of epithelial cells, of which the inner, Langhan's layer, are cubical and distinguished from each other, and the outer is but a layer of protoplasm with many nuclei. The outer layer is called the syncytium and may present budding projections. The inner layer is certainly derived from the chorionic epithelium, but it is uncertain whether the outer comes from this or from the uterine epithelium. At about the fifth month giant cells with many nuclei are found in the placenta. The decidua cells in the remaining portions are large, rich in protoplasm, and of spindle shape, and develop from the connective-tissue cells of the uterine mucous membrane.

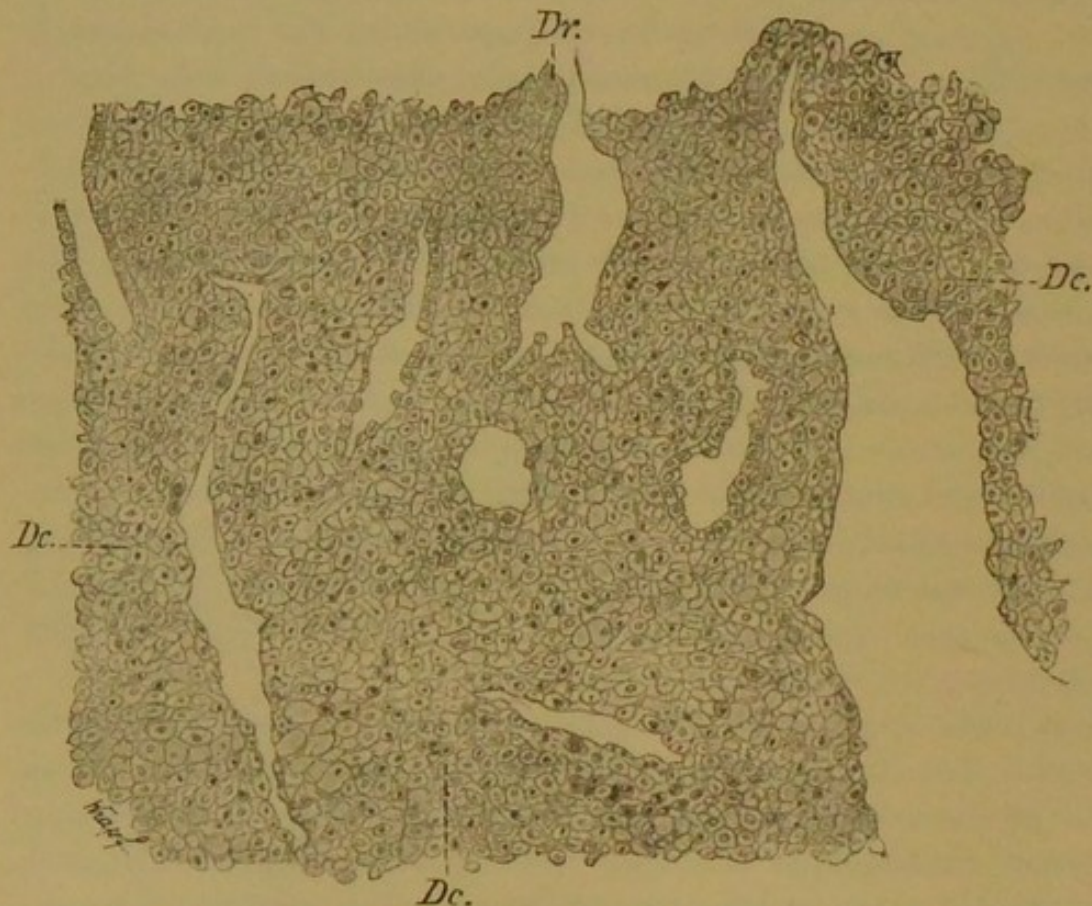
Decidual Endometritis. Pregnancy during the course of hyperplastic endometritis causes marked thickening of the decidua vera and numerous nodular formations in it and projections from it, owing to the proliferation of the large decidual cells. Similar changes in the decidua reflexa and serotina may occur. This condition is termed endometritis deciduae. Hemorrhage into the fetal envelopes and formation of a uterine mole may be the result, or the decidua vera becomes adherent to the decidua reflexa in places, and a collection of fluid between them may form. This is called *hydrorrhea gravidarum*, when the fluid escapes in quantity after rupture in the wall of the sac. Endometritis after abortion has been mentioned above (p. 356).

Uterine Moles. Abortive ova, which have remained for a long time in the uterus, after the death of the fetus may be infiltrated with blood. As the blood lies between the envelopes in layers they become very thick, and the cavity of the amnion is decreased, but the blood

may be found in this also. The fetus may be already dissolved and lost, or found in a macerated condition. After a long time these bloody moles lose their color and become light brown or yellow, when they receive the name fleshy mole, or they may calcify.

Placental Hemorrhage. At birth this occurs in the serotina when the placenta separates from the uterus. Occurring during pregnancy it may cause the death of the embryo and premature labor. Placenta previa, by which name is meant the location of the placenta over

FIG. 345.



Decidua in normal pregnancy. *Dc.* Cells of the stratum proprium transformed to large decidua cells. *Dr.* Glands with dilated cavities and flattened cells. (After AMANN.)

the uterine os, is dangerous because of the liability of this hemorrhage in the early stages of parturition. Placenta previa marginalis forms when the edge of the structure reaches to the uterine os. When it is partly over the opening it is called placenta previa lateralis, and with this a process may enter the cervical canal and appear at the external os (*p. previa cervicalis*). The adjective *centralis* is used when the attachment wholly covers the os.

Hemorrhages into the tissue of the placenta may cause destruction

and necrosis of parts of it. These foci then appear dark red, or lighter and yellowish, and may heal by fibrosis.

Placental infarction forms firm wedge-shaped yellowish areas of the size of a pea or a walnut, on the edge of the placenta or involving its entire thickness, and often multiple. Microscopically in the intervillous spaces there is hyaline fibrin, and the villi may be necrotic. Old infarcts may be organized and the scar depresses the surface. Puriform softening is not common. These lesions have been explained as due to degeneration from the pressure of proliferated decidua cells, closure of the vessels of the villi, thrombosis in the intervillous spaces, and disorders of the uterine circulation. The supposed relation between these lesions and syphilis has not been proved.

Vesicular Mole, Hydatid Mole, Myxoma Chorion Multiplex. All these names apply to a transformation of the chorionic villi which converts them to cystic vesicles filled with fluid. They consist of gelatinous connective tissue, rich in fluid, with many fine vessels and an epithelial covering. On puncture of a vesicle mucous fluid escapes. The whole formation has been likened to a bunch of grapes. It is made up of numerous small vesicles with slender pedicles, and one of these may be common to several vesicles in a series. Developing in an early period of pregnancy the entire fetus and its envelopes may be lost in the mass; at a later time it causes death of the fetus and abortion.

When the change involves only a limited portion of the chorion or placenta the fetus may develop normally.

According to Virchow, there is a mucoid change in the chorionic villi. Marchand's view is that the chorionic epithelium becomes hyperplastic and undergoes a later hydropic change, by which the inner layer of the villus becomes fluid, while the outer persists.

Cases of this nature occur in which the mole acts destructively, invading the uterus to the serosa. This is called destructive uterine mole. Probably malignant epithelial tumors may arise from these villi.

FIG. 346.

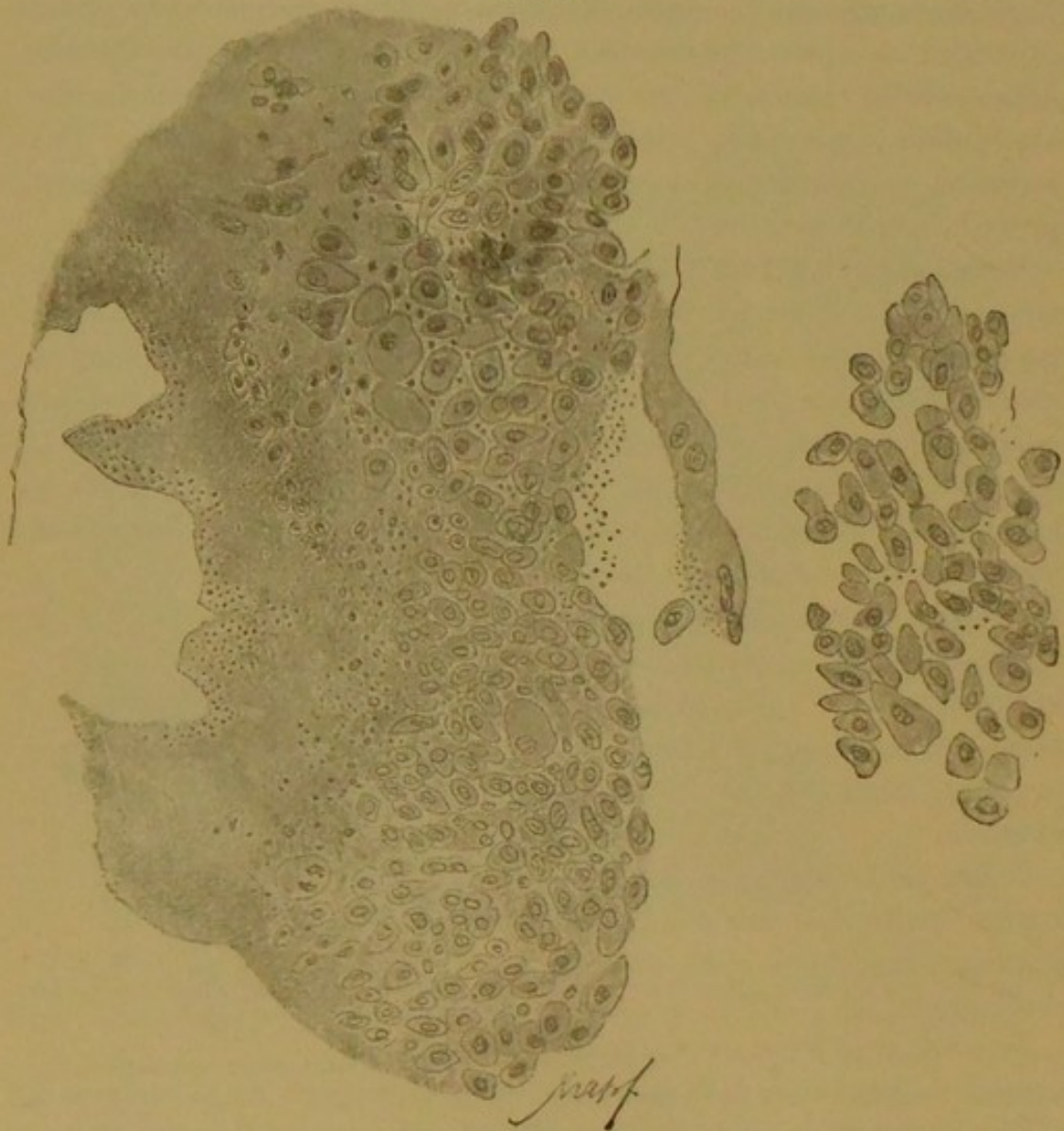


Hydatid uterine mole. Natural size.

Inflammation and Infectious Granulomata of the Placenta. Productive inflammation indurates the placenta and causes loss of the villi. Some cases begin as periarteritis fibrosa. The lesion causes early separation of the placenta, or, on the other hand, abnormal fixation.

Syphilis may be responsible for many of these indurative lesions. Gumma of the placenta is rare.

FIG. 347.



Synecioma malignum. The uterine tissue infiltrated with decidua cells. (After AMANN.)

Typical tubercles occur in the placenta at times when the mother suffers from general miliary tuberculosis, and the bacilli have been recovered from the fetal tissues.

Placental Polyps and Tumors. Fibrinous placental polyp, also called hematoma uteri, develops when there is copious bleeding at the site

of the placenta and its fragments are enclosed by the clots. The latter become firmer, their attachment to the uterus is lengthened, and thus they assume a polypoid form. They may be of the size of the fist, cause severe hemorrhages until they are cast off, or become calcified.

Deciduoma is an adenomatous neoplasm starting in remnants of the placenta and membranes. Destructive placental polyps have the outer appearance of the variety mentioned above, but at their uterine attachment they grow into the muscular tissue and destroy it. There is, in other words, a destructive proliferation of chorionic villi.

Malignant deciduoma, or syncytioma malignum, or chorionic epithelioma, is the name of a tumor which starts in retained portions of placenta and behaves like an epithelial neoplasm in its local and metastatic effects. The tumor has been explained as a proliferation of decidual cells, but it is now clear that the essential feature of the process is malignant proliferation of the chorionic epithelia. Hence the tumor contains two varieties of cells, large elements of irregular shape and size with transitions to giant cells, corresponding to cells of the syncytium, and smaller cells from Langhan's layer. They are arranged irregularly, or nests of the smaller variety are surrounded by syncytial masses, or trabeculae of syncytial cells run perpendicularly to the base of the tumor. The neoplasm infiltrates the uterus, or is enclosed in the wall, or sessile upon it. It destroys the muscle fibres and breaks into the vessels and causes secondary tumors (lungs). In the gross it is a soft, red mass, with a spongy section.

Diseases of the Amnion.

The liquor amnii is formed by transudation from the maternal vessels with admixture of fetal products from the kidneys and skin. It resembles thin blood serum (1 per cent. albumin), and contains small amounts of urea and grape sugar. Toward the end of pregnancy the percentage of urea in the fluid exceeds that in the maternal blood (0.029 to 0.059 per cent.), and urine may be mingled with it.

Hydramnion refers to excess of liquor amnii, more than 1 to 1½ litres, and the amount may reach ten times the normal. The condition develops with many maternal diseases, but the relation between them is not always clear. Inflammation of the decidua, hypoplasia of the placenta, anemia, maternal syphilis, and dropsy may be associated with it. From the fetus, syphilis, imperfect development, and

other conditions may be causative. Large collections may atrophy or destroy the fetus.

With twins from a single ovum acute hydramnion may develop in the course of a few weeks about the better developed of the two.

Too slight a quantity of fluid permits adhesions between the amnion and the fetus, and from this various deformities result (p. 186).

Meconium is found in the liquid only with asphyxia of the child; blood pigments and products of decomposition color it dark or make it turbid.

Affections of the Umbilical Cord. Abnormal insertions of the cord include the marginal and the velamentous. In the latter the cord does not reach the margin of the placenta, but sinks into the envelopes and runs in them for a space without its layer of Wharton's jelly. Knots form in the cord when the fetus passes through a loop of it. A coil about the fetus may be dangerous to its life, especially during parturition. Marked twisting of the cord may close its vessels, and it may be unusually long. With syphilis there may be arteritis and phlebitis of its vessels, and occlusion of them has been found with macerated embryos.

Abortion. Changes in the Fetus and Its Envelopes.

Expulsion of the embryo during the first sixteen weeks is called *abortion*, during later periods it is called *partus immaturus* or *partus prematurus*. The commonest cause of abortion is the death of the fetus, which may be due to lesions of the placenta, the fetal envelopes, or the mother. Among maternal diseases which produce abortion are poisons, diseases of the heart and kidneys, syphilis, and acute infectious diseases. The fetus dies by direct infection or intoxication, or because of nutritive disturbances. Diminution of the uterine cavity, severe physical exertion and emotions may lead to the same result. Malformation and fetal diseases, especially syphilis, are the commonest causes of abortion in the growing individual.

The entire ovum and its membranes may escape, or a tear in the latter permits its expulsion while the other structures are retained. After the death of the fetus the chorionic villi may continue to grow for a long time, and, though dead, the fetus need not be expelled at once. Dying in the early weeks, the frequent result is formation of a fleshy mole. It may be absorbed or make an imperfect mass which is called an abortive malformation. When death occurs later in the intra-uterine period the fetus becomes macerated, the epidermis strips

off in flakes, the bones are separated from their attachments, the cranial bones are shifted over each other, all the organs are softened and blood-stained, and bloody serum collects in the cavities of the fetal body (*fetus sanguinolentus*). Externally are the signs of syphilis, and in all the organs are numerous crystals of hematoidin. When the membranes are torn infection may cause putrefaction of the fetus. In other cases it is mummified or calcified. The dry mummy is called *fetus papyraceus*.

Extra-uterine Pregnancy. Three forms are recognized: (1) The abdominal, when the fetus develops at some point of the peritoneum, often in Douglas' pouch; (2) the tubal, and (3) the ovarian. In tubal pregnancy three possibilities occur: the ovum may develop at the outer end (tubo-abdominal form), or in the median section of the tube (simple tubal form), or in the isthmus (interstitial form). In all cases the placenta forms from the allantois. In the tubal form the decidua develops from the tubal mucosa. In the ovarian form the membrana granulosa serves the purpose. In the abdominal form there is a copious formation of false membranes. The fetus may die early and become calcified (lithopedion), or suppurate and cause peritonitis, or perforate into the small intestine or the rectum and be expelled. The commonest result is rupture of the membranes and hemorrhage into the peritoneum, forming a recto-uterine hematocele which becomes encapsuled. In the uterus imperfect decidua may form.

Diseases of the Uterine Ligaments, Parametrium, and Pelvic Peritoneum.

The parametrium is a collective name for the connective tissue about the cervix and vault of the vagina and in the ligaments, partly covered by peritoneum and partly enclosed in its folds. Its lesions are similar to those in the pelvic peritoneum, and are usually secondary to those in the pelvic viscera.

Circulatory Disorders. The veins about the cervix and in the broad ligaments may become varicose, thrombosed, and the seat of phleboliths. Rupture of such varicose veins, of hematosalpinx, and tubal pregnancy, and hemorrhage from Graafian follicles, may lead to the accumulation of large amounts of blood in the pelvis. Severe and profuse menstrual flow and traumatism, infections and intoxications, may lead to the same condition. The blood collects at first in the rectovesical pouch, and if copious in the anterior cavity also. It may be large enough to cause death, or, with infection, it is followed by

peritonitis. Such masses may become organized and encapsuled. This formation is called hematoma or hematocele, and consists of strands of connective tissue and masses of clotted blood. The blood may thicken and be partly absorbed, and the remainder organizes.

Inflammation of these parts, parametritis, may be due to extension from the uterus, gonorrhea, proctitis, fistula in ano, and rectal syphilis, and, as in the puerperal cases, may be of any variety, serous or purulent. Perforation or induration may be the consequence, and the perforation may involve the rectum, bladder, vagina, and other organs, or take place under the psoas muscle, and caries of the pelvic bones may occur with it.

Perimetritis and pelvic peritonitis are the names for inflammation of the serous lining of the pelvis and of the organs contained in it.

Chronic perimetritis is primary or secondary, especially with periophoritis and hematocele. Fibrous adhesions between the various surfaces and retraction may follow, with resulting displacements of the uterus, tubes, and ovaries. When the adhesions form hollow spaces serous fluid may accumulate in them, and this may become purulent.

Cysts of the broad ligament may begin in the parovarium or remnants of the Wolffian body, or, with a partially patent processus vaginalis, hydrocele of this structure is possible.

Of the tumors, lipoma, myoma, and sarcoma, and subserous ovarian cystoma may be mentioned.

Tuberculosis occurs with tubal lesions and general infection.

Diseases of the Vagina and External Genitals.

Acute and chronic catarrh of the vaginal mucous membrane results from gonorrheal and puerperal infection, irritation from cancerous discharges, diabetes, scrofula, and other general diseases. The surface is red and swollen, the columnæ and papillæ are prominent, and there is excess of secretion, which may be turbid or purulent (*fluor albus*). If the inflammation is chronic the surface is pigmented and gray, or spotted and mottled with livid or red hues, and atrophy of the mucous membrane may occur.

Croupous and diphtheritic colpitis may accompany cholera, variola, and scarlet fever, from hematogenous infection.

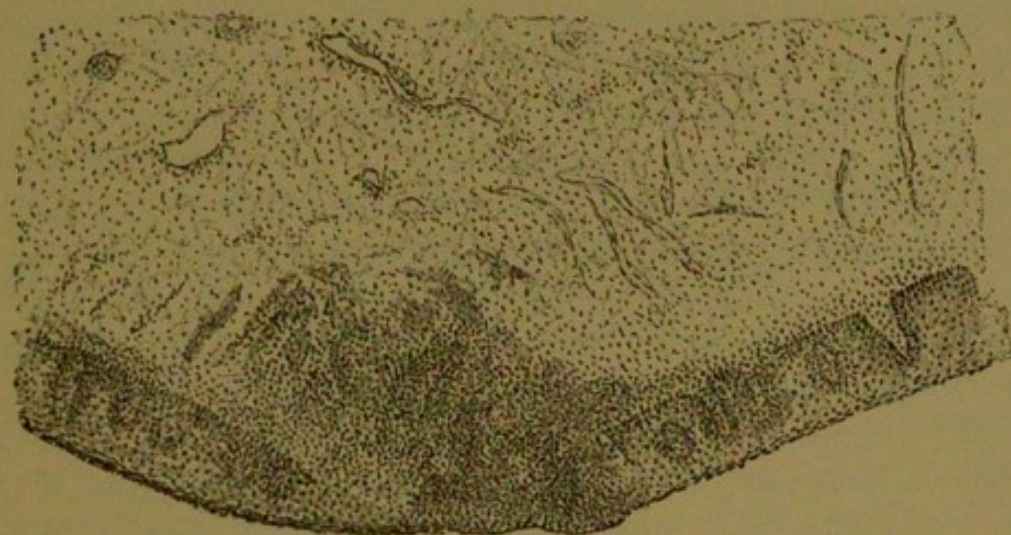
In advanced age adhesive ulcerative colpitis may be observed with infiltration of small cells at certain points, loss of the epithelium, and consequent adhesions between the walls of the canal. Complete closure of the vagina is possible in this lesion.

Miliary follicular colpitis in the upper section of the canal may follow chronic inflammation of the vagina. Scattered over this surface there are numerous sharply limited spots, of the size of a pin's head and gray or pigmented in color. The epithelium over them is lost, or there are small vesicles. Microscopically there is an infiltration of small cells, more or less circumscribed, which resemble the lymphoid collections in the intestinal follicles, and in them there may be a lymph space with lymphectasia in the vicinity.

An unusual form of colpitis is the herpetic, with vesicles.

Among other rare affections of the vagina are dysentery, erysipelas, tuberculous and syphilitic inflammation, and gummata. In the cadaver the initial lesion or its scar may be found.

FIG. 348.



Chronic colpitis. (After VEIT.)

In senile atrophy the vagina is narrowed and its walls become thin and relaxed.

Inversion of the anterior or the posterior vaginal wall may occur, or a ring-like protrusion when both walls collapse. If the displaced wall protrude from the vagina it is called inversion with prolapse. The condition is due to looseness of the vaginal attachments, as after childbirth, or prolapse of the uterus. The anterior vaginal wall may draw down the bladder and contain part of it, the posterior wall displaces the anterior rectal wall; these conditions are known as vaginal cystocele and vaginal rectocele. Ring-shaped inversion is usually secondary to uterine prolapse and begins in the vaginal dome.

Organs which usually lie much higher than the vagina may invert

the posterior wall, forming vaginal ovariocele, enterocele, or, if the inversion is due to exudate, hydrocolpocele and pyocolpocele.

Injuries to the vagina may produce fistulæ and scars. The former may be due to foreign bodies, parturition, softening tumors, and gangrenous inflammation, when the vagina is adherent to other organs normally or pathologically. Hence rectovaginal fistulæ, vesical and urethral fistulæ, and communication with the small intestine may be found.

Tumors. Myoma, fibromyoma, sarcoma, and carcinoma may start in the vagina, but the latter are almost always secondary to cervical tumors.

Cysts are relatively common, and may be due to retention in the glands, dilatation of lymphatics, and collection in portions of the persistent Wolffian duct. In pregnant women the vagina may be covered by a multitude of small cysts (colpohyperplasia cystica or colpitis emphysematosa).

Among the parasites found in the vagina trichomonas, oxyuris, and *oidium albicans* may be mentioned.

The Vulva. The inner surface of the vulva is covered by mucous membrane which gradually passes into the external skin. Lesions of mucous and cutaneous surfaces may be found here. Injuries, pointed and broad condylomata, chancres, and lupus are among the commonest. Hypertrophy of the labia majora (elephantiasis), circumscribed fibromata, sarcoma, and lipoma are also found. Carcinoma may attack the labia and the clitoris as epithelioma. Dermoid and atheromatous cysts, and cystic and suppurative dilatation of the glands of Bartholin are other lesions of the part.

Diseases of the Mammary Gland.

Anomalies. Agenesis of one or both glands or the nipples may be observed. Hypoplasia is common with imperfect sexual development, especially of the ovaries. Supernumerary breasts are sometimes found between the normal glands or on distant parts, and the condition is called polymastia.

Normally the breast undergoes marked development at puberty, and when completely formed consists of connective tissue and ducts with but few acini. In pregnancy the breast enlarges and the acini multiply.

Atrophy of the breast may be senile or due to inactivity.

Hyperemia of the breast occurs with menstruation, lactation, and inflammation. The latter condition is called *mastitis*, and may appear in the newborn, at puberty, or during the puerperium. Puerperal infection usually occurs from injury and fissure of the nipple, and may alter the composition of the milk.

The inflammation may resolve, but most often it ends in the formation of abscesses with external perforation. If the abscess heals imperfectly a so-called milk fistula may remain. In other cases there is a diffuse induration from fibrous hyperplasia, and if the ducts are occluded in this way, galactocele, or retention cysts filled with milk, may be the result.

Tuberculosis of the breast is very uncommon.

The initial lesion of syphilis may be found on the nipple.

Hyperplasia and Tumors. True hyperplasia leads to uniform enlargement of both breasts, and progresses for a long time until a certain size is reached. The enlarged organs may weigh many kilogrammes. In structure they are normal, and during pregnancy go through the customary changes.

Adenoma is characterized by proliferation of the glands, so that the numerous acini have the appearance of the breast during pregnancy. The epithelium in the acini may have many layers. Adenomata are usually unilateral and circumscribed. Many of them are encapsuled and may be shelled out of their envelopes.

Pure fibroma is not common in the breast. Usually there is also a growth of glands, just as the adenomas may be rich in stroma. Hence adenofibroma and various transition forms occur, of firm consistence, and lobulate or nodular in outline.

Myoma and adenomyoma may be diffuse and cause a general atrophy of the gland, or more localized. Similarly lipoma is either diffuse with atrophy of the glands, or circumscribed.

Sarcomata have the same forms as benign tumors. They consist of round or spindle cells and are at times cystic and infiltrating. They invade the surrounding tissues, but make metastases to the axillary nodes late or not at all.

Many tumors of the breast become cystic, from dilatation of old or newly formed glands. Cystofibroma and cystadenoma are common. Papillary outgrowths which fill the glands and ducts constitute the variety of adenoma called a. phyllodes or a. intracanalicular proliferum. Sarcoma proliferum is a similar malignant tumor. The cysts usually contain clear and thin mucus.

Carcinoma of the mamma is distinguished from adenoma by the growth of the epithelia into the connective-tissue spaces and a consequent destructive character. The new cells are arranged in columns (carcinoma simplex) and tubular groups (adenocarcinoma). Medullary and scirrhous carcinomata are common. Carcinoma gelatinosum is sometimes found, and a cystic tumor of this type results from dilatation of the proliferating glands.

Carcinoma tubulosum affects the lacteal ducts, and contains nests of cells which resemble ducts. Carcinoma acinosum starts in the acini and resembles them microscopically. Epithelioma of the nipple occurs.

Cysticercus and echinococcus are the only animal parasites of importance in the breast.

B. DISEASES OF THE MALE GENITALS.

Malformation.

In the male the genital gland becomes the testis, the Wolffian duct furnishes the vas deferens and the tail of the epididymis, the upper section of the primitive kidney (Wolffian body) forms the head of the epididymis and from its lower part the paradidymis develops, while the prostate sinus (uterus masculinus) is formed from the Müllerian duct. The testis lies at first on the posterior abdominal wall, covered by the peritoneum. Complete descent of the testis transfers it to the bottom of the scrotum, and on its way it pushes before it a double serous sac, the processus vaginalis peritonei. The sac is closed off later by fibrous tissue.

Anorchia is complete absence of the testes, and with it the infantile type persists. *Microrchia* implies imperfect development of one or both organs, and *monorchia* the absence of one. Imperfect descent of the testis is called *cryptorchism*, and is either unilateral or bilateral. The testis may remain in the abdomen or in the canal. Cryptorchism is commoner with the newborn than the adult, for the testis often descends later. When the normally descended testis does not develop, the condition is called hypoplasia. In the retained organ primary tumors (sarcoma) may develop, and with cryptorchism inguinal hernia is common. The empty half of the scrotum atrophies.

Aberration or dystopia of the testis is a false position of the organ, as in the perineum or at the crural ring. Traumatic luxation may

also occur. Inversion may be caused by torsion of the cord, and places the epididymis in front and the testis behind.

When the vaginal process of the peritoneum does not close, inguinal or scrotal hernia and also congenital hydrocele are possible.

The vas deferens and seminal vesicle may be absent on one side, or the vas may be closed or end blindly without connection with the testicle, or open into the urethra.

The epididymis may share in anomalies of the testis or lack some of its parts, as the cauda.

The penis may present aplasia, hypoplasia, or defect of the corpora cavernosa, or be doubled and fissured. Hypospadias is present when the urethra opens on the under surface of the penis, epispadias when it opens on the upper surface. Congenital penile fistula is due to fusion of the vasa deferentia to an independent canal, opening above the urethra. Bony plates in the prepuce, atresia with congenital phimosis, hyperplasia and elephantiasis of this structure and the scrotum, are other malformations of the parts.

Diseases of the Testis, Epididymis, Tunica Vaginalis, and Spermatic Cord.

The testicle and epididymis are the glandular parts of the seminal apparatus, and their seminal canals empty first into the vas of the epididymis, and thus into the vas deferens. On section the testis presents bands of fibrous tissue which run from the inner side of the albuginea to the corpus Highmori, itself a mass of fibrous tissue, and between the septa lie the seminal canals and a little delicate connective tissue. In these fibrous structures run the vessels. The canals are made up of various kinds of epithelial cells on a tunica propria, and in certain of these cells spermatogenesis takes place.

The vas of the epididymis terminates blindly at one end as the vasa aberrantia. The vas deferens, with the pampiniform plexus of veins and the spermatic artery, runs to the seminal vesicle of the same side, and consists of fibrous tissue, smooth muscular fibres and a lining of cylindrical epithelium.

The tunica vaginalis of the testis has two layers, the inner fused with the tunica albuginea, the outer separated from it by a serous interval, the cavum vaginale.

Regressive Processes. Fatty changes and pigmentation may affect the stroma and the canals of the testis, and the walls of the

canals are apt to be hyaline and swollen. In the gross the organ is small, yellowish, or even brownish, and varies in consistence with excess of fat or of fibrous tissue.

Atrophy may be senile or presenile. The atrophy of old age resembles that which occurs with general cachexia, orchitis, the pressure of hydrocele, tumors, and herniæ. In other cases there is a neurotic lesion, as injury to the cerebellum, concussion of the brain, and paraplegia, or a circulatory disorder, as atheroma. Resection of the vas may lead to similar atrophy.

A commonly associated condition is azoospermia, in which the spermatozoa are diminished or lacking, or cannot be discharged owing to occlusion of some of the seminal channels.

Disorders of Circulation. Varicocele is a dilatation of the veins of the pampiniform plexus, the separate veins becoming thick and tortuous, which commonly develops in young subjects. Hemorrhage may follow injuries and inflammation.

Closure of the internal spermatic artery or the spermatic vein leads to atrophy of the testis, hemorrhagic infarction, necrosis, or gangrene. Anemia of the testis may be due to pressure from fluid in the serous sheath; venous congestion is due to compression of the spermatic veins, as by epididymitis with swelling of the part. In the epididymis similar lesions may occur.

Inflammation. These lesions include orchitis, epididymitis, and periorchitis.

Primary orchitis is usually traumatic. Secondary orchitis may follow extension of gonorrheal or other lesions from the urethra, bladder, or prostate, or hematogenic infection in cases of variola, ulcerative endocarditis, glanders, etc.

Acute orchitis causes redness and swelling of the testis and a serous exudate into the serous cavity (acute hydrocele). Microscopically the tissue is infiltrated with fluid and round cells, and small hemorrhages may be present. Purulent orchitis may become encapsuled, and its exudates may thicken and become atheromatous, or contain cholesterin and calcareous salts, or the tunica albuginea may be perforated and the granulations appear as a *fungus benignus*. Formation of scars or further progress to gangrene may follow.

Chronic orchitis produces great thickening of the fibrous septa, generally or in parts of the organ, often affecting the corpus of Highmore, and accompanied with atrophy and degeneration. On section the atrophic organ presents the thick line of fibrous tissue, with a

few yellow masses of parenchyma between, all enclosed in a thicker albuginea.

Epididymitis is usually caused by infection through the spermatic cord. Hyperemia, edema, and swelling, with desquamation of the epithelia and distention of the canals with pus and mucus, are the various features of the lesion. It is usually gonorrheal, and completely resolves, but abscesses and chronic inflammation are other possibilities, and the latter causes occlusion of the vas deferens. Cystic dilatation of the vas develops at times. The inflammation may pass from the epididymis to the testis and surrounding tissues.

Hydrocele is usually the result of inflammation of the serous covering of the testis. In simple cases the fluid is serous or cloudy with fibrin. It exudes after injuries, gonorrheal infection and with other lesions of the parts, and may fill the cavity to distention; as much as 3 litres has been observed. When blood is mixed with the exudate the lesion is known as hematocele, or this condition may develop apart from inflammation with the hemorrhagic diathesis and scurvy. When the fluid contains spermatozoa, from the free communication of a vas aberrans with the serous cavity, it is called spermatocele, which may arise also from cystic enlargement of the aberrant canals.

Purulent periorchitis is usually traumatic or follows suppuration in the testis or scrotum. The pus collects in the serous cavity, and may thicken and heal, with obliteration of the space.

Chronic periorchitis is often the sequel of acute inflammation, from injections of iodine, gonorrheal and other infections, or develops with chronic orchitis. Serous exudate may be present, or fibrinous and organizing material; the latter is called plastic periorchitis. The serous membrane becomes thickened, and the scars may be converted into cartilage or bony tissue, or adhere to each other. Floating bodies may also form, as in joints, from thickened fibrin. Hematocele occurs from the bleeding granulations.

Funiculitis, or inflammation of the vas deferens, may be traumatic or gonorrheal, and phlebitis of the adjacent veins and fibrous induration of the cord itself are common results. *Perispermatitis* is the name sometimes given to inflammation of the tissue about the cord. Congenital hydrocele of the processus vaginalis occurs when the canal does not close, and the exudate may be displaced into the abdomen. If the closure of the canal is partial, in the open spaces hydrocele of the cord may develop. *Hematoma funiculi* means a col-

lection of blood in such cavities. *Hydrocele herniosa* is an exudation of serum in the sac of an inguinal hernia.

Infectious Granulomata. Tuberculosis of the testis and epididymis may be secondary to any other form of genital lesion, or due to hematogenic infection, and it is possible that the organ may be the first point of deposit for bacilli which circulate in the blood; and it is suggestive that the tubercular lesion sometimes follows traumatism of the organs. The urethra is the port of entry for primary affections.

The extension of tuberculosis to the testis affects the epididymis first and then the testis, and here the corpus of Highmore is involved. The epithelia of the canals proliferate, giant cells develop and necrotic changes follow. Caseation of the walls occludes the lumina. Large masses of caseous appearance result from destruction of the canals and surrounding stroma. Fibrous hyperplasia and encapsulation may shut off the focus, but newer ones form, and the process thus resembles caseous bronchitis and peribronchitis. Many small nodules or a few large ones are observed, and the organ is decidedly enlarged.

In the hematogenous lesions interstitial tubercles are found.

The tunica presents tubercles or caseous masses, serous exudates, and adhesions. When the tuberculous granulations rupture the tunica vaginalis and the scrotum, fistulae and *fungus malignus testis* result. The lesion occurs fairly often and at any time of life, and may be bilateral but of different stages on the two sides.

Tuberculosis of the vas deferens may be associated with such lesions, and causes caseation in the walls and plugging of the lumen.

Syphilis. This disease usually affects the testicle first and the epididymis later. Indurating orchitis of the usual type may be the form of the lesion. Congenital cases are bilateral. The corpus of Highmore and the fibrous septa become infiltrated with mast cells, among others, and atrophy with induration follows. Small or large caseous gummata may be found in the fibrous tissue. They are surrounded at times by a fibrous capsule from which radiate fibrous bands. Rupture of the coverings of the testis with fungous granulations may also be observed. The organ in general is small and scarred and very dense. The coats are thickened, adherent or also caseous, and serous or adhesive periorchitis is apt to accompany the process; the disease develops late with constitutional syphilis. Gumma and fibrosis of the epididymis and cord are frequent.

Leprous and leukemic nodules may be found in the testis.

Hypertrophy may be compensatory in the young for the loss of the accompanying organ. Regeneration of the glandular epithelium may occur.

Tumors are usually mixed in character. Fibroma, chondroma, myxoma, and sometimes rhabdomyoma and osteoma are observed. Melanosarcoma and round-celled forms, endothelioma and mixed tumors, and cystosarcoma from dilatation of seminal canals have also been found. These sarcomatous tumors are malignant and make metastases. Carcinoma is frequently medullary or combined with adenoma. Chondrocarcinoma may develop.

Papillary and proliferating cystic tumors, like those of the breast, sometimes are found, and combinations, as cystochondroma, consisting of tumors with cavities lined with epithelium and containing seromucous material or masses like those in cholesteatoma. Dermoid cysts and teratomata are less frequent than in the ovary. Simple cysts of the testis or the epididymis may be due to retention or spermatocele from vasa aberrantia.

Injuries of these organs include punctured and bullet wounds, and crushing, and result in hemorrhage, inflammation, and formation of scars. With division of the scrotum the granulations may be termed fungus benignus testis.

Diseases of the Prostate.

This gland consists of a few glandules clothed with cylindrical epithelium embedded in muscular tissue.

Prostatitis in most cases follows extension of a neighboring inflammation, especially from the urethra with gonorrhea, but it arises also with injury and from thrombophlebitis of the prostatic veins. Temporary hyperemia, edematous swelling which may compress the urethra, or purulent infiltration, may result. The abscess, if small, may be encapsuled, but it frequently spreads to the vicinity and perforates into the rectum or urethra. General infection may be due to purulent thrombi in the prostatic plexus of veins.

Tuberculosis of any part of the genital system, but most often of the epididymis, is associated with miliary tubercles or large caseous foci in the prostate, and perforation into various hollow organs may complicate the lesion.

Hypertrophy is very common in old age, from increase of the glandular tissue or from fibromyomatous hyperplasia of the stroma. The gland is then hard, and on section the bands of fibrous tissue may be

seen. Adenomatous growth of the glandular canals, with budding from the single tubes, makes the gland large and soft, of a uniform grayish yellow on section, and light pressure squeezes out a milky fluid due to fatty degeneration of the epithelium. Small cysts of the tubules may also be noted. Large cysts develop from rudiments of Müller's ducts. The middle lobe of the gland is most often hypertrophied, and as this compresses the urethra and the vesical neck it causes difficulty in expulsion of the urine, and leads to hypertrophy of the bladder, retention of urine, and cystitis.

Atrophy, fatty degeneration, hyaline and fatty changes in the muscular fibres, hyaline thickening of the walls of the glands, and pigmentation with brownish granules are the most common regressive lesions. They accompany inflammations or follow them, and often result from castration. Upon this fact is based the operative treatment of prostatic hypertrophy by castration.

Corpora amylacea and other prostatic concretions are very common, and are probably explained as hyalin deposited in dead cells from the secretion of the gland. Sometimes they give the amyloid reaction, others contain lime salts and brown pigment. The larger specimens are concentrically marked, and may project into the urethra.

Tumors of the prostate include adenoma, lymphosarcoma, and adenosarcoma, and primary or secondary carcinoma, the latter from the rectum or by transformation of an adenoma. Carcinoma causes destructive ulceration of the distorted urethra and adjacent tissues, and early metastases to bones and elsewhere.

In Cowper's glands, urethral and prostatic inflammations commonly cause similar lesions, and these may go on to the production of abscesses. The gland may swell to the size of a bean. Fistulæ, occlusion of the ducts, cysts, and complete destruction are the various terminations of these lesions.

Diseases of the Seminal Vesicles and the Ejaculatory Ducts.

Catarrhal and purulent inflammation may pass from the vas deferens to the vesicles, and dilatation, abscesses, perforation, or in chronic cases, great thickening of the walls may follow. Concretions with enclosed spermatozoa sometimes form in the cavity.

In tuberculosis of the genito-urinary organs the vesicles are frequently much involved, and their mucous lining is caseous and their cavities filled with caseous material at times. Isolated tubercles result probably from the access of single bacilli from the testes. The ejacu-

latory ducts are usually involved in such lesions and may be occluded. Retention cysts of the vesicles follow.

Carcinoma as a primary tumor has very rarely been observed in the seminal vesicles.

Diseases of the Penis and the Scrotum.

Injuries of the penis include crushing of the organ, so-called fracture, when the investing fibrous sheath is ruptured, penetrating wounds from the urethra with consequent infiltration of urine and necrosis of the tissues, and luxation to the inguinal region. Severe hemorrhage from the corpora cavernosa may accompany such traumatism, and after healing the fibrous scars may distort the organ.

Balanitis is an inflammation of the glans, and is usually associated with balanoposthitis, a similar inflammation of the prepuce. Gonorrhea, chancre, and chancroid, decomposition of smegma, and mechanical injuries may be the causes of the inflammation. When the prepuce is swollen the condition is termed *phimosis*, and when the prepuce is also irreducibly retracted, *paraphimosis*. The latter condition arises without inflammation when the opening of the prepuce is too small and it is forcibly drawn back, causing venous stasis and swelling of the glans. If not relieved, gangrene of the glans may result. In total phimosis the urine may be retained and dilate the part to the size of the fist. Small collections of pus are found with balanitis. The two layers of the cavity of the prepuce often become adherent in places.

Inflammation of the corpora cavernosa follows injury, extension of inflammation, and hematogenic infection. It may be diffusely purulent, or single abscesses form which empty through the urethra and leave dense scars.

Chancres are commonest about the glans, and, if seated at the frenum, either a tubercular or a syphilitic ulcer may break through into the urethra. Syphilitic scars in the scrotum lessen the movability of the skin upon parts beneath. Fungous granulations have been mentioned. Broad and acuminate condylomata have a less intimate connection with subcutaneous tissues than the carcinomata.

Papillary epithelioma is apt to begin in the glans or the prepuce, and often with phimosis. It may be confused with papillary condyloma. Lipoma, steatoma, cutaneous horns, and telangiectases are other lesions observed in these parts. Elephantiasis of the prepuce occurs. In the scrotum elephantiasis frequently develops in tropical

countries and converts it into a thickened sac as large as the head, into which the penis is retracted, or the lesion may affect the penis also. Epithelioma in the form of several ulcerating nodules occurs in chimney-sweepers and workers in paraffin. Atheroma, dermoid cysts, and teratoma of the scrotum are rather frequent.

Preputial stones result from collection and inspissation of the local secretion, with epithelial desquamation and precipitated urinary salts.

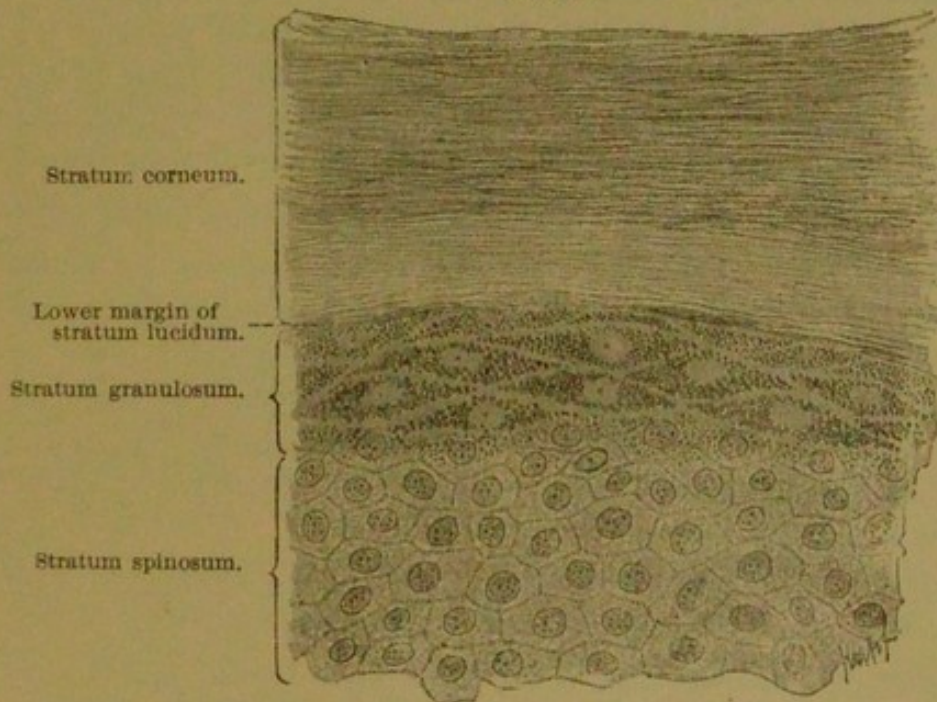
CHAPTER XV.

DISEASES OF THE SKIN.

THE skin consists of three layers, as follows :

1. Epidermis, presenting from without inward, the stratum corneum or horny layer, with the stratum lucidum as its lower portion, then a layer of polygonal cells with granular protoplasm, the stratum granulosum, beneath this a layer with prickles, the stratum spinosum, and below this a layer of cylindrical palisade cells, the basal layer, or stratum cylindricum. The last three together form the rete Malpighi.

FIG. 349.



Transverse section through the human epidermis ; the deeper layer of the Malpighian stratum is not shown. $\times 720$. (After BÖHM-DAVIDOFF.)

2. The cutis presents the cutis vasculosa, beneath the epidermis, which sends papillary bodies into the epidermis and between these presents epithelial processes. The cutis vasculosa consists of collagenous fibres in a meshwork and elastic fibres mingled with these, and is richly provided with vessels and nerves. The deeper cutis propria has few vessels and consists of bundles of connective tissue

arranged in large rhomboid spaces, whose greatest diameters lie parallel with the planes of cutaneous tension. These bundles are covered with a network of elastic fibres.

3. The subcutis is made up of collagen bundles and elastic fibres, and contains large quantities of fat.

The general surface is marked by large folds about the joints and fine subdivisions which are especially distinct about the hands.

Functionally the epidermis and the cutis vasculosa are closely related, both in normal and in pathological conditions, and as the cutis propria presents fewer lesions it is considered as the cutaneous stroma, and the former structures are grouped as the parenchyma.

Alterations in the Cutaneous Pigmentation.

The normal pigment of the skin is melanin, free from iron, and lies in granules in the lowest layer of the epidermis, especially in the basal layer. It is probably derived from the specific activity of the cells here and not directly from the blood. Since the cells normally proceed outward to the surface and become free from pigment we assume that it is converted into a colorless substance. Some of the cells of the connective tissue contain pigment also. The normal pigment is increased in the following conditions:

In pigmented *nævi* the pigment lies in large so-called nevus cells, and outside of these in the connective tissue and the epithelia. *Nævus pigmentosus* may be of small or broad extent and flat, or warty (*nævi verrucosæ*). Similar small collections are known as *ephelides* or freckles, which develop under the influence of sunlight on the uncovered skin and disappear during the winter. They are most marked in blondes about the sixth to eighth year, and are usually lost in old age.

Lentigo is the name of nevus-like spots, of the size of a pin's head or a lentil, which are not congenital but acquired in later life.

Other cases of pigmentation occur with physiological and pathological conditions, and especially with functional activities of the genital system. *Chloasma uterinum* occurs in pregnant women and those suffering from disease of the genitals, and has a physiological type in the common darkening of the areolæ and the linea alba in pregnancy. *Chloasma cachecticorum* accompanies exhausting diseases, as phthisis, and similar pigmentation is observed with congenital syphilis.

Thermic and mechanical causes lead to other cases of pigmentation, and are known as *chloasma caloricum*, *toxicum* (cantharides, arsenic),

or *traumaticum*, and in the course of various diseases of the skin similar pigmentation is very frequently observed. Part of this is due to hemorrhage and transformation of the blood pigments, but more frequently and persistently to specific epithelial activity.

General increase of the physiological pigment is a symptom of Addison's disease.

After hemorrhage into the skin both hemosiderin and hematoidin are found in granules and crystals. (For icterus, see p. 75.)

Argyria is an example of pigmentation from ingested matter and occurs with long use of nitrate of silver. It consists of precipitates of silver of grayish-brown color. Tattooing also colors the surface.

Leucoderma is due to decrease of the cutaneous pigment, and in a congenital form, known as albinism, affects the skin, eyes, hair, or only certain parts, as groups of hairs or small areas of skin.

Vitiligo, or *leucopathia acquisita*, causes circumscribed spots of decoloration, and the hair may lose its color in these areas, and as the condition spreads the entire surface may become lighter. Certain sections may become darker.

Leucoderma syphilitica is commoner among women than men, and especially about the neck. It is probably due to resorption of pigment during the specific exanthem. A similar change accompanies psoriasis.

Disorders of Circulation.

Congestion of the skin is called *erythema*, in small spots it is termed *roseola*. During life slight pressure causes these congestions to disappear, but after death they are seldom to be recognized.

Erythema may be reflex, due to heat, wounds, and poisons, and accompanies many exanthematous diseases. In these latter cases the effect is due to local action of the micro-organism and to reflex from the action of its toxins. Erythema leads into inflammation very often.

Passive congestion is more easily observed on the cadaver, most clearly in the lips and extremities. The skin is livid and its vessels may be seen, and after a time the diffusion of the blood pigments produces spots of cinnabar red upon a livid background.

Atonic or asthenic hyperemia of the skin is due to insufficient supply of arterial blood and inability of the capillaries, accustomed to a larger stream, to accommodate themselves to the smaller. It occurs in the palm, the nails, lips, nose, and ears, which normally are full of blood, and hence they become cyanotic with lessening cardiac

activity, from failure of the blood to flow out of the capillaries. Similar hyperemia comes under observation with central nervous lesions, frost-bite, and bed-sores, in which anemia first results from pressure and then the vessels become atonic.

General anemia is distinct in the cadaver after death from hemorrhage or anemic diseases. Local anemia may be due to local pressure, or vasomotor contraction from cold. Probably ergot causes a similar vasoconstrictor effect from the central nervous organs.

Edema of the subcutaneous tissues is called *anasarca* or *hyposarca*, and causes the skin to swell. If of doughy consistence it retains the pressure of the finger for a time. The fluid loosens the bundles of fibrous tissue and may be pushed from place to place. This condition is common with stasis from local or general causes, and is most often observed with dyscrasia in certain regions of the body. Edema of the papillary layer is always local and causes a bulging of the surface, which gradually subsides into the surrounding skin, and is called an edematous papule. The type is seen in *urticaria*. Both of these forms of cutaneous edema may occur with local causes, as bites of insects, irritation by nettles, and by certain drugs and foods. Many persons are particularly disposed to such *urticaria*. Nervous influences produce the lesion at times. *Urticaria* is distinguished from inflammation by the rapid disappearance of the swelling, but it may also be the initial stage of an inflammation. Active edema may occur in the same places where the passive form is usually most marked, as in the eyelids and the scrotum. *Edema fugax* is usually due to nervous influences.

Chronic edema of the skin may result in hyperplasia of its elements, as elephantiasis, or in myxedematous changes.

Hemorrhages occur in the skin and from it in many varied conditions, and have names according to the form of the bleeding.

Petechiæ are small spots, sharply outlined; *vibices* are longer stripes; *ecchymoses* are large and flat, with irregular boundaries; and larger collections with clearer outlines are *suggillations*.

Cutaneous hemorrhage may be traumatic or accompany infectious diseases, scurvy, and pernicious anemia. In ulcerative endocarditis small hemorrhagic infarctions may occur. Other non-traumatic hemorrhages are called purpura, and divided as purpura hæmorrhagica (morbus maculosus of Werlhoff), rheumatica, and senilis. Some cases of purpura are due to infection, chemical action, alterations of the blood, or nervous influences.

Inflammation.

Cutaneous inflammations may affect the parenchyma or the deeper layers.

(a) **Inflammation of the Parenchyma.** The slightest grades of cutaneous inflammation are associated with active hyperemia and slight exudation, and are superficial and temporary. Among such are many infectious and toxic erythemas, as in scarlet fever, measles, etc., and these are seldom noticeable in the cadaver. The epidermis may desquamate after the lesion subsides.

More severe forms with swelling of the skin may be diffuse or localized. In the latter case the inflammatory papule forms, a cone-shaped elevation of the skin from edema of the papilla and epidermis; there may be larger nodules and wheals. The exudation of serum converts the papule to a vesicle. Severe irritation may be followed by copious serous exudation, and a large section of the skin (epidermis) may be raised from its bed. The fluid collects between the papillæ and the epidermis. In other cases the fluid spreads through the interepithelial spaces and distends them, or softens and breaks down the cells (colliquative necrosis). The contents of the vesicles is clear serum with few leucocytes, and the cover either dries or ruptures, and healing follows. If the inflammation persists the secretion may escape externally and dry to crusts and scales.

When the contents of the vesicle become purulent it is called a pustule, and this may furnish a moist discharge or crusts of yellow or brownish color, without the subsequent formation of scars.

Mechanical, thermic, and toxic causes produce such lesions, and trophoneurotic influence is at times important, as in herpes with lesions of the spinal ganglia. In prurigo and herpes of the lip and genitals the nerves play a large part. Reflex edema has been mentioned. The various forms of exanthemata follow:

Measles. Round, flat, or little elevated spots with central nodule, never uniformly confluent; catarrh of the air passages and catarrhal pneumonia common; scaling afterward, branny.

Scarlatina. Flat or slightly elevated, first on neck, red spots which quickly spread and fuse, of uniform color; catarrh of the air passages, pharyngeal diphtheria, pneumonia, nephritis, etc., common; desquamation lamellated.

Erythema Exudativum Multiforme. Congestion and edema of skin (papillæ), which latter remains after the hyperemia; begins with small

papules which grow to the size of a penny and become depressed in the middle; blebs and other eruptions may occur; probably infectious.

Eczema. Begins with *stadium papulosum*, followed by *stadium vesiculosum*, pustules may form later. Papules and pustules may break and form excoriations which excrete thin fluid, *stadium madidans*; drying with crusts makes the *stadium crustosum*; pus beneath the crusts, the *stadium impetiginosum*; chronic desquamation, the *stadium squamosum*. A single case seldom goes through all these stages. Fissures of the skin may be left called rhagades.

Miliaria. Small vesicles with clear, watery contents, remain but a few days; with typhoid, puerperal fever, articular rheumatism; chiefly on the body.

Herpes. Groups of vesicles with clear contents which grows turbid and dry, with small desquamating cells. Destruction of the tips of the papillæ leaves small scars. *Herpes facialis*, with various fevers, about the lips and alæ of the nose. *Herpes genitalis*, on glans, prepuce, or labia. *Herpes zoster*, vesicles along the course of a nerve, idiopathic or with infection and intoxication; with blood in vesicles called *herpes zoster hæmorrhagicus*; gangrenous forms occur.

Variola. Contagious general disease with two weeks' incubation, fever, erythema, and hemorrhages in skin, and characteristic eruption in three days. Papule in hemorrhagic area, becomes vesicle, then pustule, may be hemorrhagic, pustule umbilicated; vicinity markedly swollen and red; pustules dry or break and form crusts; often fatal. Microscopically papillæ and epidermis swollen and coagulation necrosis in the latter, causing the umbilication; inflammation of papillæ and cutis may be severe and leave deep scars after healing.

Varicella. Pustules like those of variola, occurs as mildest type of variola or independently.

Impetigo. Lenticular pustules, confluent; if very large called ecthyma; both kinds dry to thick crusts.

Pemphigus Vulgaris. Pustules of size of hazelnut or palm of hand, contents may be serous at first; dry to dark-brown crusts, and heal without scars. *Pemphigus neonatorum*, small rapidly growing pustules, irregularly located, usually without constitutional symptoms. *Pemphigus syphiliticus*, in newborn as sign of hereditary lues; symmetrical on hand (palm) and sole. *Pemphigus foliaceus*, chronic with wide extent of surface involved, large sections of corium laid bare or covered by crusts; occurs with marasmus, and may be fatal. *Pemphigus vegetans*, serpiginous progress and fatal.

Chronic parenchymatous inflammations are characterized by the lesions discussed, and clinically by a tendency to frequent relapses, and hence there are cellular infiltration along the vessels, swelling, and enlargement of the entire papilla, and thickening of the epidermis. In this way large sections of the surface become elevated and papillary, lose the inflammatory congestion, and suffer marked desquamation of the outer layers.

Such a desquamation has as its foundation an imperfect cornification of the epidermis and loosening of the connections of cell with cell. In some cases the scales are small and branny, in others large plates of superficial cells separate. In many chronic cases, as in psoriasis and eczema, the desquamation is called essential, as it is the distinguishing feature of the disease.

Complete resolution of chronic inflammation is possible. In some cases, however, the thickened papillary layer forms a kind of granulation tissue, with spindle and epithelioid cells, and enlarged papillæ, and from this cicatrices result. Examples of this kind are:

Chronic Eczema. Persistent relapses or proceeding from acute form, with marked cellular infiltration of papillæ, chronic secretion, crusts, and scales; causes hyperplasia of papillæ and thickening of cutis and subcutis, at times like elephantiasis. *Eczema seborrhæicum*, small vesicles, red papules and scaling, like psoriasis.

Psoriasis. The type of scaly anomalous cornification; nodular and larger eruption on whose surface there is chronic formation of white, dry scales, which make large shield-like plates. According to form and size, punctate, guttate, nummular, and diffuse forms; common location about knee, elbow, and scrotum.

Lichen. Nodules which remain as such and suffer no further change, papillæ enlarged, often by infiltration of large cells; cicatricial contraction later. *Lichen acuminatus*, small, scaly nodules; *L. ruber planus*, at first red nodules with central depression, then white with epidermis marked in network, without scaling; *L. scrofulosus*, flat with small scales on summit, corresponding to openings of follicles, benign, occurs in scrofulous subjects.

Lupus Erythematodes. Papillæ usually infiltrated with large and giant cells, with marked atrophy later; in fresh stages red and slightly elevated; cause unknown.

Prurigo. Common in children during second year, incurable in advanced stages, and persists through life. Eruption of blains and papules, with itching; pigmentation after scratching; infiltration and

thickening later, over whole skin, and scaliness; swelling of lymph nodes called prurigo bubo; localized especially on extensor surfaces of legs, sacrum, and buttocks, less often on abdomen and arms; face, elbows, and knees free.

(b) **Inflammation of Cutis and Subcutis.** The cutis contains only the vessels going to the papillæ, while the subcutis is very vascular, hence their inflammations differ.

Erysipelas is localized especially in the cutis and caused by infection of wounds, or through the blood, by streptococci. It is frequent in the skin of the face. There is marked hyperemia with infiltration of leucocytes in the lymph spaces between the bundles of connective tissue, but, as a rule, suppuration is not present. The lesion disappears rapidly, though it may migrate over large areas. Vesicles and pustules and crusts may form, and with large blisters the lesion is called *erysipelas bullosum*, or, if accompanied by necrosis, *erysipelas gangrenosum*.

Phlegmon is a rapid melting of the skin by suppurative inflammation in the subcutaneous tissue, and it may spread laterally and also in the depth to the muscles and the periosteum. A special form on the finger is called *panaritium*.

Gaseous phlegmon is due to a malignant infection of wounds by dirt and dust of various kinds, or rather by the organisms contained in these. Collections of gas in the tissue form early, which crepitate on palpation, the epidermis is elevated by fluid, and the rest of the tissue infiltrated by red fluid, the muscles necrotic. Suppuration may be associated with the infection. The lesion spreads rapidly and causes general infection through the lymphatics, with parenchymatous degeneration of the organs, and death.

Malignant pustule is the primary lesion of anthrax in the skin. At first there is a rapidly formed nodule on a reddish area, and a pustule follows, which becomes a slough. The adjacent tissue swells for a distance about the lesion, all the layers being involved, and in the fluids of the part there are numerous anthrax bacilli (carbuncle). With the initial lesion there may be marked and general edema.

Infectious Granulomata. Tuberculosis of the skin includes lupus, scrofuloderma, and true cutaneous tuberculosis.

Lupus is the most frequent form of tuberculosis of the surface. It appears as flat elevated nodules of the size of a pea, developing from the cutis or the subcutis as a cellular granulation tissue, in which epithelioid and giant cells may be found. Bacilli are scarce. The

lesion may be healed and leave scars and depressions. In many cases the lesion forms masses of cicatricial tissue with nodules in it, called sclerous or verrucous lupus. In other cases there is a diffuse infiltration of the skin, of a round or irregular outline. With marked proliferation of the cutaneous and subcutaneous tissues the form known as *lupus hypertrophicus* results, and, with decided scaling from the surface, *lupus exfoliatus*. Softening of the nodules may produce ulcers with thickened edges which show but little tendency to heal, but rather extend through the skin and to the deeper tissues; it is called *lupus exulcerans*. If the ulcers heal the scars are large and distort the parts.

FIG. 350.



Lupus hypertrophicus; atypical growth of epithelium. *e*. Superficial epithelium. *c*. Corium.
e', *e'*. Masses of epithelial tissue growing into the deeper parts.

Lupus affects the face, especially about the nose and cheeks, and the end of the nose may be completely destroyed by the lesion. The mucous membranes of the nose and lips, pharynx and larynx, eyelids and cornea, and other regions are unusual places for the lesion. In mucous membranes lupus makes diffuse infiltrations and ulcerations with large deforming scars.

Scrofuloderma occurs as circumscribed nodules in the skin which increase to large prominent tumors of tuberculous granulation tissue. They reach the surface, and cause fistulæ by breaking through, and if

the process continues, large defects may result. The secretion is thin and mixed with crusts, and the process is very sluggish. Healing with scars may be observed. The disease affects children, often with other similar lesions, and attacks the skin of the neck, the forearm, and leg. It usually proceeds from the lymph nodes to the skin.

Tuberculosis vera cutis is very unusual. It begins with the eruption of tubercles in the skin from hematogenic infection, and rapid caseation produces small ulcers, with fresh tubercles on their edges. In the discharge numerous bacilli may be found.

Tuberculous infection of wounds occurs on the hands of those who handle tuberculous material, as firm bluish-red nodules from the corium, with proliferation of the adjoining cells and horny crusts on the summit. Inoculation of the skin may occur during ritual circumcision from infection by sputa of the officiating person. The so-called post-mortem tubercles are found on the extensor aspect of the fingers and hands, and contain tubercle bacilli at times and pyogenic bacteria in other cases.

Syphilis of the skin has several forms :

1. The initial lesion, the *chancre*, is a pronounced infiltration of the tissues with small cells, with proliferation of the connective-tissue elements and of the intima of the vessels. The newly formed cells make a thick mass in the spaces of the tissue, and among the numerous small cells are many large epithelioid elements. This proliferation is most marked about the vessels, and their walls are thickened. The gross lesion is a firm papule on which the epidermis is at first intact. Further changes may be absent, and the lesion may heal without a scar, or the epidermis may be lost, and an erosion or a deeper ulcer occurs with consequent scarring.

2. In secondary syphilis inflammations in the parenchymatous layer develop which heal without scars. Broad condyloma, mucous patches, erythema, papules, pustules, and scaling forms occur, with acne, pemphigus, ecthyma, and rupia.

3. In the tertiary stage gummata and gummous inflammation may develop which involve the deeper layers and heal with marked cicatrices. Gumma of the skin may be as large as the fist, round and firm, seated in the cutis or the subcutis. The papillæ are involved later, and the epidermis may scale. These nodules may be absorbed and the surface may sink in over their former site, or there may be pustular and ulcerative lesions of the surface. Large nodules may soften to a viscous mass and perforate externally, and the resulting

large ulcers may progress as a serpiginous destruction. The scars which follow are large and very irregular and of a white color. Many of the cutaneous forms of syphilis resemble the lesions of tuberculosis, and hence the name *lupus syphiliticus* has been employed for some of them. Hereditary syphilis causes syphilitic pemphigus of the palms and soles.

Leprosy produces red and temporary spots of the skin or prominent nodules of red-brown color (*lepra tuberosa*) which may make large confluent ulcers when they break (*elephantiasis Græcorum*). With trophoneurotic influences, lepra nodules result in widespread and deep ulceration, which may cause the loss of fingers and toes (*lepra mutilans*). The nodules consist of cellular and fibrous granulations with giant cells, and the bacilli are found in large epithelioid cells which are probably derived from endothelia.

Glanders usually arises from infection of a wound and causes inflammation of the skin, with rapid formation of ulcers which spread by necrosis of their edges. Erysipelatous and phlegmonous forms occur, and pustules are common. When the infection of the skin is hematogenic a red spot appears on which a pustule like that of variola or pemphigus forms, and after rupture this pours out a thick, red, and mucoid discharge. In other cases there are blisters and ulcers. The lesion may involve the entire surface. Acute cases last two to four weeks, the chronic two to six months.

Rhinoscleroma is a nodular, and later diffuse, thickening of the skin and mucosa of the nose and lip, which is due to a slow hyperplasia of cellular connective tissue. The bacilli are found in large, light cells, or spheres without nuclei and of hyaline appearance.

Mycosis fungoides is a diffuse neoplastic formation which usually has an early stage of chronic inflammation like an eczema, with frequent relapses. Then there appear many scattered nodules in the skin, of flat or half-spherical form or mushroom-shaped, which grow to the size of a hand and become confluent. Their surface is dry, red, or moist and covered with crusts. Marasmus and death are the constant termination of the case. The neoplasm consists of round cells, spindle cells, and plasma cells. Metastases to internal organs do not occur. The cause is unknown.

In leukemia and pseudoleukemia many growths like sarcoma may develop.

Dermatomycoses and Dermatozoonoses.

A *dermatomycosis* is a lesion of the skin caused by a fungus, and one of the most common of these is favus, due to the *achorion Schoenleinii*. It occurs in round crusts of the size of a lentil, yellow in color, depressed in the centre, and pierced by a hair. These crusts, called *scutula*, consist for the most part of hyphæ and spores of the fungus. The organism grows in the epidermis and invades the hair, its sheath, and the sebaceous glands.

Herpes tonsurans is caused by the *trichophyton tonsurans*, and appears at first as vesicles and then as scales, characterized by its ring form, and pale centre. In parts with hair the fungus invades the follicle and the shaft of each hair and causes it to fall out. In other regions the fungus lies in the deeper layers of the rete. A form of the disease occurring on the bearded parts is called *sycosis parasitica*.

Pityriasis versicolor makes brownish spots with scaling of the epidermis, especially on the breast and back, and is due to the microsporon furfur. The fungus is found in the epidermis and the scales.

Of the *dermatozoonoses*, scabies and molluscum contagiosum are the most important.

Oidiomycosis is a rather common blastomycetic inflammation of the skin, clinically resembling tuberculosis (p. 229 ff).

Regeneration. Cicatrices. Atrophy.

Lesions which affect the epidermis heal as already given on p. 92.

Defects in the cutis heal by the proliferation of new connective tissue, but this tissue does not act like normal cutis. Sebaceous and sweat glands are lacking, and the bundles do not assume the rhomboid arrangement which is normal, but take the direction of greatest tension upon the scar. Elastic fibres are lacking, and hence the scar is firmer and denser and less yielding than normal skin. Its surface is smooth because of the absence of papillæ. When only the cutis vasculosa is affected the healing is more complete, and the scars are more like the normal tissue.

Atrophy of the skin implies thinning of the single layers which compose it, and may be due to local pressure, as from a tumor, or certain nervous conditions. The lines on the skin are lost, the papillæ are flattened. Such changes are found in the abdominal surface after pregnancy from stretching of the tissues and rupture of

certain fibres of the connective tissue, and arrangement of the bundles in the course of greatest strain. Any great distention of the abdomen may cause the same effects.

Senile atrophy causes general thinning of the epidermis and cutis, and the fibrous bundles of the cutis, being less extensive, allow the surrounding elastic fibres to lie closer together. Both varieties of fibres suffer hyaline changes, and the elastic fibres may degenerate and disappear. Hence the skin loses its elasticity and becomes relaxed, so that large wrinkles form instead of the normal folds. In marasmus and cachexia similar changes may occur.

Cicatrices with depression of the surface cause cicatricial atrophy, which differs from the preceding only in being connected with reparative processes. After severe burns and with ulcerations and infectious granulomata there may be simple atrophy, or scars and cicatricial atrophy.

Scleroderma is the name given to a peculiar hardening of the skin in various regions from unknown causes. The surface feels as hard as a board, and at last becomes atrophied. Microscopically there is a formation of cicatricial tissue with fusion of the fibrillæ, loss of elastic fibres, and some cellular proliferation. Neurotic atrophy may present the same picture.

Sclerema neonatorum is explained as rigidity of the skin and subcutaneous fat, with collapse. The skin is thickened, hard, and tense.

Hyperplasia and Tumors of the Epidermis.

Hyperkeratosis is the name given to hyperplasia of the corneous layer. With such a lesion the underlying tissues may also be hyperplastic or atrophic from the pressure, so that the corneous layer lies almost directly on the cutis propria. The cause is a sclerotic change in the cutis vasculosa.

Callosities are local thickenings of the corneous layer, especially of the palm and sole, from constant pressure.

Clavus, corn, is also the effect of local pressure with circumscribed hypertrophy of the corneous layer and atrophy of the papillæ. The thickening may involve the corium also, and redness and edema, even suppuration in the adjacent tissues, may coexist.

Ichthyosis is a diffuse hyperkeratosis, in which the skin is covered with horny plates and lumps. With hypertrophy of the papillæ at the same time the variety called *i. hystrix* is formed.

Cutaneous horns are a special form of localized hyperplasia of the

corneous layer, and at times the long papillæ reach for a distance into the horn. This form occurs about scars, tumors, etc.

Fibro-epithelial tumors. (See p. 152.)

Nevi may be congenital soft warts and small tumors, pigmented or not, with or without hair, flat or projecting. They vary in size from a pin's head to a bean, or, as giant forms, may be much larger. They may be lobulated, and the single papillæ may be recognized. The peculiar cells called nevus cells are mostly endothelia, or, according to some, cells snared off from the epidermis. Nests of these cells are found also in freckles, xanthelasma, lentigo, etc.

Verruca vulgaris, the ordinary wart, consists of long, slender papillæ, and a larger proportion of epithelial hyperplasia. The corneous layer is very thick and reaches in between the papillæ. Flat warts are common on the back of the hand or foot; other kinds are senile and seborrheic, the latter containing corneous, pearly, and fatty masses.

Condyloma acuminatum develops from the irritation of various discharges, especially with gonorrhea, about the corona glandis and the labia, the vaginal and anal openings. They develop rapidly and consist of branching papillæ with hyperplastic, corneous epithelia.

Molluscum contagiosum is a multiple tumor of the skin which may affect the face, the forearm, and the penis, especially, and the single nodules are about the size of a pea. The color of the growth is like that of the skin; they are soft, and on pressure exude a white, tallow-like material. On section they have a lobulated structure with septa, and the lobules contain cells like those of the rete Malpighi of cylindrical form. In the centre of the nest, at first enclosed in cells and then free, there are "molluscum bodies," of round or oval form without apparent finer structure, looking like swollen grains of starch. Probably these are gregarinæ, and their resemblance to the epithelioma contagiosum of chickens and doves renders the presence of a parasite probable.

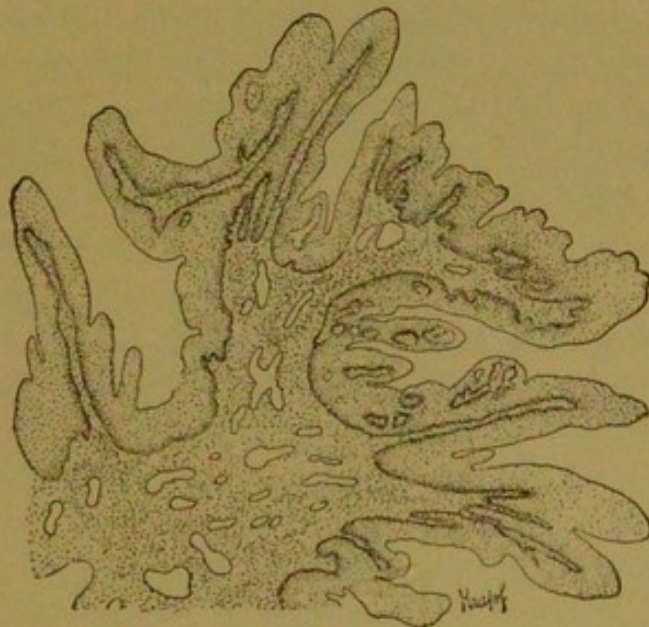
Hyperplasia and Tumors of the Cutis.

Elephantiasis is a hyperplasia of the cutis and subcutis which leads to diffuse thickening and prominence of the parts involved, and irregular pendulous masses on the surface or smaller warty growths. It is most common in the lower limbs and the external genitals. Various causes produce it, among them erysipelas and other inflammations.

Elephantiasis arabum, myxedema, and the skin lesions of cachexia strumipriva are characterized by edema of the skin, and may result in elephantiasis, and this condition may be due also to the *filaria sanguinis*.

Of the tumors of connective tissue nodular fibroma is common. In the nerves of the skin neuroma containing newly formed nerves, and neurofibroma from the sheaths of the nerves may develop. They are often multiple, and extend over large sections of the body. In size they vary from that of a small seed to that of a fist, and since their consistence is soft they have been called fibroma molluscum. In large tangled masses of branching cylindrical formation they are called plexiform neuromata.

FIG. 351.



Acuminate condyloma.

Keloid is a flat tumor, with branches to the vicinity, composed of dense, sclerotic, connective tissue without elastic fibres, and developing below the unchanged papillary layer. Cicatricial keloid develops in scars, and differs from the former by including the papillary layer. The epidermis is smooth over the tumor.

Xanthelasma occurs as small, yellowish masses, flat and slightly elevated, in the eyelids and other parts of the face. They are usually of the size of a lentil or the finger nail, but may form larger tumors. In the superficial layers of the cutis there is a cellular tissue containing much fat, and to this the sulphur or straw-yellow color is due.

Lipoma is common in the subcutaneous tissue of the buttocks, back, and thigh. **Lipoma polyposum** projects from the surface. Myofibroma, myxoma, sarcoma and myxosarcoma, and melanotic sarcoma are also rather common in the skin. Lymphangioma, cavernous angioma, and dermoid tumors occur. Telangiectasis develops with acne rosacea and lupus, or spontaneously in old age. Lymphangioma is usually congenital. The so-called lymphangioma tuberosum multiplex is an endothelioma.

Carcinoma of the skin is commonest where cutaneous and mucous surfaces come in contact. It may develop from warts, scars, or lupus, or the site of inflammation and chronic irritation, as about ulcers of the leg, syphilitic affections of the tongue, and as chimney-sweeper's cancer.

Three varieties of flat-celled carcinoma are recognized. **Ulcus rodens** usually begins as a small nodule which spreads laterally and infiltrates the tissues, and then slowly breaks down and forms a sluggish ulcer, in which partial healing may occur. Nodular infiltrating cancer may make large tumors and equally large ulcers when they break down. Papillary forms occur, especially about the external genital organs, as cauliflower tumors, but they also send processes into the depth.

Secondary glandular tumors, as with such tumors of the breast, include scirrhus forms which infiltrate the skin and appear as many small nodules in the corium, with intact epidermis. The skin becomes hard and fixed to the tissues beneath. If general this form is called cancer *en cuirasse*.

Melanoma is a malignant tumor developing from nevi, and is usually deeply pigmented. It may have the structure of alveolar endotheliomata, in which the large endothelial cells of the nests correspond to the nevus cells. When the cells in these nests correspond with displaced superficial epithelia the tumor may be a true carcinoma. In other cases the formation is that of a true sarcoma, with bundles of long spindle cells and stellate chromatophores. Such masses arranged about the vessels are characteristic of perithelioma.

Necrosis and Ulceration.

Embolism, thrombosis, and atheroma of the cutaneous arteries may cause necrosis, and this is especially frequent in old age as senile gangrene of the feet and legs. When the necrosed tissues simply

dry the part is spoken of as mummified, or in dry gangrene. Putrefactive organisms usually complicate the case with decay of the affected part.

Many cases of peripheral gangrene are due to inflammatory causes associated with small wounds of the toes or feet. Secondary thromboses of the arteries of the foot may form. Noma and hospital gangrene are due to infections. The latter, known also as diphtheria of wounds, covers the wounded surface with a tough, fibrous layer, which is not easily removed, and which is formed by necrotic granulations. Before the general use of antiseptic measures this affection caused many deaths. Other cases of gangrene are due to pressure, frost, and burns.

Ulcers arise by the casting off of small necrotic portions of the surface with progressive molecular death of the tissue. According to their form ulcers are called callous when their edges are prominent and infiltrated, sinuous when undermined, fungous when the granulations project markedly, fistulous when making canal-like defects, and serpiginous when one part progresses while others heal, and so the lesion spreads. Healing occurs by granulation and the formation of a scar.

Ulcus varicosum, or *ulcus cruris*, is connected with varicose veins of the part and stasis, since from the consequent loss of sensibility in the skin slight injuries lead to destructive inflammation and an ulcer. The tendency to heal is slight. The edge and the base of the ulcer become covered with granulations, but they lead to imperfect attempts at healing, and suffer speedy relapse, and hence the lesion extends. The edges of the ulcer are thickened by infiltration and have an irregular outline, and may be the seat of a later elephantiasis. Frequent bleeding causes pigmentation, either diffuse or in spots. The periosteum of the bones beneath may proliferate or become the seat of a neoplasm.

Ulcus molle, or soft chancre, is a contagious lesion which begins as a papule, becomes a pustule and opens, and, with much infiltration of the adjoining tissues, forms a punched-out ulcer with undermined edges and a gray, discharging base. The lesion may be multiple. It heals with a scar. This lesion causes no general infection, but only involves the nearest nodes as a bubo. Phagedenic chaneroid causes deep and wide destruction of the tissues. The serpiginous form makes progress on one side while healing on the other. When gangrenous the lesion may be very destructive.

Other ulcers of the skin are due to nervous influences, either vasomotor or trophic, and as examples of this class may be mentioned perforating ulcer of the foot, and the cutaneous necrosis occurring with lepra mutilans and syringomyelia. Edema, hyperemia, vesicles, panaritium, and necrosis of the bones may accompany such lesions, and severe injuries to the smaller extremities may be the result. Morvan's disease is an analgesic paresis with panaritium of the upper extremities, which is also probably due to syringomyelia.

Ulcers with infectious granulomata and scurvy have been mentioned.

Diseases of the Cutaneous Glands, Hair, and Nails.

(a) **The Glands.** Seborrhea is an increase of the secretion of the sebaceous glands, which may be limited to a part, as the head, face, or genitals, or more general. *Seborrhea oleosa* furnishes a fatty fluid, especially in the skin of the forehead and nose, and *seborrhea sicca* or *squamosa* causes desquamation of epidermal cells, as in the scalp.

Comedones are due to accumulations of sebum in the glands, with cystic distention, and the outer, black portion is colored by dirt. They are especially common in the skin of the nose and forehead.

Milium is a small white spot directly under the epidermis, caused by the collection of fat and epidermic cells in a sebaceous gland. It is common in the eyelids.

Atheroma is a relatively large and tumor-like retention cyst of sebaceous glands and hair follicles, attains the size of a hazelnut, and is filled with a semifluid mass of detritus surrounded by a fibrous capsule. In some cases the lesion develops from scattered bits of epithelial tissue in the cutis and subcutis, or from remains of the branchial clefts, and corresponds to epidermoids or dermoids. The atheromatous mass consists of corneous epithelium, fat, fat crystals, cholesterin, etc. In dermoids the wall has the typical structure of the skin.

(b) **Abnormalities of the hair** include early falling out, hypertrichosis, or the growth of hair in unusual places, especially on nevi pilosi. Loss of hair follows many local diseases.

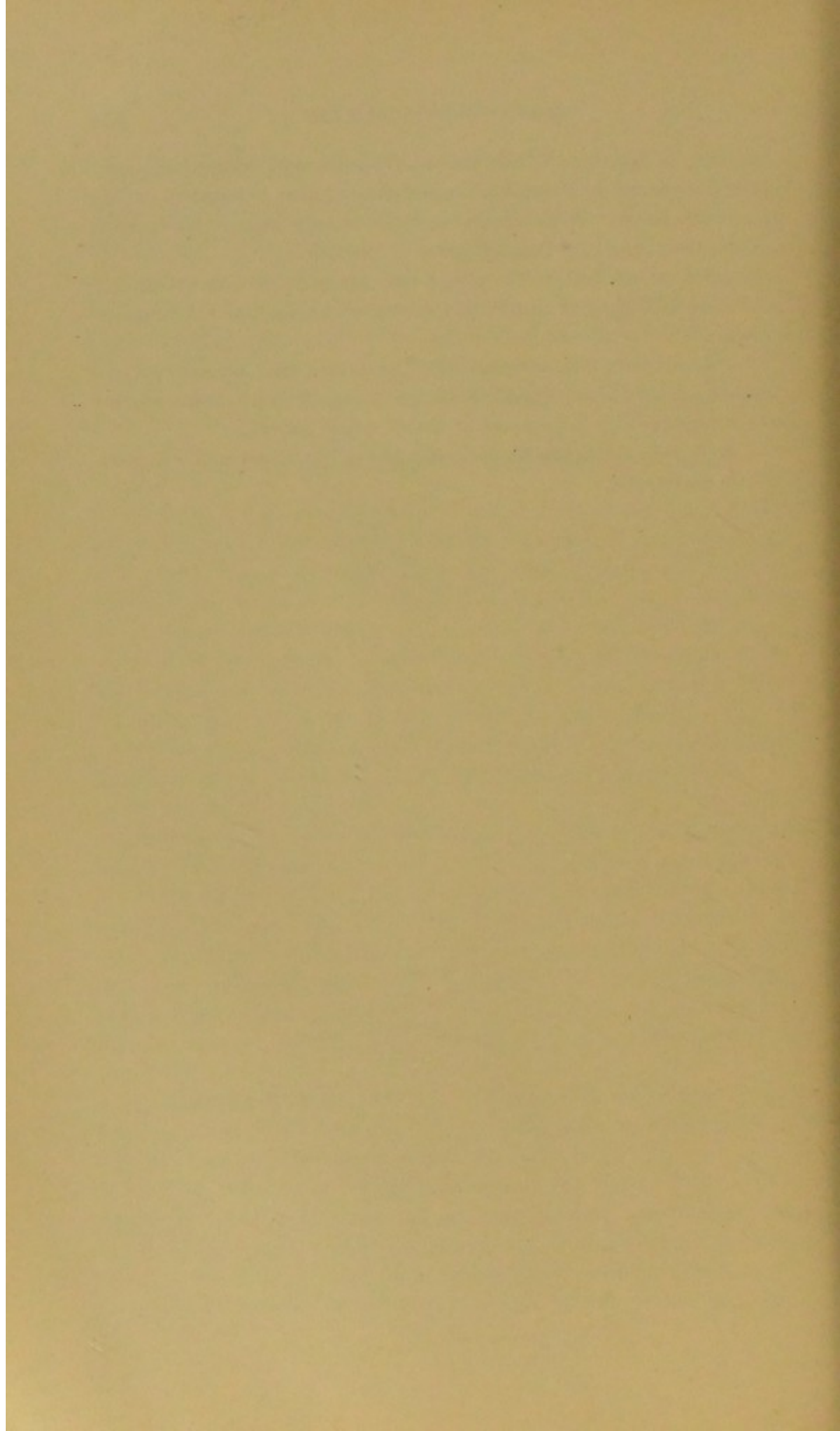
(c) **The nails** suffer an inflammation of the bed which is called paronychia, and ends with suppuration. It may be due to local injury or to syphilis. Onychogryphosis is a hypertrophy of the tissue beneath the nail by which it is lifted up and twisted like a claw. Onychomycosis is due to infection of a nail by favus or trichophyton.

Acne is a purulent inflammation of a sebaceous gland, especially about comedones, or from application of irritating substances or the administration of certain drugs, as iodine and bromine. Sycosis is a similar affection of the bearded parts of the face.

A furuncle or boil is an intense and extended inflammation of a cutaneous follicle, with a necrotic centre which may be expressed as a plug.

Carbuncle is also a circumscribed, purulent, and necrotic inflammation, but of larger extent, with gangrene of the central portion which may involve large areas of the skin and subcutis.

Among tumors carcinoma and adenoma of the sweat and sebaceous glands may occur.



APPENDIX.

STATISTICS OF THE MOST IMPORTANT BODILY MEASURES AND WEIGHTS.

Average Weights of Organs of Normal Adults. The figures are "round," and the female organs in general approach the lower of the given weights, while male organs approach the higher.

Brain	1200-1400 gm.
Heart	250- 350 "
Lung, left	325- 480 "
Lung, right	360- 570 "
Spleen	150- 250 "
Liver	1400-1600 "
Kidneys, together (the left is a few gm. the heavier)	300 "

Average Measurements of the Newborn Child at Term.

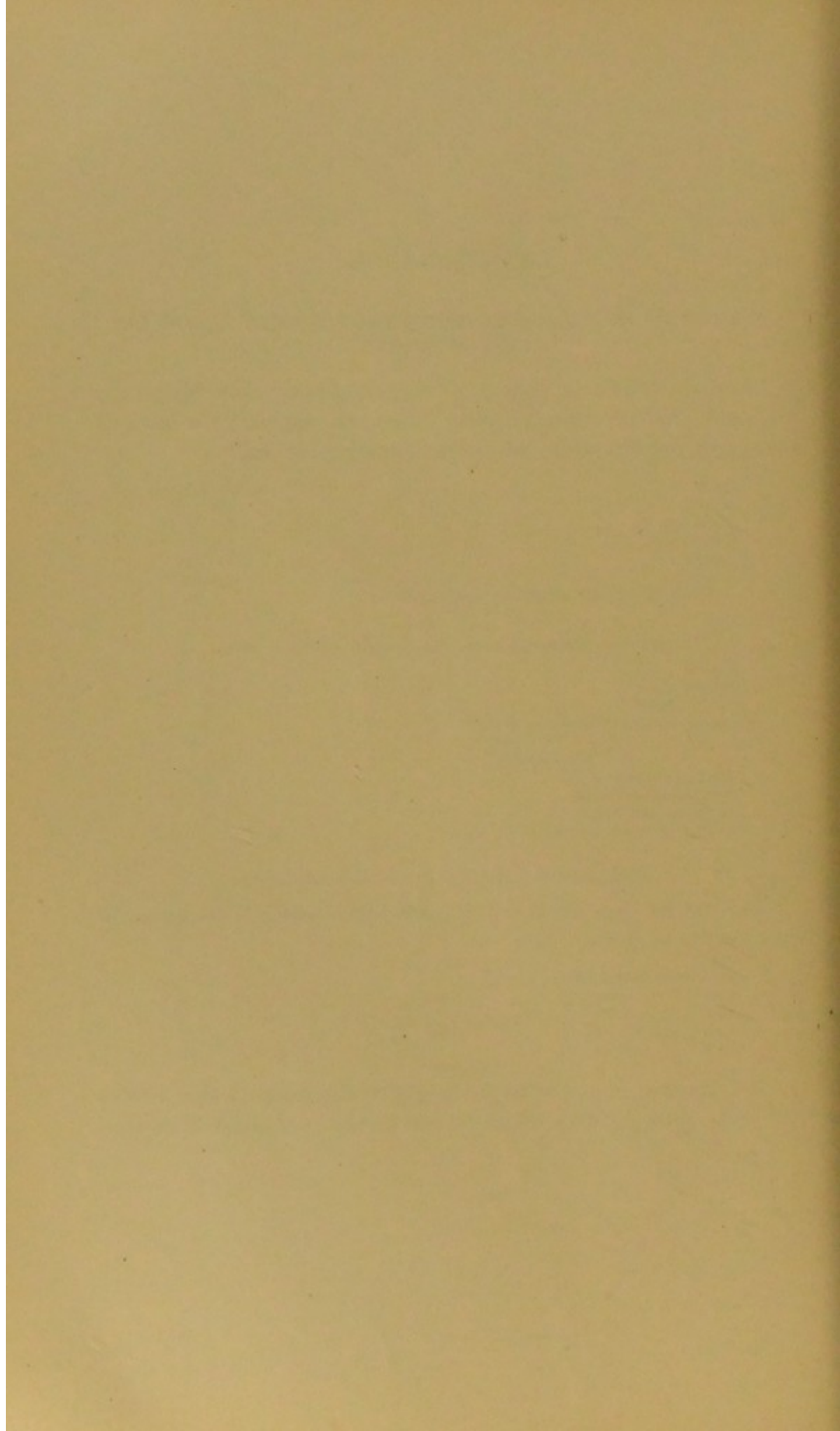
Length	50 cm.
Weight, male	3250 gm.
" female	3000 "
Diameters of head, transverse, smaller	8 cm.
" " " larger	9.25 "
" " fronto-occipital	12 "
Head, circumference	34 "
Large fontanelle, length	2-2.5 "
Umbilical cord, length	51 "
Nucleus of ossification, lower end of femur	5 mm.

Determination of the Age of a Fetus by its Length.

For the first five months of pregnancy the length is the square of the number of months, thus :

1 x 1, length in first month	1 cm.
2 x 2 " second "	4 "
3 x 3 " third "	9 "
4 x 4 " fourth "	16 "
5 x 5 " fifth "	25 "

For the last five months the length of the fetus divided by five will give the age ; thus, length 30 centimetres \div 5 equals 6 months.



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