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BY

CORNIL AND RANVIER

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PART II.

WITH 172 FIGURES INTERSPERSED IN THE TEXT

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commonest tumours of the small intestine, the colon, and the rectum. It has exactly the same gross appearances, the same form, and the same microscopical details as epithelioma of the stomach. As in that organ, it commences by hypertrophy of the tubular glands; the muscular layer of the mucous membrane is then perforated, and the saccules penetrate into the submucous tissue, where they form cavities lined with cylindrical cells; from these cavities vascular buds equally covered with cylindrical cells are often given off. These epithelial cylinders and expansions of the glandular saccules then penetrate into the muscular layers of the intestine. Part or the whole of the morbid mass often undergoes colloid degeneration. Pavement, horny, or mucous epithelioma is often found near the anus; these tumours do not differ in structure from similar epitheliomata observed in other parts of the body.

CHAPTER VII.

THE LIVER.

I. Normal Histology of the Liver.

The liver differs from other glands by the fact that the glandular cells composing it are in direct relation with the capillaries. It is they which elaborate glycogen and secrete bile. The liver is developed in a fibrous membrane called Glisson's capsule, which is itself covered by the peritoneum. It is reflected with the vessels, and is insinuated between the hepatic lobules, which are formed by the glandular cells. Though all the hepatic lobules are not exactly alike as regards shape and size, they so closely resemble one another in structure, that by studying one of them the entire organ can be understood.

Structure of the hepatic lobule.—The hepatic lobules are polygonal in shape. They vary in diameter from 1 mm. to $1\frac{1}{2}$ mm.; they are suspended from the ramifications of the sub-lobular vein in the same way as the glandular cells from their excretory ducts. From the extra-lobular branches of the sub-lobular vein spring smaller branches, which after a short course penetrate singly into a lobule, and are then called the intra-lobular, or central vein of the lobules. From this central vein springs a radiating network of capillaries, anastomosing with one another by short transverse branches. These capillaries, the diameter of which is $10\,\mu$, and which are separated only by a mean distance of $15\,\mu$, form a network of meshes elongated in the direction of the radiating veinules. Communicating at the centre of the lobule with the central vein, they receive blood at the periphery of the lobule from the portal vein, and are thus directly continuous with the interlobular portal veinules. These latter ramify in the prismatic-shaped spaces which are left between the hepatic lobules, and they penetrate into the lobules at their periphery, so that each lobule receives capillaries from four or five branches of the portal vein. In the same interlobular spaces

are found branches of the hepatic artery and the interlobular bile ducts, surrounded by connective tissue, which is continuous with Glisson's capsule. The capillaries of the hepatic artery supply the walls of the portal vein and the interlobular bile ducts; they are therefore chiefly present at the periphery of the lobules, where they anastomose with the capillaries of the lobule itself. The lobules are thus seen to be in contact with one another, separated only by the ramifications of the portal vein, the bile ducts, and the interlobular hepatic artery, accompanied by a little connective tissue. Within the lobules the spaces left between the meshes of the capillaries are entirely filled by liver cells.

The cells of the liver.—These cells are small blocks of a soft granular substance containing one or two round or oval nuclei from 9 μ to 12 μ in diameter; the shape of the cells is easily modified by pressure exercised by the capillaries, or by neighbouring cells. They may be obtained singly by scraping the cut surface of the liver, when they are seen to be polygonal, with four, five, or six facets. Examined *in situ*, in very delicate sections of the liver, the cells are seen to be in close contact, so that one cell may touch five, seven, or nine neighbouring cells and one or more capillaries. The semi-fluid, granular protoplasmic mass composing the liver cells often contains the fine yellow granules of bile pigment. It also contains diffused glycogen, which stains with a solution of iodine, or with serum strongly iodised. Generally also during digestion the cells at the periphery of the lobule contain some fat granules. The liver cells have no membrane; at least all we can say is that their protoplasmic substance becomes condensed in the neighbourhood of the bile canals, and forms a delicate cuticle which serves as a wall to these canaliculi.

Considering their reciprocal relations with the centre of the lobule, the liver cells seemed to Eberth to form a series of trabeculæ radiating from the centre to the periphery and anastomosing transversely. He compared these networks or trabeculæ of liver cells with tubes containing these cells, such as may be seen in certain species of animals, fishes, reptiles, &c. This appearance of trabeculæ is simply due to the general configuration of the capillary network, as Hering and Kölliker have shown. Neither in man nor in other mammalia is there a membrane comparable to a glandular sac containing liver cells and separating them from the capillaries. In the rabbit, in particular (Hering), the liver cells adhere to the capillaries and are not detached on placing a portion of the liver in alcohol and chromic acid—reagents which strongly

contract the elements—whilst in the dog and man the hardening action of these fluids separates the cells from the walls of the capillaries. The hepatic lobule can therefore be considered only as a continuous mass of cells, intersected by a capillary network, the arrangement and shape of the cells being modified by the vascular meshes.

The **bile ducts** commence in the hepatic lobule in a network of fine canaliculi, forming narrow meshes, and they are all in contact with the liver cells. This network is an emanation of the interlobular bile ducts which accompany the branches of the portal vein (Büdge, Andréjevie, MacGillavry, Eberth, Kölliker). The intralobular bile canals pursue a straight and regular course. They have a diameter of 1·5 μ, and their meshes, in the rabbit, of from 14 μ to 17 μ. They have no internal epithelium, and their walls are solely constituted by the liver cells, of which the substance is slightly condensed. The meshes formed by the bile canals are rather larger, but in the same direction, as those of the capillaries. The canaliculi are formed by the approximating surfaces of two cells. They never come in contact with the capillaries, from which they are separated by at least half the surface of a liver cell. The meshes of this network of canaliculi are polygonal, their form depending on those of the liver cells. Each cell is

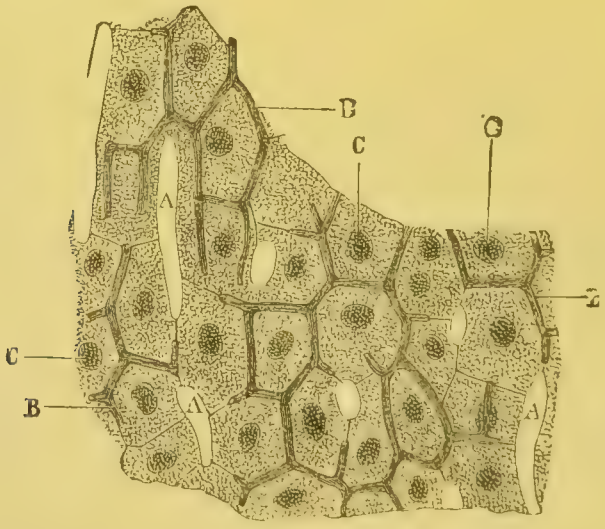

FIG. 126.—SECTION OF A LIVER IN WHICH THE INTRALOBULAR BILE DUCTS HAVE BEEN INJECTED.
(Fig. borrowed from Kölliker.)
A, blood capillaries; B, bile canals; C, nuclei of the liver cells.

consequently in contact with a blood capillary on one side, and by many of its surfaces with the bile canals. At the periphery of the

lobule the bile canals unite to form slightly larger canaliculi, which empty themselves into the interlobular bile ducts. The latter have quite a different structure; they are formed of a delicate membrane completely lined internally with cubical epithelial cells containing a round or oval nucleus. Inside is a narrow channel for the flow of secretion. In diameter they vary from 30 μ to 50 μ. The bile is secreted by the liver cells, passes first into the fine intralobular canaliculi, and then into the intralobular ducts.

Such are the essential elements of a hepatic lobule: it only remains to describe the connective tissue and lymphatics of the lobules. The connective tissue which emanates from Glisson's capsule, and the bundles which accompany the interlobular vessels, penetrate into the lobule in the form of scanty fibrils. They cling to the walls of the capillaries, forming at certain points a kind of adventitious membrane, or extended between the capillaries they form a reticulate tissue. These fibrils can be isolated and observed in very delicate sections on brushing out the cells, when they are seen to form, together with the capillaries, the framework which supports the liver cells. The peripheral connective tissue of the lobule does not always form a complete investment; sometimes two lobules are in contact, there being no process from Glisson's capsule between them.

Glisson's capsule, which is rather thick on the surface of the liver, can be separated into two layers: the serous, composed of loose connective tissue, covered by the endothelial cells of the peritoneum; the other, deeper and thicker, is in relation with the liver cells, and is composed of fibrous tissue.

The existence of **lymph vessels** in the lobules has been admitted by MacGillavry, who in injecting the bile ducts produced extravasations around the blood capillaries, between them and the liver cells. Kölliker has seen the injection pass thence into the perilobular lymph vessels which accompany the portal vein. It is certain that in man, the cat, and the dog, the liver cells become easily detached from the capillaries, leaving perivascular spaces which MacGillavry looks upon as lymph lacunæ. Hering is not favourable to this point of view, and according to him fresh researches are necessary before this theory is adopted, he remarking that there is nothing similar in the rabbit, in which the liver cells are always adherent to the walls of the vessels. The perilobular lymph vessels consist of trunks or networks which accompany the portal vein and unite on the surface of the liver with the superficial network seated under the peritoneum.

Nervous filaments have never yet been discovered in the hepatic lobules, and they have not been traced further than the walls of the interlobular portal veins, for it must be stated that no credit can be placed in the observations of Pflüger, who pretended that he had been able to trace nervous filaments into every liver cell.

The **blood vessels** of the lobule have been already described; we must refer our readers to treatises of descriptive anatomy for all that relates to distribution of the interlobular vessels in the liver. We will only add that if the hepatic vein remains gaping on dividing the liver, this is due to the fact that not being enveloped, like the portal vein, by Glisson's capsule, it is closely connected with the glandular parenchyma and cannot collapse.

The excretory bile ducts.—The bile canals of the hepatic lobule empty, as we have already seen, into the interlobular ducts. These latter accompany the ramifications of the portal vein and unite, forming large trunks which follow the principal branches of this vein. The two principal trunks join at their exit from the liver in the transverse fissure, to form the hepatic duct, which uniting with the cystic duct forms the common bile duct, which opens into the duodenum at a depression in the upper third. Besides these principal ramifications, there are accessory branches which unite the two branches of the hepatic duct and form a network in the transverse fissure. At different spots on the surface of the liver the bile ducts spread out into the connective tissue, anastomosing together; such are the ducts which penetrate into the broad ligament as far as the diaphragm (*vasa aberrantia*). The interlobular bile ducts are composed of a membrane of connective tissue and a lining of epithelial cells, the smallest of which are cubical, the largest cylindrical. In the smallest interlobular ducts the membrane is not distinct, and the cells are often flattened as well as their nuclei. The fibrous membrane of the large ducts and the medium-sized ducts contain smooth muscle fibres. They have also small simple or composite glands composed of round or elongated vesicles. The epithelial lining of the hepatic and cystic ducts and of the common bile duct consists of a single layer of long cylindrical cells, the nuclei of which are ovoid or elongated. The subepithelial connective tissue contains a rich network of capillaries. In the gall-bladder a layer of connective tissue is found beneath the mucous membrane, intersected by bundles of smooth muscle cells which give it an alveolar appearance. It is covered by the peritoneum and contains a network of subserous lymph vessels.

II. General Pathological Anatomy of the Liver.

The lesions of the liver are best studied by first considering the general pathological anatomy of this organ. To the position of the liver in the track of blood which is loaded with the products of digestion, and to the large quantity of blood which unceasingly passes through it, is due the fact that diseases of the intestine and spleen, and morbid changes of the blood in all those diseases which profoundly modify the constitution, invariably result in producing lesions of the liver. It is also always affected in those organic affections of the heart and lungs which modify the portal circulation. Thus we see that most of the changes in the liver are secondary to other general or local diseases. In hot climates, where liver diseases are common, the most acute are consecutive to attacks of intermittent fever, yellow fever, dysentery, or alcoholism. In temperate climates the most frequent affections of the liver follow in like manner intermittent fevers and dysentery of less serious types than those of tropical countries; they may also result from alcoholism, typhoid fever, small-pox, scarlet fever, purulent infection, &c. In other cases lesions of the bile ducts may be the cause. The diseases of this organ are almost always deuteropathic.

We will first consider the anatomical changes of the elementary parts of the liver, that is to say of the liver cells; then of its cellulo-vascular tissue, and finally of its bile ducts.

1. **Morbid changes in the liver cells.**—We have already stated that the liver cells are polygonal in shape, that they have generally one, and exceptionally two, nuclei, and that their granular protoplasm contains proteic granules and also pigment and fat granules. Under the influence of various morbid conditions they become profoundly modified. Their shape is easily changed by the pressure of other contiguous cells, so that a capillary may be often observed grooving the surface of a cell. In the case of tumours in the liver, the cells compressed by the tumour become flattened in the direction of the pressure; in cross-section they appear like fusiform cells slightly swollen centrally at the level of the nucleus. All the cells of a compressed lobule take the same form; thus the entire lobule becomes flattened and spread out around the tumour. The softness of the liver cells enables us partly to understand how the entire liver may become modified in form by an abdominal tumour, by ascites, or even by tight lacing. In the

latter case, the base of the thorax being narrowed by the tightening of the body, the entire liver is displaced downwards and its

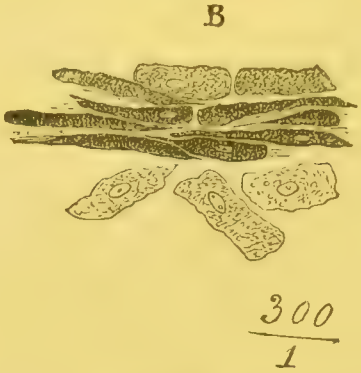

FIG. 127.—LIVER CELLS FLATTENED BY PRESSURE, SOME SEEN SIDEWAYS, OTHERS FULL FACE. Magnified 200 diameters.

upper surface becomes anterior. This surface, which is smooth in the normal condition, becomes puckered and seamed with grooves from above downwards, the result of lateral constriction. The lower edge of the liver, which is then below the false ribs, sometimes projects beneath the ribs following the convex line of the abdominal walls. These deformities become permanent in consequence of atrophy of the lobules, which are compressed in the folds on the surface of the liver, and also of thickening of Glisson's capsule at the same spot. A similar deformity is also very frequent in aged persons in whom the back is bent, in which case the lower border of the thorax presses against the anterior surface of the liver. The form of the cells is also often modified in cardiac and pulmonary diseases by the increase of blood pressure in the inferior vena cava. The pressure in the inferior vena cava is directly transmitted to the hepatic vein and to the central veins of the lobules; the capillaries leading from these are distended, and consequently the liver cells are compressed and flattened. Owing to the blood stasis they simultaneously fill with reddish-brown pigment granules; later on, if the pressure continues, they become granular, more and more thin and atrophied, and they may even entirely disappear, so that here and there may be seen groups of distended vessels no longer separated by cells. Such is the lesion which is caused by cardio-pulmonary affections, particularly those of the mitral valve, and which has been called *red atrophy*.

In acute diseases, such as the exanthemata, and particularly in hæmorrhagic small-pox, and also in acute tuberculosis, another

series of changes is almost always observed in the liver cells. These changes are also present in some cases of poisoning, but reach their maximum in acute icterus, or acute yellow atrophy of the liver. They have been grouped by Virchow under the name of *parenchymatous hepatitis*, a name which is rather misleading, as the symptoms of inflammation are little marked. The changes consist essentially in lesions of nutrition of the cells, which become cloudy, rounder and larger than normally; the granules which fill them often prevent the nucleus being seen; nevertheless on staining the cells with picro-carminate of ammonium the nuclei become visible without the addition of any other reagent. Acetic acid causes a great number of these granules to become paler or to disappear, as they are of a proteic nature; others persist, and their dark borders as well as their refrangibility enable one to recognise them as fat granules. In the cells thus cleared and stained two nuclei are very often discerned. Half of them may, for example, contain two nuclei, while others may have three or more. If the liver cells have two nuclei in the normal condition it is exceptional, while here it is common and consequently abnormal. Besides these large cells which are in the condition of *cloudy swelling* other small cells are found in the fluid obtained by scraping, which have but one nucleus, and in which the protoplasm is soft and easily lets the nucleus escape; also free nuclei are found which have been separated from their protoplasm by the method of preparation. Such is the lesion found in the first period of acute fevers: it is due to the presence of microbes in the circulation, and probably also to the high temperature of the blood. Later on, a large number of fat granules is found in the cells—a true fatty degeneration of the liver—as may be observed at the end of typhoid fever. In other diseases of this group, particularly in acute icterus, which seems to be caused by bacterial infection, the cells atrophy, become filled with fine granules, and fall to pieces. They are then infiltrated with yellow bile granules, as well as with proteic and fat granules. Lobules or parts of lobules are replaced by a mass of cells in a state of disintegration. It must not, however, be thought that acute yellow atrophy of the liver is the only parenchymatous hepatitis in which the cells are infiltrated with bile pigment. The same lesion may be found in cases of hæmorrhagic small-pox. The organ is then large, rather soft, of an uniform greyish-yellow colour. Nearly half the cells have two nuclei and are cloudy with proteic, fat and pigment granules. Though the same degree of parenchymatous hepatitis

is not reached in all acute febrile diseases, and the lesion may show a slightly different evolution and intensity, yet nevertheless the facts are comparable and point to an identical nutritive lesion of the liver cells. This series of nutritive changes of the cells in parenchymatous hepatitis is related to changes, still little understood, of the blood in infectious fevers. A similar granular degeneration, followed by disintegration, is observed at those points where the circulation of the blood is arrested, as in thrombosis or embolism, and where the cells are surrounded by suppuration.

Fatty degeneration, amyloid degeneration.—Another series of lesions of nutrition in the cells is observed in cachectic chronic diseases, such as phthisis, chronic suppuration, scrofula, cancer, &c., and is characterised by fatty degeneration, or by amyloid degeneration of the liver cells. Fatty degeneration consists in infiltration of the cells by small drops of fat. In chronic diseases the nucleus is generally preserved, and consequently the liver cell is not destroyed; it is simply surcharged with fat. The protoplasm shows many small drops of fat, or a single large drop which occupies almost the entire cell, which then consists only of a hollow sphere of protoplasm surrounding the fat; at some spot in this protoplasm the well-preserved nucleus is seen. The element then greatly resembles the fat cells of the subcutaneous cellular tissue. In adiposity, or fatty deposit, the nucleus is intact, and the cell shows no tendency to disintegrate or disappear, while in parenchymatous hepatitis the degenerated cells, filled with proteic and fatty granules, split up and disintegrate. In fatty degeneration, as each one of the fatty liver cells has increased in size, it follows that the entire liver becomes hypertrophied. Physiologically, fatty deposit takes place in the liver cells during suckling and at the end of parturition in women, as well as in other mammalian females.

Amyloid degeneration is also frequently observed in the liver cells; they are then changed into small blocks of a refractile transparent substance, which often splits up. The nuclei and granules have disappeared. These small refractile masses stain brown with even a weak solution of iodine, and on adding sulphuric acid they often pass from brown to violet, blue, green, and dark red.

Besides these two important series of general causes, febrile infectious diseases, and cachectic chronic diseases, which profoundly modify the liver cells in consequence of blood changes, these elements undergo other changes resulting from liver disease

not originating with them. Thus in retention of the bile an accumulation of pigment is found in their interior; in acute suppurative inflammation they are destroyed after becoming granular; in chronic cirrhotic inflammation and in tumours they may show every kind of nutritive lesion. We will return, later on, to these various points.

2. **Changes in the cellulo-vascular tissue.**—Owing to the fact that the connective tissue of Glisson's capsule surrounds the interlobular branches of the portal vein and of the hepatic artery, penetrating even with the capillaries into the lobules, it is difficult to separate its lesions from those of the walls of the vessels. It is around the hepatic lobules, and precisely in the neighbourhood of the portal vessels, that morbid changes in the connective tissue most frequently occur; but they are also present and sometimes even predominate around the extralobular branches of the hepatic vein. They are in fact generally related to the presence of substances in the blood of the liver which do not exist there normally, or of normal elements which are found there in abnormal quantities. These foreign substances cause an irritation of the vascular walls, which is transmitted to the neighbouring connective tissue. The following examples justify this proposition. Take first the case of leukæmia, in which the blood is loaded with a considerable quantity of leucocytes; these embarrass the capillary circulation, and the pressure being increased, they have a tendency to pass through the walls of the vessels, and to be extravasated into the surrounding connective tissue. There might be positive infarctuses of white cells in the connective tissue which surrounds the interlobular veins of the portal vein, and around the capillaries of a lobule. In chronic intermittent fever with cachexia, when the tumefied and indurated spleen is affected with interstitial splenitis, when the leucocytes contained in the lacunæ of the splenic tissue are charged with black pigment granules (melanæmia), the blood of the portal vein contains a large number of the same pigmented lymph cells. The walls of the small interlobular portal veins soon also show black pigment in their cells; the pigmented lymph cells escape from the vessels, and infiltrate the interlobular connective tissue as well as that surrounding the capillaries of the lobules. Thus the connective tissue is almost always found to be inflamed and infiltrated with lymph cells, some of which are filled with pigment. This is one of the varieties of cirrhosis of the liver,

or chronic inflammation, with thickening of the connective tissue.

Alcoholic excess, which is the most frequent cause of hepatic cirrhosis, acts most probably by direct irritation of the vascular walls and of the connective tissue surrounding them. In alcoholic cirrhosis, as in malarial cirrhosis, the hepatic connective tissue is inflamed; in the periods of exacerbation a large number of lymph cells are found between the fasciculi of connective tissue; soon new fibrous bundles are formed and sclerosis unites the walls of the vessels with the surrounding tissue; actual phlebitis, obstruction of the hepatic vein, fibrous organisation of the thrombus, in which finally lacunæ are formed by means of which the circulation of the blood is re-established (Sabourin)—all these changes of cirrhosis follow, taking more or less time to develop, and they terminate, as we shall see when studying the disease in detail, in cicatricial contraction of the new fibrous tissue.

In **purulent infection**, when small metastatic abscesses arise in the liver, the blood and the tissues do not only contain a larger quantity than normally of lymph cells, but more particularly microscopic germs, micrococci, diplococci, or bacteria, derived from the primarily inflamed part and carried thence by the blood. This is the conclusion drawn from the most recent researches on this important question of metastatic abscesses and suppuration, the theories regarding which have changed frequently during the course of the past twenty years. In some autopsies made in the year 1870–71, a very short time after death and under quite exceptional conditions, and at a temperature below freezing, one of us observed the above-mentioned microscopic germs extravasated with the lymph cells outside the vessels in small metastatic abscesses of the liver. There is moreover during life an actual putrid fermentation in these abscesses, which is proved by the presence inside them of bubbles of gas. On treating a section of a liver affected with pyæmic abscesses with glacial acetic acid, and staining with safranine or B. violet, the capillary vessels are easily seen to be full of masses of microbes.

The blood vessels are sometimes altered primarily, sometimes secondarily. Among primary inflammations we must mention that of the portal vein, pylephlebitis, in which the vascular trunk is found after death to be filled with pus and coagulated fibrin. This occurs in consequence of intestinal lesions, the ulcers of tropical dysentery being often the starting-point; at other times it is a sequela of general disease, and there are cases in which it

is impossible to discover the primary lesion of pylephlebitis. On opening the liver small purulent collections are found, varying in number. They are actual canaliculated abscesses, having the form and direction of branches of the portal vein. What we have said regarding the part played by microbes in metastatic abscesses equally applies to those of pylephlebitis. In cirrhosis and other chronic affections of the liver the walls of the portal vein and hepatic vein are changed like the rest of the organ; here also the cellular coat undergoes a very marked kind of cirrhosis. Vascular tumours are rare in the liver, though aneurisms of the portal vein have been observed. The same may be said of induration of its internal wall or of atheroma, which is extremely rare. Angiomata of the liver are, on the contrary, much more common; they are found as small cavernous tumours in the midst of the hepatic tissue.

III. Special Pathological Anatomy of the Liver.

Post-mortem changes.—At the autopsy, the liver is generally found to be pale. Its parenchyma contains very little blood, the large vessels alone containing a notable quantity, more particularly the branches of the sublobular veins. The small vessels and branches of the portal vein contain very little. If a rather considerable quantity of blood is present it is owing to the fact that the liver was congested during life. On the convex surface of the liver, a little above its anterior border, whitish opaque spots are often found. These spots, the extent and form of which vary, are due to partial anæmia, which seems to be produced by pressure on the hepatic parenchyma after death. These spots are extremely superficial, and must not be confounded with pathological changes, such as, for example, fatty degeneration, nor with neoplastic growths, after one has been forewarned of their existence. The liver may also be found to be softened. Some time after the death of an animal the protoplasm of the hepatic cells solidifies and the liver becomes rigid; but this condition disappears at the end of a few hours, so that at the autopsy, which takes place twenty-four hours after death, the liver is softened. The extravasation of the bile also gives origin to another post-mortem phenomenon, namely, to the greenish-yellow staining of the parts near the gall-bladder, particularly the intestine. This must not, however, be mistaken for rupture of the gall bladder, nor for any other lesion existing during life. After death the surface of the gall bladder and the ducts is green. Under the microscope the cylindrical

cells of the mucous membrane are also coloured green; but this appearance is never observed in animals which have been killed, in which case they are found to be entirely colourless. This diffusion of the bile in the neighbourhood of the gall bladder is seen also in the hepatic parenchyma. Bile, as is well known, destroys the red blood corpuscles; thus in hardened sections of a perfectly healthy liver, made twenty-four or forty-eight hours after death, the intralobular capillaries are seen to contain no red blood corpuscles, but only a few leucocytes. It is quite otherwise in diseases which prevent the secretion of the bile —in acute yellow atrophy, for example; also when a tumour has been formed by dilated capillaries in the substance of the liver. The mass of the blood is then too considerable or too distant from the bile ducts for the bile to affect the red blood corpuscles, which are well preserved. Putrefaction also gives origin to changes in the hepatic parenchyma which might lead to error in those little accustomed to pathological research. In fact it produces constant changes in the fluids of the body, more particularly in the blood. Putrefaction gives origin to sulpho-hydrogen gas, which combines with the iron derived from the destruction of the red blood corpuscles, whence results a greenish or black point of sulphate of iron, which certain observers, among them those who have studied the diseases of tropical countries, have often mistaken for a pathological lesion. Before completing this account of causes of error we must mention a phenomenon often observed in certain cases of putrefaction, and described as a pathological lesion—namely, the formation of gas in the tissue of the liver. The gas forms vesicles, varying in size, regularly circular and often opening one into another so as to form an areolar cavity. In purulent infection gases are formed a short time after death, and perhaps these vesicles may even be produced during life. In other diseases it is only during the great heat of summer, during periods of storm, or twenty-four hours after death, that this cadaveric change is observed. It is, however, important to avoid these causes of confusion.

Congestion of the liver.—Congestion of the liver is a very common lesion, for it is met with at the commencement of most diseases of the liver, and constitutes the most frequent anatomical change of the liver in diseases of the heart and lungs. Congestion is often accompanied with fatty degeneration, hypertrophic cirrhosis, &c. We divide hepatic congestion into two groups according as

it depends upon a more considerable afflux of blood by the portal vein or upon stasis in the sublobular veins.

Firstly, after eating the portal vein is more full of blood than at any other time of the day. After a copious dinner, in which one has eaten spiced meats and has drunk wine, liqueurs, coffee, brandy, &c., the blood of the intestinal and splenic veins, charged with the absorbed fluids, is poured into the liver, which it congests and enlarges. A sensation of fulness is then experienced in the hypochondrium, sometimes a sensation of malaise and even occasionally pain. The liver may increase a third owing to the repletion of its vessels, which fact may be proved by percussion. We have here an exaggeration of a physiological function, namely the elaboration of the blood drawn from the intestine by the hepatic gland. Excesses in eating, if often repeated and if they become a habit of life, may lead to cirrhosis. Gout seems also to be a cause of congestion of the liver; in fact the authors who have made a special study of this disease have shown that the attack in certain gouty subjects is preceded by congestion of the liver ('Treatise on Gout,' Garrod). In hot countries acute congestion of the liver is very common, whether produced by heat or due to the influence of certain morbid germs. In fact malaria and dysentery, which diseases especially affect the organs placed at the region of the portal vein, are the most frequent causes of congestion of the liver in hot countries, a congestion which is followed either by the peculiar pigmented cirrhosis of malaria or by abscesses of the liver. In cases of pernicious fever the liver on section is always found to be red, and ecchymoses are often found under Glisson's capsule. Congestion of the liver is seen at the commencement of the hæmorrhagic icterus of hot countries and of the intermittent fevers of a bilious character described by Dutroulau, in which the secretion of bile is so abundant that the patients secrete from two to four pints of bile in the day, while at the same time the colouring matter infiltrates the tissues of the liver, the skin, &c., and red blood corpuscles pass into the urine. Congestion of the liver may be carried to such a high degree that the tissue of the gland becomes itself ecchymosed. On section, it is seen to be uniformly red, the blood oozing from the small vessels and distending the large trunks. Without having had ourselves the opportunity of observing these facts it seems that these morbid changes in the liver are almost identical with those observed in Egypt by Griesinger in bilious typhoid fever, that is to say congestion followed by infiltration

and by granulo-fatty degeneration of the liver cells. In the last stage the liver is normal in size or diminished, and is yellowish-grey in colour and opaque as in yellow fever. A similar condition, though much less severe, is produced in our climate during the heat of summer, in a disease characterised by icterus, excessive production of bile, vomiting, and bilious stools, and which coincides with an increase in size of the liver, and a febrile condition of short duration. It is a hypersecretion of bile with congestion of the liver, which must be carefully distinguished from another form of simple icterus, also accompanied with congestion, which is due to intestinal catarrh, catarrh of the bile ducts, and obstruction of these by mucus. Most of the acute infectious fevers of our climate, variola, typhoid fever, measles, erysipelas, &c., are accompanied at the commencement with congestion of the liver, which precedes and leads to cloudy swelling and fatty degeneration of the cells. It is a temporary condition, and is particularly observed at the commencement of hæmorrhagic small-pox and scarlatina.

Secondly, when congestion of the liver is caused by increase of blood pressure in the hepatic veins it is generally shown by distension of the central veins of the lobules and the nearest capillaries, so that the internal half or two-thirds of the lobule are red while its periphery is grey. All cardiac diseases, but especially those of the right and left auriculo-ventricular valves, stenosis or insufficiency, aortic aneurism, chronic diseases of the lung, emphysema, pulmonary induration, chronic pleurisy, tuberculosis, &c., in which the cardio-pulmonary circulation is impeded, have the same result. On the other hand, if asphyxia has been rapid and takes place from poisoning by carbonic acid gas, the congestion, instead of being limited to the central part of the lobule, is general. Congestion of cardiac origin lasts as long as the cardiac disease itself, that is to say months or years; whence ensue a series of lesions of nutrition of the liver, which, commencing with hypertrophy, terminate with atrophy of the organ.

The cardiac liver.—The surface of the hypertrophied and congested cardiac liver is at first smooth, and Glisson's capsule is distended. In section, the lobules appear to be larger than normally, and they generally show at their centre a zone of dark red colour, which occupies one-half or two-thirds of the lobule, while the periphery is grey or opaque.

At the spots where the section passes through the divisions of a sublobular vein, a leaf-like figure is observed with red branches

surrounded by grey zones. If the section is made perpendicularly to the direction of the sublobular veins they form regular circles,

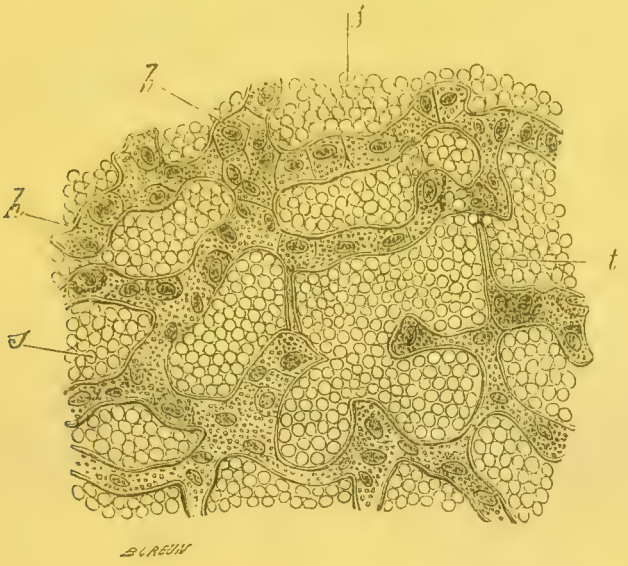

FIG. 128.—SECTION OF PART OF A HEPATIC LOBULE AFFECTED WITH CONGESTION OF CARDIAC ORIGIN (RED ATROPHY).

The hepatic cells, *h*, are atrophied, while the capillaries, *s*, are very much dilated and filled with red blood corpuscles: the liver cells have even entirely disappeared at certain spots, as at *t*. Magnified 250 diameters.

the centre of which is red, while the periphery is grey. This distribution in the same lobule of red and grey parts is surely what led Andral to suppose that in the normal condition two different substances existed in the liver. This colour has been compared to a muscat nut, and hence this lesion has been called the nutmeg-like liver or cardiac liver. This latter name is, however, not exactly correct, as the same kind of lesion is observed in pulmonary diseases, and it were better to call this morbid change red atrophy, under which name it is now generally known.

On examining delicate sections of a liver affected with this lesion the central vein is seen to be very much dilated in the middle of the red part; sometimes its lumen may be perceived even with the naked eye. The rest of the red region of the lobule contains very much enlarged capillaries, two or three times larger than normally, and filled with blood. The liver cells, interposed between these capillaries, are, on the contrary, flattened and atrophied. They nevertheless contain their nucleus, but their protoplasm is finely granular and frequently contains at the same time pigment granules of hæmatic origin, and even crystals of hæmatoïdin may be discovered. Some of these cells also contain

the yellow granules of bile pigment; these may be found in the centre of the lobule as well as in the periphery of the red region. The grey peripheral part of the lobule is composed of capillaries, normal in size or less dilated than the preceding, and of cells in a condition of complete fatty degeneration. These contain large granules, or even one or two large drops of fat, which distend them fully, giving them a round form. Such is the first stage of this lesion, which may be shortly stated to be that the blood of the sublobular vein distends the central vein and the capillaries of the lobule, impregnating the cells with the colouring matter of the blood and atrophying them, while the blood of the portal vein, stagnating at the periphery, deposits in the cells surrounding them the fat which is derived from digestion. Soon, however, graver lesions follow. The dilated capillaries, after the more or less complete atrophic destruction of the cells which separate them, come into contact with one another, their walls being separated only by the connective tissue which normally surrounds them, and from place to place by a flattened hepatic cell which still contains its nucleus. The dilated capillaries, filled with blood, separated by a little connective tissue, form small foci in the centre of the red zone or irregularly disseminated throughout it, which foci greatly resemble blood tumours in the liver, only that the diameters of the latter are larger. In the cardiac liver these spots appear, on section of the red zone, as clear reticulated spaces, the meshes of which are filled with red blood corpuscles. Later, the liver, primarily hypertrophied, contracts and atrophies. Its surface is then unequal. On section, the lobules appear smaller than normally, and the red substance seems at first to be more unequally distributed. Moreover, newly formed connective tissue is very often found around the central veins of the lobules as well as around the sublobular veins, whence the red colour of the centre is less uniform than at the commencement of the process. In sections, examined under the microscope, a zone of newly formed connective tissue is seen around the dilated central vein, in which a few connective-tissue cells with oval nuclei are found. The liver cells are atrophied, finely granular, and are often reduced to a small mass of proteic and fatty granules. The capillaries are not always as dilated as in the preceding case, but sclerosis is invariably present around the hepatic vein. It has been said that actual cirrhosis may be produced, comparable to the cirrhosis of alcoholic origin. This complication is very rare. We have, however, observed it in a case of stenosis with double regurgitation of

the mitral and tricuspid valves, in which the perilobular vessels were surrounded by a zone of sclerosis. Around some of the intralobular branches of the portal vein, not around all, fibrillar connective tissue containing cells was found, and it formed small circles enclosing the hepatic arteriole and the bile ducts which accompany the portal vein. But the new connective tissue does not form complete circles around each hepatic lobule, as may be seen in well-accentuated cirrhosis; it simply forms isolated bands around some of the portal veins. In sections these bands, appearing from place to place around the lobules, look like small round islets of connective tissue. In treating of cirrhosis generally we shall return to this subject of cirrhosis of cardiac origin.

As a consequence of congestion of the liver and stasis of the blood in the heart and in the veins and capillaries of the liver, great difficulty is always experienced in the circulation of the blood in those organs from which the portal vein derives its supply; whence result congestion of the spleen, stomach, and of the intestines as far as the rectum, varicose dilatations of the veins in these parts, varices of the lower part of the œsophagus, hæmorrhoids, &c. Sometimes ecchymosis of the mucous membrane of the stomach may be observed. Red atrophy is characterised by chronic catarrh of the stomach and intestine, and sometimes by a yellowish discolouration of the sclerotic membrane, and also by a certain amount of ascites.

Congestion may be due to traumatic causes, such as a blow over the region of the liver, as, for example, a blow from a buffer, from which accident railway servants frequently suffer. The lesion in such a case may be so severe as to produce attrition of the liver substance, ecchymoses, apoplexy, the most serious consequences, and even abscesses. In his experiments on contusion of the liver of the dog, Terrillon examined the changes following fissures and rents produced in the liver. The solutions of continuity are immediately filled by blood, which coagulates on the spot. In the middle of the clot white blood corpuscles arrange themselves in masses and ultimately constitute an actual embryonic tissue in which fibres and vessels are subsequently developed. Repair, according to Terrillon, takes place much quicker when Glisson's capsule is torn than when it is preserved intact. In the latter case, long after the contusion, extensive ecchymoses are found around the lobules, in which the blood undergoes its usual destructive changes. Collections or infiltration of blood may also be found in the liver in the very rare cases of atheromatous lesion of the

portal vein followed by perforation, or in the exceptional case of aneurism of the hepatic artery.

To recapitulate, hepatic congestjon accompanies most of the lesions of nutrition of the liver, and it marks the commencement of inflammation and cirrhosis. It also constitutes a quite peculiar and permanent morbid condition in all diseases of the heart.

IV. Hepatitis.

We distinguish three principal kinds of hepatitis: parenchymatous hepatitis, suppurative hepatitis, and interstitial hepatitis or cirrhosis. The first is particularly characterised by inflammatory and degenerative changes of the liver cells.

Parenchymatous hepatitis.—The word hepatitis scarcely includes all the cases known under the name of parenchymatous hepatitis, particularly if one considers suppuration as the final result of inflammation; for this particular form of hepatitis is scarcely ever followed by the formation of abscesses.

A. **Acute yellow atrophy of the liver.**—Of all the forms of parenchymatous hepatitis the best determined, from the anatomical point of view, is that which has received the name of acute yellow atrophy (acute icterus, hæmorrhagic icterus, or typhoid icterus). It is characterised by icterus, hæmorrhage, delirium, coma, and always terminates fatally. These accidents, it is true, do not always correspond to acute yellow atrophy of the liver, for they are observed as the result of a series of hepatic lesions accompanied by retention of the bile, in biliary lithiasis, cancer, &c. There are, moreover, cases of idiopathic icterus, which show all the accidents of acute icterus and which are followed by death, without the characteristic lesions of acute yellow atrophy being found at the autopsy. Vulpian and other equally competent observers in pathology have given examples. In the monograph of Frérichs, in 177 cases of acute icterus there are 7 in which the hepatic lesion is absent. This disease presents other incomprehensible characters, as we shall see when studying its pathological physiology. We must, however, admit that we have always found the characteristic lesions of acute yellow atrophy in a great number of subjects who have succumbed to acute idiopathic icterus. In well-observed cases it may be ascertained, during the short duration of the disease, that the liver, at first normal or slightly increased in size, progressively diminishes. At the autopsy, the organ is more or less

atrophied, though it may be nearly normal in size if the disease has lasted a short time. It is always softer than in the physiological state, and its softness is more marked the smaller it is. Its thinned capsule may be pinched up between the fingers. On placing the liver on the post-mortem table, and on taking it between the hands and pressing it, it seems so soft as to deceive one into imagining one has got hold of a semi-fluid mass. Its surface is of a yellow ochre colour, and, on section, the same colour and the same flaccidity are observed. It can be torn with the greatest ease, and on scraping it with a scalpel a cloudy yellowish fluid is obtained. On section, the lobules are not distinguishable from one another, the whole surface being of the same colour. The gall bladder and bile ducts contain very little bile, or a bile slightly coloured and sometimes even transparent.

On examining the opaque fluid obtained by scraping, under the microscope, a small number of liver cells are seen having their normal form and size; some of these are finely granular, and they contain proteic granules, fat, and a considerable quantity of yellow bile pigment. The majority of the cells are much smaller than normally and their edges are thin. Others are broken into fragments having a granular protoplasm and containing fat and bile granules. In some very much softened spots, liver cells can be found which have preserved their physiological form and diameter. The fluid then contains small masses of granulo-fatty pigmented matter, in the midst of which nuclei can always be found. These have in fact become free by the softening of the protoplasm of the cell. Such is the series of lesions of the liver cells, commencing with a cloudy condition and bile infiltration and ending in disintegration and softening. At the same time the peripheral connective tissue of the lobules, and even that which accompanies the capillaries into the lobules, undergoes, according to most observers, an albumino-fibrinous infiltration into which lymph cells are extravasated. This is more particularly the view taken by Frérichs. This inflammation of the peripheral connective tissue of the lobule seems to be the initial lesion of atrophy, according to Winiwarter, who met with it in a case of atrophy in which death took place only twenty-four hours after the commencement of the disease. This author speaks moreover of a similar case quoted by Holm and Hüttenbrenner, in which segmentation of the liver cells led to their changing into connective-tissue cells. This is, we think, an error of interpretation. We have never seen marked thickening or inflammation of the perilobular connective tissue in this

disease. In a case published in the 'Archives de Physiologie,' 1871, describing an autopsy in the wards of M. Sée, one of us saw the network of bile ducts around the hepatic lobules penetrate as far as the external third or even half of the hepatic lobules. This was a case of acute yellow atrophy of rather old standing, in which a very advanced stage of destruction of the liver cells had been reached.

FIG. 129.—BILE DUCTS IN ACUTE YELLOW ATROPHY OF THE LIVER.

o, section of the central vein of a lobule; *l*, atrophied liver cells; *a*, intralobular bile ducts; *b*, interlobular bile canal.

In section, obtained after hardening of the organ in absolute alcohol, these ducts were seen in the midst of a fibroid tissue. The liver cells had completely disappeared, and only the fibro-vascular framework of the lobule remained. As to the bile ducts, they were characterised by the presence of an anhistic membrane around the largest interlobular ducts, and by being lined with small cubic epithelial cells. From these ducts sprang similar ducts in which the membrane was seen with greater difficulty, and which were lined by the same cubic cells, or by flatter cells, which completely filled the lumen of the ducts. These ducts formed a distinct network in all that part of the lobule where the cells had disappeared. These epithelial cells, which contained neither pigment nor fatty granules, stained easily with carmine. They could not be confounded either with trabeculæ of liver cells or with blood vessels. Sabourin, in a case of acute atrophy, published in the 'Revue de Médecine,' July 10, 1882, observed, besides the destruction of the liver cells, an extravasation of leucocytes into the portal spaces and a certain degree of angiocholitis of the interlobular bile ducts. This case may be compared with the pre-

ceding one, but the inflammatory lesions observed in the connective tissue of the portal spaces and in the interlobular bile ducts are far from being constant or frequent, for we have not found them in the many cases of acute yellow atrophy which we have examined during recent years. On examining very delicate sections of a liver which has undergone this change, and on spreading them out and brushing away the free cells with a camel's hair brush, a reticulum is seen formed by the large vessels and capillaries of the lobules, while the liver cells leave empty spaces at the spots where these cells are fragmented or destroyed. At other spots, and often throughout the whole extent of the altered liver, the cells, though granular, infiltrated with pigment, and partly atro-

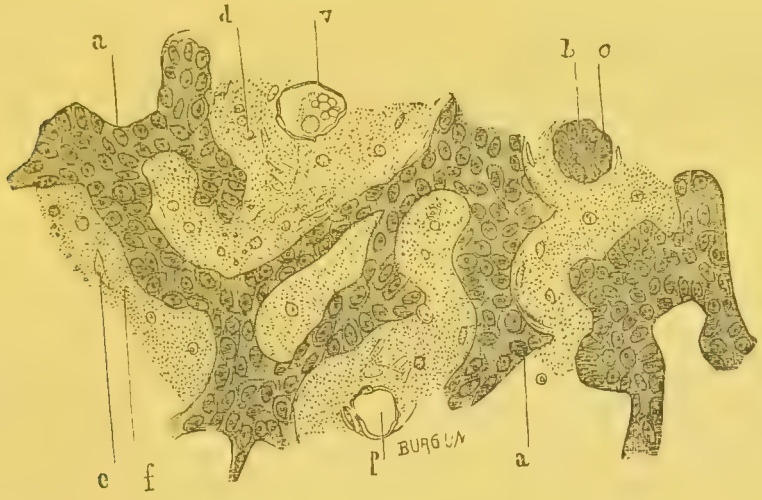

FIG. 130.—BILE DUCT REPRESENTED AT *a* IN THE PRECEDING FIGURE.

The ducts, *a*, filled with epithelium, are situated in the midst of a granular tissue, containing a few cells of embryonic connective tissue and blood vessels: at *b* a transverse section of one of these bile ducts is seen. Magnified 150 diameters.

phied, remain and are not destroyed. In certain cases of acute yellow atrophy the cells, though profoundly altered, granular, infiltrated with bile pigment, and atrophied, are yet found throughout the extent of the lobule. The bile ducts show no change, and the perilobular tissue is neither thickened nor inflamed.

Before attempting to discover the cause of these lesions and their relation to the symptoms observed in acute icterus, we must state the changes of the fluids and the different organs in this disease. The blood is much less rich in red blood corpuscles than in the normal condition. It contains not only a much larger quantity of urea than physiologically, but also other products of incomplete oxidation, proteic matters, leucin, tyrosin, xanthin, &c.

These substances exist in rather considerable quantities in the blood of the general circulation. The same substances exist in the urine, which is sometimes albuminous, and contains less urea than normally, but is stained by the colouring matters of the blood and the bile. Urine coloured by hæmoglobin does not necessarily contain red blood corpuscles. The spleen is invariably tumefied and diffluent. The heart is flaccid, and its muscular tissue is in a state of granulo-fatty degeneration. The kidneys are constantly altered, as is always the case in icterus, that is to say, the epithelial cells of the tubuli are infiltrated in places with the colouring matter of the bile, and the tubes contain hyaline casts filled with granules of bile pigment, and are lined with cells equally pigmented. Moreover, in a considerable number of cases in which albumen has or has not been observed during life, the cells of some of the tubuli of the cortex are in a state of granulo-fatty degeneration ; in other words, subacute catarrhal or parenchymatous nephritis is present.

We will now consider the relation between these divers lesions. The blood contains fewer red blood corpuscles, which is due principally to the fact that they have been in a great measure destroyed by the bile introduced into the general circulation. The blood contains bile colouring matter and the products of incomplete combustion of proteic substances. These may be derived from the profoundly altered liver. The lesions of the spleen and kidney seem to be the consequence of the presence in the blood of a considerable quantity of bile. The accidents of acute icterus have been successively attributed to uræmia, cholæmia, or to the accumulation of cholesterin in the blood (A. Flint); but it is probable that the accidents observed depend on the presence of a single substance, and that acute icterus is a febrile disease caused by microbes. According to the researches of Klebs, Waldeyer, Eppinger,[1] and Balzer, the post-mortem lesions of the liver cells are due to the presence of micrococci.

B. **Poisoning by phosphorus and arsenic.**—Acute idiopathic icterus and acute yellow atrophy may be compared to the parenchymatous hepatitis which is observed in certain cases of poisoning and in acute fevers. The hepatitis due to poisoning by phosphorus is that which most closely resembles them in its anatomical lesions (fatty degeneration and destruction of the liver cells) and in its symptoms, among which icterus, hæmorrhage, and delirium may be principally noted. But in poisoning, fatty degeneration

[1] *Prager Vierteljahrsschr.*, 1875.

of the cells predominates. In the rabbit and guinea-pig, at the commencement of the poisoning, that is within the first twenty-four hours, the liver cells near the portal spaces become swollen and their fluid protoplasm is more considerable than in the normal condition. Soon a few fat granules appear in the protoplasm. The fatty degeneration is most marked at the periphery of the lobules, the cells of which are larger than normally. In delicate sections of specimens, hardened in osmic acid, the lobules are seen to have an areolar appearance, for the tumefied and softened cells of the periphery disintegrate and leave empty spaces in their places. At the end of twenty-four or forty-eight hours the lobules are found to be composed of cells full of fat granules, the cells of the periphery always being larger and fuller of fat than those of the centre of the lobules. This difference is still observed when the degeneration has reached its height, that is to say on the third or fourth day. The cells, in fact, are replaced by large drops of fat, their protoplasm and nuclei having disappeared. In delicate sections of specimens hardened in osmic acid, the capillary vessels are seen to be preserved even in this advanced stage of degeneration, and are separated by masses of fat granules partly disintegrated, while the normal parenchyma of the liver is entirely destroyed. In poisoning by antimony or by arsenic the changes in the liver are comparable to those produced by phosphorus, but are less pronounced.

C. **Parenchymatous hepatitis in infectious fevers.**—The whole series of infectious fevers, such as typhus, yellow fever, typhoid fever, the exanthemata, particularly hæmorrhagic small-pox, scarlatina, erysipelas, pyæmia, septicæmia, &c., the hæmorrhagic icterus of tropical countries, and febrile diseases such as pneumonia, tuberculosis—in all these diseases lesions of parenchymatous hepatitis, comparable to those of acute yellow atrophy, are found, but much less marked, and vary in character and intensity according to the disease. Thus, in hæmorrhagic icterus the liver becomes, according to the few histological data given by naval physicians, first congested and ecchymosed, and finally reaches a condition of fatty degeneration of its cells characterised to the naked eye by a yellowish discolouration. It is the same in yellow fever. Babes recently found microbes in the capillaries of the liver in this disease (*vide* fig. 131). In typhoid fever, in the middle or at the end of the second week, a state of softening of the liver is often observed, which coincides with the acute swelling and lesions of the cells already described. Later, the fatty condition

predominates, and sometimes at the end of the disease, instead of showing an uniform surface, the lobules of the liver are red

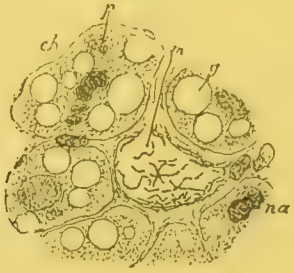

FIG. 131.—SECTION OF THE LIVER IN A CASE OF YELLOW FEVER. (After Babes.)

c h, liver cells; *g*, vacuoles in these cells; *n a*, nuclei; *m*, microbes contained in a capillary. Magnified 600 diameters.

centrally and grey at their periphery. Most cases of parenchymatous hepatitis show a condition resembling that of the liver in typhoid fever. In all slight cases the blood is more or less altered, and catarrhal and parenchymatous nephritis is also found at the same time, accompanied or not by albuminuria. The changes in the blood and hepatic parenchyma observed in the infectious diseases already mentioned are most probably caused by the presence of micro-organisms in the fluids and tissues.

D. **Nodular parenchymatous hepatitis.**—Parenchymatous hepatitis sometimes takes an anatomical form, which has been well described by Kelsch and Kiener[1] in diseases of the liver occasioned by malarial fevers. These authors have given it the name of *nodular parenchymatous hepatitis*, or *nodular epithelial hyperplasia*. It is characterised to the naked eye by small islets or granules of a yellow ochre colour very marked on section of the liver, which is always softened. On microscopic examination these spots are seen to be composed of tumefied hepatic cells, which are granular and multi-nucleated, and which finally become filled with fat granules and disintegrated. A part of a lobule is thus profoundly altered; the trabeculæ, composed of liver cells larger than normally, are thickened and their arrangement altered. Instead of forming lines radiating from a centre, the trabeculæ are irregular, imbricated, and without order. The trabeculæ of liver cells near such a lobule of parenchymatous hepatitis are compressed by it, and become concentrically arranged in consequence of pressure. These nodules of parenchymatous hepatitis greatly resemble in form the

[1] *Arch. de Physiologie*, 1878 and 1879.

lesions which have been described under the name of adenoma of the liver, and which will be found again described in the article devoted to cirrhosis.

Purulent hepatitis.—This form of hepatitis is characterised by the presence of purulent foci, some small and numerous, such as are observed most frequently in temperate climates in purulent infection; others larger, in the form of large collections of pus, are observed principally in tropical countries. The latter are preceded by congestion of the liver, and difficulties in the bile secretion; they are frequently consecutive to dysentery and to intermittent fever. We will consider with purulent hepatitis thrombosis and inflammation of the portal vein and biliary abscesses.

a. **Metastatic abscess of the liver.**—Metastatic abscesses in the liver seem to be always due to transmission of pyæmic microbes by the blood; they are observed in purulent infection caused by injuries, surgical operations, puerperal fever, &c. Small metastatic abscesses are also sometimes observed in typhoid fever, probably as the result of eschars, and in small-pox during the period of suppuration. In most of these cases metastatic abscesses are coexistent with more or less marked parenchymatous hepatitis. In purulent infection with abscess of the liver, the liver is found to be hypertrophied, and on its surface are observed a more or less considerable number of round, irregular, yellowish elevations lifting up Glisson's capsule: some are miliary, others may reach the size of a millet seed or even that of a pea. The largest give evidence of fluctuation and contain fluid pus. On dividing the liver, it is seen to be of a dark red and is highly congested, and yellowish opaque spots are seen on a smooth surface, which on scraping yield a variable quantity of pus. These spots vary in diameter from that of a pin's head to a nut. It is easily seen that the large spots are formed by the confluence of smaller ones, for their edges are sinuous and festooned. Their centre contains pus in a fluid condition, while their periphery is composed of yellow hepatic lobules infiltrated with a small quantity of pus, but not yet completely softened. On carefully examining the lobules with the naked eye, at the commencement of the changes which transform them into miliary abscesses, some of them are seen to be of a dark red colour, as if ecchymosed. In the midst of these lobules a yellow opaque spot is observed, which is either dry or which yields a drop of pus on scraping. Besides these, other spots are found which are quite

yellow and more or less infiltrated with pus. From this cursory examination it may be inferred that an abscess commences in a hepatic lobule which gradually becomes itself converted into a small abscess; microscopic examination of the section confirms this opinion. On examining a preparation containing many spots, one of which is undergoing change, very marked lesions of the vessels and of the trabeculæ of cells will be found in the latter.

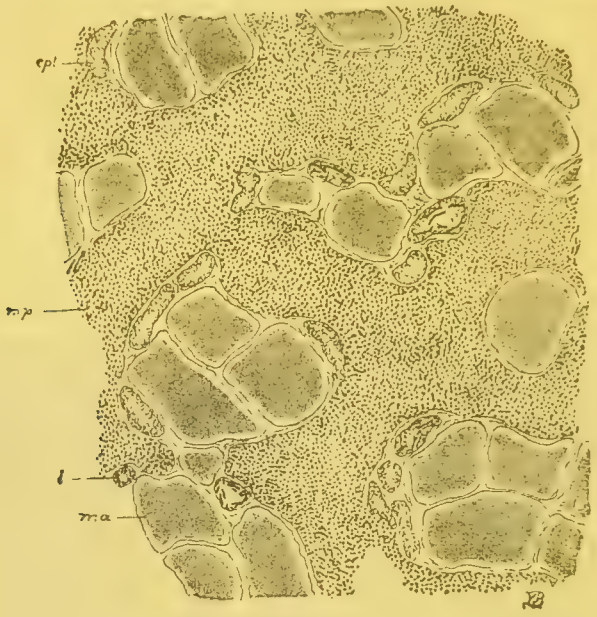

FIG. 132.—SECTION OF THE LIVER IN A CASE OF LEPROSY.

cpl, plasmatic cells showing the leprosy bacilli in their protoplasm; *mp*, capillaries filled with round microbes; *ma*, liver cells in a condition of amyloid degeneration. Magnified 600 diameters.

The capillaries of the spot are more or less filled in places with micrococci collected into zooglea, which are easily shown either by treating an unstained section with acetic acid, or by staining with safranine or B. methyl violet. The capillaries also contain more or less altered leucocytes and a small quantity of red blood corpuscles. At the periphery of the spot along the portal vessels and around the central vein migratory cells may be seen. All the trabeculæ of the liver cells of the diseased spot are pale and granular. They are necrosed, stain badly, and their nuclei are less visible or are destroyed. They finally atrophy and undergo granular disintegration, and their debris, mixing with the migratory cells, forms the puriform fluid with which the spot is infiltrated. Spots in the neighbourhood of those just described present simple congestion of their capillary vessels and inflammation of the perilobular connective tissue, which is shown by the

presence of round cells in the portal spaces. Thus a spot which has been the seat of capillary thrombosis, or of embolism caused by pyæmic micrococci, is changed, after the molecular destruction of the cells which composed it, into a small collection of pus. The connective tissue and the walls of the vessels belonging to this spot soften and rapidly undergo destruction in the midst of the pus. These suppurating spots increase in size by their union with neighbouring foci and form large cavities full of pus. The liver is in general of a yellowish or of a red colour around these purulent foci. The contents of these abscesses is composed of the débris of the liver cells, or of liver cells themselves, which are still recognisable, mixed with leucocytes. In the yellow and

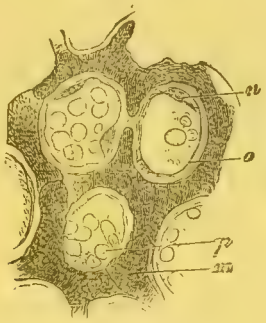

FIG. 133.—SECTION OF THE LIVER THROUGH AN ABSCESS.

m, trabeculæ of liver cells; *o*, wall of a capillary detached from the liver cells and showing endothelial cells, *n*; *p*, white blood corpuscles and fibrin contained in the capillaries.

opaque liver tissue which surrounds the abscesses, either a kind of fatty degeneration of the liver cells is found, or subacute interstitial inflammation of the connective tissue of the portal spaces, or hepatic spots in which all the capillary vessels and sublobular veins are filled with fibrinous coagula, while the trabeculæ of the liver cells are atrophied and necrosed. Thus in a case of metastatic abscess of the liver, consecutive to deep whitlow, the hepatic lobules in the neighbourhood of the abscess were yellow in colour and had preserved their form, but their capillaries and sublobular veins were filled by fibrinous coagula and lymph cells. Between the capillaries dilated by these coagula, the trabeculæ of liver cells were found to be so thin as to have nearly disappeared in places, and the necrosed and atrophied cells were compressed between neighbouring capillaries. It is easily ascertained that the fibrin and the cells are really situated within the capillaries, for the delicate endothelial membrane of these vessels is recognisable. Often also between the wall, *e*, *e* (fig. 134), of the capillaries and the atrophied liver cells, lymph cells, *a*, are found extravasated from

the vessels, and also granular fibrin. The hepatic veins at the centre of the spot and the larger trunks belonging to the sub-

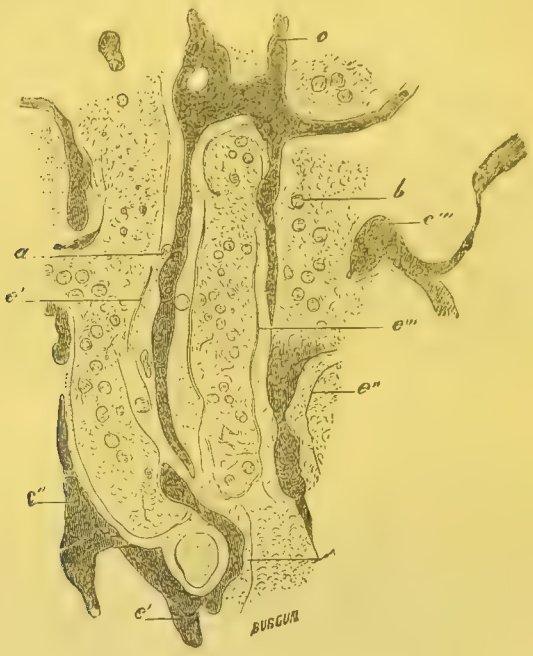

FIG. 134.—A SECTION OF A LIVER IN THE NEIGHBOURHOOD OF AN ABSCESS.

c, *c'*, *c''*, necrosed and compressed liver cells; *e*, *e'*, *e''*, wall of the capillaries; outside of the capillaries leucocytes are seen, *a*, situated between the wall of the capillaries and the hepatic cells; the capillaries are filled with leucocytes and granular fibrin. Magnified 300 diameters.

lobular vein are thrombosed and their walls are equally infiltrated with lymph cells. There is at the same time thrombosis and phlebitis of the portal vein. The interlobular branches of this vein are normal as well as the hepatic arterioles.

Such are the alterations which signalise the commencement of metastatic abscess. It remains now to ascertain the cause and the mode of formation of the abscess. For a long time it was thought, according to the researches of Virchow, that metastatic abscesses of the liver were caused by emboli, and that the fragments of fibrin derived from endocarditis or phlebitis, being carried into the arterioles or capillaries of the liver, produced an infarctus or a small abscess. Independently of the criticisms which we have made of this doctrine in general it was found particularly easy to attack it in the liver. To explain the presence of abscesses in the liver as the result of phlebitis of the limbs, a wound in the head or of the bone, it had to be supposed that clots detached from a peripheral vein passed through the whole course of the pulmonary circulation before returning to the left side

of the heart, and thence passed into the hepatic artery. How could it be explained in such a case that metastatic abscesses were produced in the liver without there being any in the lungs? The doctrine of phlebitis and migratory emboli gave a plausible explanation of abscess of the liver consecutive to inflammation of the radicles of the portal veins, caused, for example, by ulcerative inflammation of the intestine, dysentery, typhus, &c. Later the knowledge of diapedesis was added to this pathogenesis. But Pasteur and Koch [1] have now demonstrated that pyæmia and septicæmia are caused by microbes, which are easily recognised in the spot primarily affected, as well as in the metastasis of pyæmia. These authors also succeeded in isolating and cultivating several species of microbes which may be the cause of pyæmia and septicæmia. In the organs affected by metastatic abscesses micro-organisms are found in the capillaries, and it is probable that they reach the hepatic circulation by means of the general circulation, when the initial lesions are referred to the integument and more particularly to the bones of the skull. They would be conveyed by the portal vein in the case of ulceration of the intestine or of primary lesions of the spleen. The micro-organisms in the capillaries of the liver arrest the blood in the vascular network of one or more lobules. A fibrinous coagulum is formed and the capillaries are plugged with white corpuscles, some of which pass out by diapedesis, while those that remain in the vessels undergo granular degeneration. At the same time the liver cells of the diseased lobule die from inanition, their nuclei become pale, fragmented into granules, and are incapable of being stained, as in the normal condition, by colouring reagents. Such are the lesions caused by transmission of the micro-organisms of pyæmia to the liver. But it must not be thought that all the micro-organisms carried by the blood produce abscesses. The bacilli of anthrax, for example, which are diffused throughout the vascular system of the liver in such large quantities that all the vessels are full of them, do not cause any appreciable lesion in the hepatic cells of the animals affected, and never produce abscess. It is the same with the bacilli of the septicæmia of mice (Koch), and we shall see when treating of the localisation of the bacilli of tuberculosis in the liver that they also have no tendency to form abscesses.

There is not an organ in the body which is more predisposed to form abscesses in purulent infection than the liver, and this more particularly when the focus of primary suppuration is seated

[1] *Ueber die Aetiologie der Wundinfectionskrankheiten.* Leipzig, 1878.

in the bones, and especially in the bones of the skull. What causes this predisposition of the liver to suppuration and its coincidence with wounds of the head is a fact which has struck surgeons of all ages. Magendie tried to explain hepatic suppuration in cases of wounds of the head by the mixing of the blood of the superior vena cava and inferior vena cava in the right auricle, and by the possibility of the reflux of the blood of the superior vena cava into the hepatic vein. This hypothesis is in contradiction of what we know concerning the circulation. But it may be said that the passage of pus elements from a suppurating bone into the vessels is favoured by the arrangement of the osseous veins. It may also be supposed that the lymph cells and microbes contained in the blood accumulate and stagnate by preference at the spots where the circulation is slowest. Now the circulation of the liver, carried on between two veins, cannot but be accomplished slowly. Here may be the cause, not only of the frequency of metastatic abscess in the liver, but also of all other secondary affections—cancer, sarcomata, &c. Such is at least the tolerably satisfactory explanation proposed by Klebs.

From what precedes it may be concluded that thrombosis, inflammation of the external and internal walls of the branches of the portal vein are elements not to be neglected in the study of hepatic abscess; in fact, on the contrary, that thrombosis and phlebitis of the portal vein, or pylophlebitis, are very common and very important. The following are the conditions under which they are observed.

1. **Thrombosis and phlebitis of the portal vein may be consecutive to the formation of metastatic abscesses.**—Take, for example, an abscess composed by the fusion of two, three, or a greater number of miliary abscesses. It may be of the size of a pea or small nut, it is limited by connective tissue and is bounded on one or more points of its periphery by large interlobular branches of the portal vein. Here the connective tissue which formed the external wall of the vein is infiltrated with pus cells, and at this spot periphlebitis arises, thence by continuity endophlebitis, and finally coagulation of the blood in the interior of the vein, that is to say, thrombosis. This infiltration of the peripheral connective tissue of the interlobular veins and the suppuration which is the consequence explain the extension of the abscess to neighbouring parts. Hence we see that thrombosis and periphlebitis are lesions following one another consecutively.

2. **Thrombosis of a branch of the portal vein is sometimes primary,**

resulting, for example, from phlebitis of a branch caused by intestinal ulceration. A fibrinous clot formed in the trunk of the portal vein may become detached and arrested in one of the hepatic branches of this vein, whence results an interruption of the circulation in a more or less considerable group of lobules. Here we have an embolism following from thrombosis of the portal vein. In the part in which the circulation has been arrested there is neither active congestion, nor hæmorrhage, nor pus, as is observed at the commencement of miliary metastatic abscesses; but, on the contrary, a condition of local anæmia in which the part is dryer and greyer than normally, and in which the cells undergo granulo-fatty degeneration. This is simply a case of infarctus, resembling those observed in the spleen and kidney of old persons in atheroma, or in the course of valvular disease of the heart, and these infarctuses do not give origin to abscesses. Similar infarctuses of the liver are extremely rare, which is explained by the fact that when the portal vein is obliterated the hepatic artery continues to nourish the diseased part. In temperate climates, emboli of the portal vein seem to be very rarely the cause of abscesses. But many authors who have studied similar cases in hot countries think that large abscesses may be due to softening and molecular destruction of part of the liver in which the vessels have been obliterated, in which cases inflammation is set up in the parts in contact with the necrosed portion in the same way as large pulmonary cavities follow necrosis of a considerable quantity of caseous pneumonia. Laveran reports cases of large abscesses of the liver observed in Algeria ('Arch. de Phys.' 1879, p. 655) in which the edges of the loss of substance showed the liver cells and lobules in process of destruction. These facts are in favour of the mode of formation of abscesses that we have already described.

3. Purulent inflammation of the portal vein, or pylephlebitis, is rather frequent in temperate climates, so that we have been enabled to study it personally, more particularly from specimens sent us by Maurice Raynaud. In this disease suppuration commences at the centre of the portal vein, the internal coat of which is inflamed. We have then a suppurative endophlebitis. The causes of this form of phlebitis are pretty well known since the researches of Dance, Cruveilhier, Frérichs, &c. It is almost always consecutive to ulcerations of the intestine, particularly the large intestine in typhlitis and dysentery. Sometimes it has been seen to follow abscess of the spleen or phlebitis of the

splenic vein. In one case it was caused by the arrest of a poison which, passing from the stomach or duodenum, had become located in the portal vein. Phlebitis determined in one of the afferent branches was propagated as far as the trunk of the portal vein and its hepatic branches. On opening the trunk of the portal vein it is found to be filled with a fibrinous coagulum, or to be occupied by a purulent focus, which is continued more or less into the trunk and hepatic branches of the same vein. In very serious cases most of the branches are filled with thick pus mixed with a granular fibrin. The calibre of the diseased vessels seems to be large, and at many points of the liver true abscesses are found in the course of veins of medium and small size; they are oval, round, or irregular in shape, and their walls, instead of being formed by the coats of the vein, are simply formed of liver tissue, the vascular wall of the vein having been destroyed by suppuration. To properly examine this condition, specimens are hardened either in alcohol or picric acid or in Müller's fluid, gum and alcohol. On examining delicate sections, cut across the portal vein at a point where it is filled with pus, the internal coat of the vessel is seen to be thickened and infiltrated with lymph cells. The other coats are equally changed. Periphlebitis is propagated to the peripheral connective tissue, the fasciculi of which are separated by lymph cells. Tumefaction of the walls of the veins of the neighbouring connective tissue causes the vein to be considerably increased in size and to compress the hepatic lobules in its neighbourhood. These in fact appear on section to be crescentic in shape, with their concavity turned towards the circumference of the vein. In these compressed lobules the liver cells are flattened according to the direction of pressure. In a larger abscess the internal coat of the vein is destroyed. The middle coat resists rather longer, but it becomes also implicated in its turn and destroyed by suppuration, which is then limited by the inflamed connective tissue of the external coat, or by the surrounding indurated connective tissue of the liver. This suppurative and destructive process of the walls of the vein leads to the formation of abscess, which is limited for a short time by the hepatic lobules. This result is particularly observed at the level of the small branches of the portal vein, for the coats of these veins are here less resisting than in the walls of the larger trunks. Around these abscesses the venous walls are partly preserved or entirely destroyed, and along the branches of the portal vein a new formation of embryonic connective

tissue is always observed, which tissue surrounds the vessels like a sleeve. Also, on examining delicate sections of the liver passing through abscesses or segments of a vein full of pus, it will be observed that the portal spaces are replaced by a zone of connective tissue infiltrated with round cells, in the midst of which tissue pass the portal vein, the hepatic artery, and the bile ducts. Such is the course of abscesses produced by pylephlebitis. To recapitulate, they consist in thrombosis followed by inflammation of the vein, and they terminate by a destructive suppuration, first of the internal coat and then of the other coats, and by the formation of true abscesses situated between the hepatic lobules.

b. **Biliary abscess.**—We include under this name those collections of pus, generally small and disseminated, which have their original seat in the cavity of the interlobular bile ducts, and which ultimately invade the connective tissue or the lobules of the hepatic parenchyma. These abscesses, the characters of which are variable, are generally related to the presence of small calculi or biliary sand in the ducts, and to catarrhal inflammation of the latter. But they may be distinguished from catarrhal inflammation of the bile ducts by reason of the tendency that they show to become isolated from the rest of the bile circulation, and to cause diffuse suppuration around themselves. They are seen under various aspects according to the intensity of the inflammation. In subjects who have died from large calculi, obliterating the hepatic and cystic ducts, or from catarrh of these ducts caused by small calculi or biliary sand, which filled them to the greater part, the hepatic lobules are found to be infiltrated with bile and are of a dark green colour, and small cavities are found in them of about the size of a millet seed or of a nut; these are filled with a muco-pus which is often coloured yellow by the bile. This fluid contains granular leucocytes, besides cylindrical epithelial cells, the characteristic form of which is more or less preserved, and also bile pigment. The walls of these cavities are bounded by embryonic connective tissue. They are segments of bile ducts which have become isolated by the inflammation of their walls; they contain muco-pus and are in process of being transformed into small mucoid cysts. At other times, a calculus, arrested and impacted in an intrahepatic bile duct of medium size, causes ulcerative inflammation in the walls of the duct, and this inflammation, instead of becoming limited, extends to the neighbouring connective tissue, and gives origin to an abscess which may become considerable in size. According to Niemeyer

this may be the origin of most of the large abscesses of the liver in our climate.

In another of these cases relating to single biliary lithiasis, or to biliary hypertrophic cirrhosis, with or without calculi, small

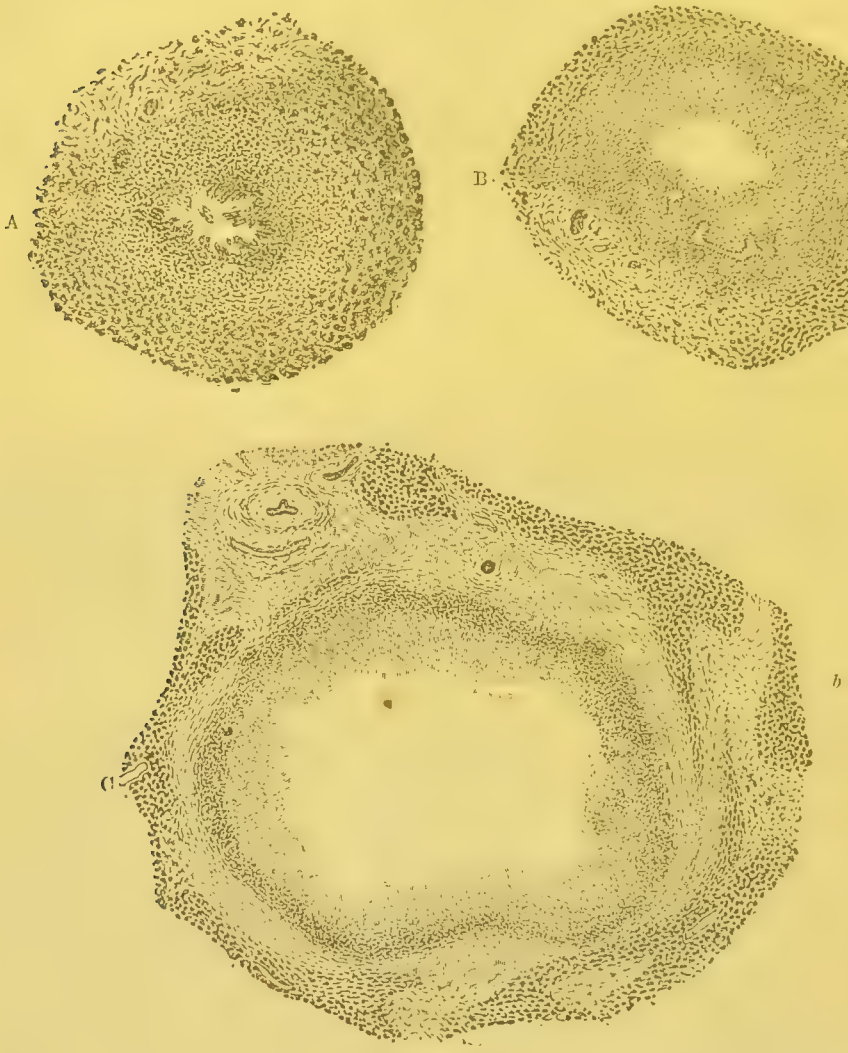

FIG. 135.—SUBACUTE BILIARY ABSCESS OBSERVED IN A CASE OF HYPERTROPHIC CIRRHOSIS.
(After Sabourin.)

A, inflammation of the walls of a bile duct at the commencement of a biliary abscess; the cavities of the duct still contain cylindrical epithelial cells (magnified 40 diameters). B, section of another abscess, the walls of which are infiltrated with small cells, and in which no cylindrical cells are seen (magnified 30 diameters). C, larger abscess, from which the contents, consisting of a magma of pus cells, has fallen out during preparation. The cavity, *a*, of the abscess is lined by a layer of pyogenic pulp, then by connective tissue, and finally by the hepatic lobules, *b*, *b*, which are flattened around it (magnified 30 diameters).

biliary abscesses are found, some of which are hardly visible to the naked eye, while the largest may attain the size of a millet seed.

In delicate sections, one or more layers of quite characteristic cylindrical cells are seen at their centre, then a thick zone of round or lymph cells taking the place of the wall of the bile duct, and of the peripheral connective tissue. Around these small abscesses there is a zone of connective tissue, which separates them from the altered hepatic parenchyma, and which is compressed by them. The section of a larger abscess, for example one measuring one or two millimetres in diameter, shows at the centre a magma formed of round granular cells, which easily falls out on mounting the preparation. The lumen of the abscess is seen to be limited by a zone of embryonic tissue infiltrated with cells of granular pus; around this layer a fibrillar connective tissue is seen, showing a few round cells in its meshes. The wall of the abscess is formed in this case by a pyogenic membrane, showing a certain tendency to become encysted.

Acute biliary abscesses run a different course; they cause acute inflammation ending in diffuse suppuration. They have received the names of miliary, pisiform, lenticular, areolar abscess; they rarely attain to the size of a haricot bean. They are the result of intermittent or permanent obliteration of the bile ducts by calculi. Sometimes they are numerous; thirty, forty, or more may be disseminated in the organ; they may be grouped together, opening into one another, so that they form purulent multilocular foci. They contain pus rendered yellow by mixing with the bile, and are surrounded by a greyish infiltrated softened tissue; they are obviously situated in the interlobular septa of the liver. The hepatic parenchyma is often intact. Malassez, Gombault, Chauffard, and Brault agree in considering that these abscesses result from inflammation of the interlobular biliary ducts accompanied with suppurative inflammation of the connective tissue. In a section made, at its commencement, through one of the smallest abscesses visible to the naked eye, one or more bile canaliculi may be seen having a diameter of from 30 μ to 100 μ, and which still retain their epithelial lining, either normal or proliferated. The canaliculi are bordered, immediately outside their ducts, by round migratory cells, which infiltrate the connective tissue and form an encircling spot of purulent infiltration. In a more advanced stage the connective tissue around the canaliculi softens, owing to the formation of pus; the proper wall of the canaliculi is destroyed, and the leucocytes developed in the connective tissue, mixing with the epithelial cells of the bile ducts, form the pus contained in the centre of the small abscess. It is very easy to follow this process

in all its details in a series of preparations. Beside the abscesses already formed with central cavities transformed into sacs full of broken-up cells, and with anfractuous walls composed of embryonic tissue, small abscesses may also be found in process of formation and visible to the naked eye, in the midst of the inflamed connective tissue which separates the hepatic lobules. These are composed of an islet of embryonic tissue, in the centre of which the biliary canaliculi are found affected with catarrhal inflammation. All successive degrees of the genesis of these abscesses may be observed. The hepatic parenchyma is normal if the abscesses are small and few in number; but around larger or confluent abscesses the hepatic lobules are more or less altered. They are separated by the inflamed, thickened Glisson's capsule, which radiates from the purulent foci. They are compressed and deformed, and their cells undergo secondary changes of nutrition; but the liver cells do not take part in the pathological phenomenon which marks the commencement of the abscess. These abscesses are sometimes seated on the surface of the liver and project. They may even become the point of departure of adhesive peritonitis, and open into the peritoneum (Meckel). Charcot and Gombault have succeeded sometimes in producing them experimentally in animals by ligature of the cystic duct.

c. **Large abscesses of the liver.**—We have hitherto studied the large abscesses of the liver occurring in purulent infection in consequence of pylephlebitis and following inflammation of the bile ducts. We are thus led to study the large abscesses of the liver which may result from the confluence of smaller abscesses of whatever cause, or from the propagation of inflammation to a considerable segment of this organ. Idiopathic abscess of the liver of a large size is rarely seen in temperate climates; Louis, however, collected a number of cases in the hospitals of Paris, and many specimens are annually shown at the Société Anatomique. Are these large abscesses caused by embolism or thrombosis of the portal vein which completely interrupts the circulation at a certain point and cuts off the blood supply of a rather considerable mass of liver tissue? This hypothesis seems to us plausible, particularly in the case of debilitated subjects or those suffering from an infectious disease, and if the blood of the general circulation or that of the portal vein contains the micro-organisms of pyæmia or septicæmia, when it can easily be understood that all that part of the liver belonging to the territory of the thrombosed part of the portal vein would necrose, soften, and become surrounded with a

zone of eliminative purulent inflammation, so that the part deprived of blood and necrosed would finally become transformed into a large abscess. All the causes of small abscesses that we have already studied above may lead to the formation of larger foci: namely, the formation and union of miliary abscesses, pylephlebitis extending to the hepatic tissue, and inflammation of the bile ducts propagated to the perilobular connective tissue and to the liver, intestinal ulceration, dysentery, intermittent fevers, congestion of long duration and faults in the biliary secretion may be the causes of abscess in tropical countries, and the same phenomena may also produce them in temperate climates. An abscess examined at a period near its commencement, whether resulting from the union of many small abscesses and consequently lobulated, or whether caused by the destruction of a considerable part of the liver, has walls more or less irregular in shape composed of hepatic tissue. The thick yellowish and granular pus which it contains is composed of lymph cells and altered liver cells. Pulpy, softened fragments of liver tissue infiltrated with pus may be found adhering to the wall of the abscess. This is the first stage in the formation of the abscess. Later, when all the parts of the liver comprised in the suppuration have become detached and softened, the surface of the sac becomes smoother and is formed of embryonic connective tissue, which is continuous around the abscess into the hepatic parenchyma, following the branches of the portal vein and the interlobular septa. This wall of embryonic tissue is more or less vascular and regular; sometimes it contains actual fleshy granulations. It is then a soft pyogenic membrane, similar to that which lines all ulcers. The abscess may continue to grow by suppurative melting of the pyogenic membrane and of the inflamed connective tissue surrounding it. As this tissue is continuous with the peripheral connective-tissue coat of the portal vein, phlebitis is, as we have said, always present, and also generally endophlebitis, with formation of a fibrinous clot at the inflamed spot in the vein. These peripheral parts may be completely destroyed by suppuration, so that the abscess increases by lateral growth following the branches of the portal vein. It is thus easily seen how phlebitis following abscess becomes suppurative and may in its turn become the point of departure of one or more secondary abscesses near to the first. The internal wall of the abscess is grey or reddish grey. Cruveilhier states having seen gangrenous abscesses. It is possible that actual gangrene, caused by the interruption of the course of the blood, may be observed at the

commencement of one of the latter periods of these abscesses; but one must be on one's guard regarding the changes of colour noticed in the connective tissue and liver tissue surrounding these abscesses. Slate colour, greenish discolouration, &c., of the wall of the abscess is often the result of cadaveric decomposition. When the abscess ceases to extend, the pyogenic membrane becomes smoother and more fibrous, and the surrounding connective tissue thickens and becomes denser. Thus an actual fibrous membrane which is thick and solid is produced, circumscribing an encysted abscess. These abscesses vary in colour; they may be brown, yellow, or chocolate, according as they contain more or less blood and as the lymph cells are infiltrated with fat granules. All parts of the liver may be the seat of these large abscesses, but they are more particularly found in the right lobe, and particularly in the thickest part of that lobe, that is to say, in its extreme right lobe or on its superior surface in the neighbourhood of the diaphragm; but they are also sometimes found on its inferior surface. They have, like every other fluid collection, a tendency to take a spherical form when old. The liver tissue allows, as we know, of being easily pushed back and flattened by pressure of the abscess, and the latter tends, by its growth and the flattening of the liver, to approach the external surface of this organ. The size and number of these abscesses vary greatly; the largest are generally solitary. They may contain from one hundred grammes to one litre or even two litres of fluid. Owing to its tendency to approach the periphery of the liver, an abscess may open spontaneously; generally they point towards the upper surface of the liver near the diaphragm or at the level of the edge of the false ribs, a little above or in contact with the abdominal walls. When brought into contact with the peritoneum, they produce a local adhesive peritonitis, and their presence is revealed by œdema of the abdominal or thoracic walls and by the sensation of fluctuation. If the abscess should open into the connective tissue of the abdominal wall, the pus may find its way along the denuded false ribs, and may extend as far as the axilla or the internal part of the thorax. Such collections of pus should be opened at once, or if the diagnosis is thoroughly made out adhesive peritonitis may be induced and the abscess opened by means of Vienna caustic. When the abscess points towards the diaphragm, which it pushes upwards, adhesive peritonitis may be produced under the diaphragm and an equally adhesive pleurisy above with pneumonia at the same spot, so that if the pus is discharged after suppurative destruction of

the diaphragm, the pleura, and the inflamed lung, it may be expectorated from the bronchi. This termination, as well as that of opening into the abdominal wall, are the most favourable. But if instead of causing adhesive pleurisy the abscess of the liver sets up pleurisy with an abundant secretion, it would empty itself into the cavity of the pleura after perforating the diaphragm. This purulent pleurisy may itself be accompanied with pneumonia, and perforation of the lung at a certain point, by means of which the pus may be evacuated. But this result is serious if a pleuritic sac is left which is incompletely emptied, and often leads to a fistula between the diaphragm and the liver. These various cavities contain blood-stained fluid and gases, and the same sounds are heard as in pyopneumo-thorax. The various ways by which abscesses may open are into the peritoneum, whence results a peritonitis which is generally fatal; into the stomach, the duodenum, and the colon, the perforation of which is generally of considerable size. They may also, though very rarely, open into the pericardium, causing instantaneous death, or into the bile ducts or gall bladder, which is the best method of evacuation, for then the pus slowly drains away by a natural route into the intestine. Finally, the liver is sometimes ulcerated, when it forms the base of an ulcer of the stomach. The tissue is then digested at this spot by the gastric juice, and a loss of substance is produced. The trabeculæ of connective tissue which pass from the base of the ulcer around the hepatic lobules are hypertrophied, whence results a kind of localised cirrhosis in the neighbourhood of the ulceration.

Interstitial hepatitis or cirrhosis.—Interstitial hepatitis or cirrhosis is anatomically characterised by a new formation of embryonic or adult connective tissue, at the expense of the cellulo-vascular tissue of the organ. The liver is very markedly indurated, sometimes hypertrophied, and is almost always granular on its surface. Cirrhosis was certainly known to Bichat, as is proved in many passages in his 'Anatomie Générale' and a brief description given by him in his last course of pathological anatomy. But it was Laennec who first gave a complete description of the disease and gave it its name—an unfortunate name, for it expresses merely the discolouration of the liver, a condition which is by no means constant, and which indicates only an accessory state, the fatty degeneration with pigmentation of the cells, while the essential hepatic lesion is thickening of the connective tissue.

The disease would be better designated by the name of *sclerosis*. The general opinion of Laennec on cirrhosis is still more incorrect, for according to him it was an accidental condition without analogy in the economy, a kind of parasitic growth resembling scirrhous or encephaloid tumours, &c. Thus he supposed that cirrhoses might be developed in other organs than the liver. Boulland, Andral, &c., had no difficulty in demonstrating that cirrhosis consisted in a change of the substance of the gland; but their theories of cirrhosis were invalidated by the ideas of the time on the structure of the liver. According to Andral the yellow granules of the liver resulted from hypertrophy of the yellow substance of the liver. Kiernan was the first to demonstrate the hyperplasia of the cellular tissue of the liver in cirrhosis. The descriptions of Rokitansky, Cruveilhier, Requin, Gubler, Frérichs, the discovery of the accessory portal veins by Sappey, and the more recent investigations of histology have completed the study of this disease. For the last ten years it has been the subject of numerous researches, published principally in France, and a number of varieties have been distinguished in the disease. Requin has described hypertrophic cirrhosis. Icterus is a rather rare phenomenon in atrophic cirrhosis; it is, on the contrary, rather frequent in hypertrophic cirrhosis. The condition of the bile ducts has been particularly examined in the latter. One of us discovered that the bands of connective tissue of new formation which surround the islets of cirrhosis are intersected by a considerable number of microscopic interlobular bile ducts. Hanot described these lesions in his inaugural thesis, and insisted that the seat of chronic inflammation was around the perilobular bile ducts. The experiments of Wickham Legg, Charcot, and Gombault have shown that actual cirrhosis may be caused by ligature of the cystic duct, and that chronic inflammation is propagated to the excretory bile ducts by the interlobular ducts. Grouping these lesions together, a new form of cirrhosis, called biliary cirrhosis, was discovered, but which for some time was confounded with hypertrophic cirrhosis. But the problem is not so simple, as we shall see when studying large cirrhotic livers.

Since then distinct varieties of fatty hypertrophic cirrhosis have been described (Hutinel and Sabourin). Kelsch and Kiener have very carefully studied the changes of the liver in malarial fevers, and have elucidated the hitherto obscure question of adenoma of the liver, a description of which lesion will be given after cirrhosis, in which we shall make particular use of the thesis

of Sabourin on this subject. The changes in the trabeculæ of the liver cells and islets, known now under the name of adenoma, are, in fact, observed in cirrhotic livers, and are so intimately related to cirrhosis that they seem to be a complication of this disease, from which it is difficult to separate them. Varieties of atrophic cirrhosis may be distinguished, according to their clinical course and their pathological anatomy. Such is atrophic cirrhosis with fatty degeneration, described by Hanot, which differs by its rapid course from common atrophic cirrhosis, the evolution of which is generally slow. Finally, Sabourin has quite lately attempted to determine the topography of the lesions, and particularly the seat of the bands of new connective tissue, which circumscribe the lobules in cirrhosis, and he has discovered that this connective tissue is found along the hepatic veins, in the centre of the hepatic lobules, as well as along the branches of the portal vein. He has in consequence given a new description of cirrhosis according to these varieties of location.

From this rapid sketch of the principal publications of which cirrhosis has recently been the subject, it is easily understood how in this disease the lesions of the liver vary according to their extent, their distribution, as well as their cause. Cirrhosis may, like every other disease, pursue a slow course, its intensity being more or less modified by the cause, the nature of this cause, the constitution of the subject, and the various lesions which complicate it. Also on examining various specimens of cirrhotic liver with the naked eye, they will be seen to differ markedly in colour, form, dimensions of the organ, and in most of the physical characters; the liver may, for example, be considerably hypertrophied, or on the contrary shrunken and in the last stage of atrophy. Its surface may be smooth or granular, more or less dented or regularly lobular. On section, the organ may show granules or islets, sometimes red, sometimes leather-coloured, sometimes of a yellowish green or of a dark green; in diameter these islets may be irregularly small, or more or less large. In spite of the apparent diversity of these lesions, due particularly to the state of the liver cells which have undergone various processes of degeneration, these cases may be grouped under one common name, for they have as an essential lesion a new formation of connective tissue around the branches of the portal vein and the intra- and extra-lobular hepatic veins, and also a profound change in the circulation of the liver, a change which ends in increase of blood pressure in the various branches of the portal system and in ascites. We will first divide

cirrhosis into partial and generalised. The first is the sequela of tumours and various lesions primarily developed in the liver; the second, which properly constitutes cirrhosis, presents many varieties. We will first give a general description, including what these forms of cirrhosis have in common, that is to say, the new formation of connective tissue; then we will pass in review their varieties—hypertrophic and atrophic—and their complications.

Partial cirrhosis.—Interstitial hepatitis is a secondary lesion of tumours and other affections of the liver. It is then partial, or more frequently may be even very limited. Thus all tumours composed of a tissue similar to fibrous tissue—tubercle, gummata, fibrous cysts developed around hydatids, abscesses, calcareous cysts, angiomata, serous cysts, carcinomata, sarcomata, &c.—are always surrounded by connective tissue of new formation, which is continuous into the interlobular septa. When, as sometimes takes place, miliary hepatic tubercles or small gummata in the newly born become generalised, there naturally follows a kind of cirrhosis which is equally co-extensive to most parts of the organ. In certain chronic inflammatory lesions of the bile ducts or of the portal vessels, the connective tissue which accompanies them is at the same time chronically inflamed and thickened. This is what occurs in the inflammation caused by calculi of the bile ducts, in pylephlebitis, &c. With partial cirrhosis must be grouped those malformations of the liver which accompany the cicatricial thickening of Glisson's capsule. Such are the lesions caused by pressure in tight lacing, of which evil practice we have already spoken. By confining the base of the thorax, the corset depresses the liver and pushes the edge of the ribs against the inferior part of the convex surface of this organ. This pressure ends in causing thickening of Glisson's capsule and a more or less regular cicatricial depression extending transversely from right to left, following the anterior surface of the liver. Above this depression the anterior edge of the liver is generally turned forwards. At the same time the gland is pressed from before backwards and undergoes a transverse pressure, which is shown by little vertical folds over the whole of its convex surface. Senile osteomalacia and malformations of the thorax are shown by cicatrices on the anterior surface of the liver, and by the change of position of its anterior edge. Beneath the much thickened fibrous capsule the hepatic islets are atrophied, flattened, and separated by fibrous trabeculæ which are continuous with Glisson's capsule.

Cirrhosis generalised throughout the liver. General description. Gross appearances.—The surface of a cirrhotic liver, whether normal in size, hypertrophied or atrophied, is generally granular. These granules, which project under Glisson's capsule, vary in size, sometimes being smaller than the normal lobules of the liver, sometimes larger, the size of a lentil or even of a small pea. They are generally unequal, small granulations being found as well as much larger ones. They are round and covered by the thickened Glisson's capsule, which pushes itself between them into the crevices separating them and shows considerable thickening. This latter forms bands or hard fibrous surfaces, at the level of which, if carefully looked for, small or granular projections are seen which have the appearance of shagreen skin. Frequently cicatricial thickening of the capsule limits large irregular lobules, so that certain parts of the liver have a mammillated, budding appearance. On incising the capsule for some distance and detaching it, a thin layer of adherent liver is removed and the granules are exposed. On section, the liver is seen to be granular, the islets of cirrhosis being generally quite limited and round. They are separated from one another by distinct zones, which are sometimes red or pink, but more often grey and semi-transparent; these zones may be thin or thick in substance and are continuous with the superficial grooves of Glisson's capsule. They are composed of a fibrous resistant tissue. The colour of these islets of liver substance surrounded by fibrous tissue varies. It is sometimes red or reddish yellow, sometimes liver-coloured or of a greenish yellow or dark green. The morbid liver is much denser and more resistant than normally, and a sensation of hardness is felt on pressing it between the fingers. On dividing it, the surface is smooth, and on removing a solid fragment with the scalpel, its edges are seen to be firm and rectilineal. On trying to indent the tissue with the nail, a quite abnormal resistance is felt, as if a fibrous tumour or a myoma were under examination. Fragments of cirrhotic liver are elastic and resistant to traction and cannot be torn into fragments like the normal liver. When the liver is highly cirrhotic and the fibrous tissue is present in great abundance, it resists the scalpel, and with the naked eye large trabeculæ and islets of a semi-transparent fibrous tissue are seen which are comparable to the fibrous tissue of the cornea. From these various characteristics it is always easy to recognise the appearance of cirrhosis with the naked eye. In spite of these profound changes in the parenchyma of the liver, the large vessels and the gall bladder have not generally undergone

a marked change. Thus the bile preserves its almost normal appearance, though it is more watery and less coloured than in the physiological condition. It is secreted in considerable quantity, a fact which struck Bichat, in the tumours of the liver, which he called by the name of steatomata, and which have always been carefully noted by all observers in cirrhosis. The bile ducts, however, which are visible to the naked eye between the lobules, may be dilated in places. Gubler has insisted on this dilatation of the bile ducts, which he has compared to dilatation of the bronchi in cirrhosis of the lung or interstitial pneumonia. The ducts, instead of being dilated, may be narrowed by the cicatricial tissue, whence results retention of the bile in the small interlobular ducts and in the hepatic lobules.

Microscopic examination.—We have seen that the naked-eye examination of sections of cirrhotic liver enables one to distinguish more or less voluminous islets of hepatic parenchyma circumscribed by fibrous trabeculæ. In certain livers the islets or granulations of cirrhosis are all equal, in which cases it is said to be an instance of *monolobular cirrhosis*. In others the islets are unequal and generally very large; this is *multilobular cirrhosis*. By these designations it is indicated, incorrectly we consider, that the granules of monolobular cirrhosis each represent a hepatic lobule, while those of multilobular cirrhosis correspond to many lobules. It will be necessary to first determine to what parts of the normal liver these islets of monolobular and multilobular cirrhosis correspond. With this object in view very large sections of cirrhotic liver should be examined under a low power, after staining with picro-carminate. In preparations of typical and long-standing monolobular cirrhosis, taken, for example, from a case of atrophic cirrhosis, it is seen that the round islets are composed of hepatic cells arranged without order, and do not in the least recall the typical arrangement of the radiating trabeculæ observed in the normal condition. These islets, the diameter of which is nearly equal or rather less than the normal lobules, are entirely surrounded by thick bands of fibrous tissue, in which the blood vessels which belong to the venous system may be recognised; the walls of these vessels are thickened and chronically inflamed. After this cursory examination it might be thought that we have here simply normal lobules surrounded by considerable thickening of the connective tissue, which normally accompanies the interlobular portal branches, and that an islet of cirrhotic liver therefore corresponds exactly to a modified hepatic lobule. At the centre of this hepatic islet

we find, however, no vestige of the intra-lobular vein, which always exists at the centre of a normal hepatic lobule, and the trabeculæ which radiate from the central vein cannot also be discovered. The researches of Sabourin on the topography of cirrhosis, and the part which the hepatic venous system plays in this disease, perfectly explain this double anomaly. According to Sabourin the islets of monolobular cirrhosis are caused by disasso-

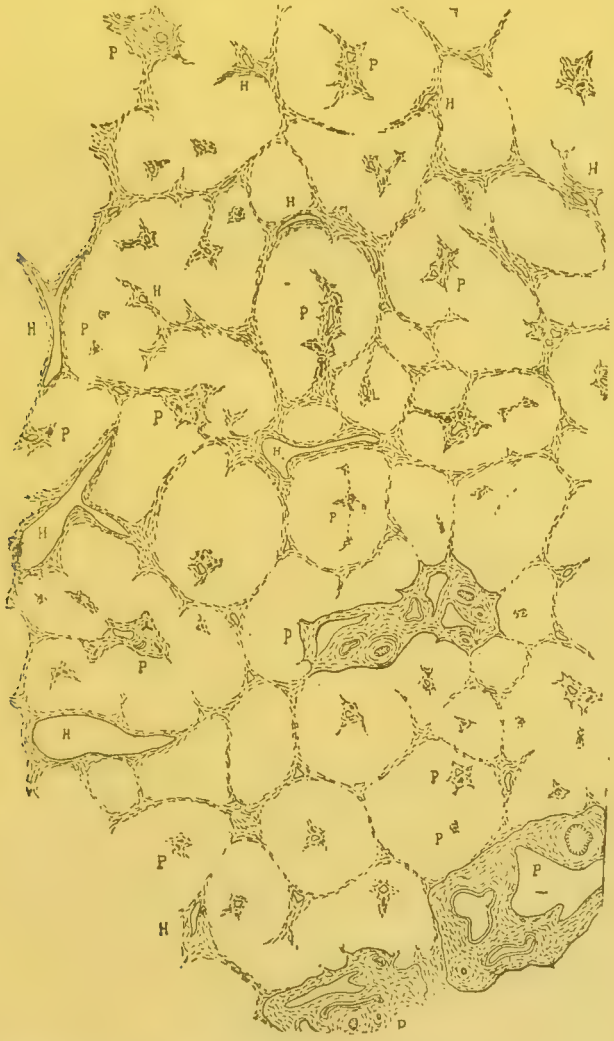

FIG. 136.—SECTION OF A LIVER AFFECTED WITH CIRRHOSIS AT ITS COMMENCEMENT. (After Sabourin.)

Around the sections of the hepatic veins, H, H, are seen the fibrous tracts which circumscribe islets of liver cells. At the centre of these islets sections of portal spaces, P, P, may often be seen. At the right and the lower part of the figure may be seen a rather large portal space with its bile ducts. Magnified 12 diameters.

ciation of the primary lobules of the normal liver and by bands of fibrous tissue, which follow simultaneously the branches of the

portal vein and those of the hepatic veins. To be convinced of this, sections of monolobular cirrhosis should be examined at its commencement. Such specimens can be obtained from alcoholic subjects who have accidentally succumbed to an intercurrent disease, acute pneumonia for example. The two figures 136 and 137 illustrate similar cases. In these figures, drawn under a very low power, may be seen the two great systems of fibrous trabeculæ which divide the hepatic parenchyma; one circumportal, P, the other circum-hepatic, H.

The first is characterised by the presence of bile ducts and branches of the hepatic artery which accompany the branches of the portal vein, while none may be seen in the fibrous tissue which surrounds the branches of the hepatic veins and the central veins of the islets. These two systems often communicate with one another by fibrous tissue which unites them by anastomoses. Thus the connective tissue of the portal spaces sends bands which unite it to the annular system of the hepatic veins. Portions of the parenchyma which primarily belong to a normal lobule, and to many normal lobules, are consequently sur-

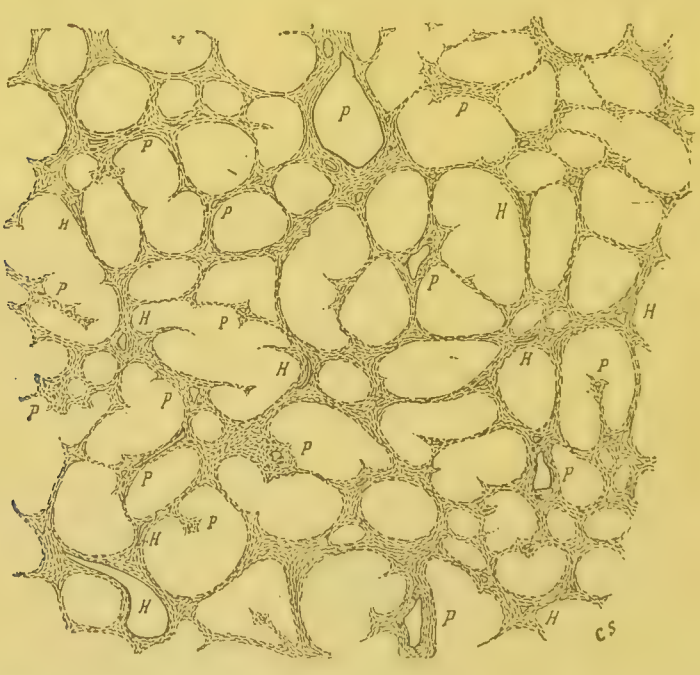

FIG. 137.—SECTION OF THE LIVER IN A CASE OF MONOLOBULAR CIRRHOSIS. (After Sabourin.)

H, H, fibrous trabeculæ surrounding the hepatic veins; *p*, *p*, trabeculæ of the same kind surrounding the branches of the portal vein. Magnified 12 diameters.

rounded by bands which are derived simultaneously from the portal spaces and the thickened connective tissue which accompanies the

hepatic veins. If circum-hepatic fibrous trabeculæ predominate at a point, they may even circumscribe a portion of the parenchyma, in the midst of which will be found a portion of the portal vein with its bile ducts.

As the cirrhosis increases and causes the formation of still larger quantities of new connective tissue, the fibrous bands derived from the portal vein and hepatic vein become thicker, and they form a complete envelope around the islets of cells, and thus it is how lobules of cirrhosis are formed. It is easily understood how the islets cease to show the central vein, and why the liver cells which compose them do not present their usual trabecular arrangement.

In multilobular cirrhosis, we consider that the prominences observed on the surface of the liver beneath Glisson's capsule, in

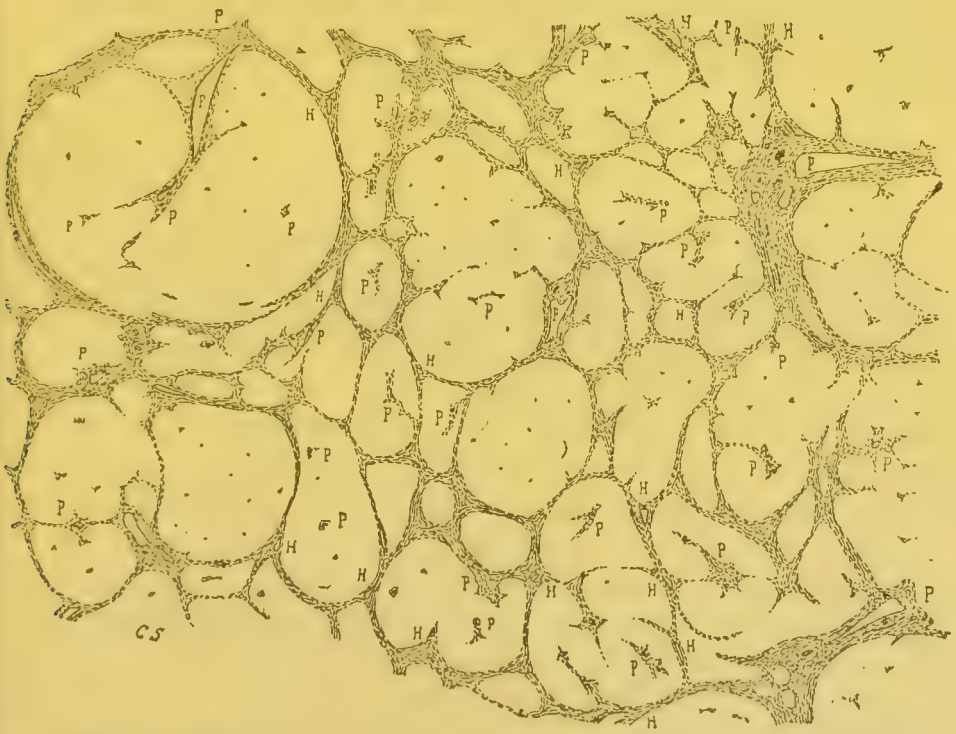

FIG. 138.—SECTION OF THE LIVER IN A CASE OF MULTILOBULAR CIRRHOSIS. (After Sabourin.)

H, H, fibrous trabeculæ developed around the hepatic veins; P, P, trabeculæ developed around the branches of the portal vein. Magnified 12 diameters.

the form of small round grains the size of a lentil or small pea on section, are the result of the union of many lobules surrounded by a common fibrous capsule belonging to the fibrous tissue which accompanies the portal veins. But this is not entirely correct according to Sabourin. The thickened fibrous tissue around the

hepatic veins takes at least as large a part in the formation of this capsule as that of the portal veins. The large islets of monolobular cirrhosis seem at first to be formed by a homogeneous hepatic tissue; they are generally spherical, and on studying them with the naked eye it is seen that they have contracted no intimate adherence with the fibrous membrane which contains them, so that they can easily be separated from it, which is impossible in the case of monolobular cirrhosis. Sections of these islets examined under the microscope appear at first to be divided by fibrous trabeculæ, which cut them up into round segments, and these trabeculæ seem to be continuous with the common envelope, only that the common fibrous shell is much thicker and more resistant than the secondary structure. Each of the large granules is then composed of small islets enclosed in single fibrous envelopes. In small sections of the liver examined under the microscope with a low power, it is seen that the centre is composed of the connective tissue which accompanies either the branches of the portal vein or many branches of the hepatic vein united by fibrous trabeculæ. Between the affected vascular territories a variable number of branches of the portal vein and hepatic vein remain intact, which tracts correspond to the secondary islets, and which by uniting together constitute the large granulations of multilobular cirrhosis. The cirrhotic liver, whether hypertrophied or atrophied, may be wholly composed of these large granulations, but besides them others may be found varying in size or quite small. Having now studied the topographical arrangement of the islets of monolobular and perilobular cirrhosis, we will examine the minute changes which the various elements undergo.

Lesions of the connective tissue.—Thickening of the connective tissue constitutes the essential characteristic of this disease. It is the connective tissue which accompanies the portal vein and the hepatic vein which is chiefly altered. As this lesion is almost always caused by abuse of alcohol, it may be supposed that the passage and arrest of alcohol in the blood of the portal vein and the liver are the causes of chronic inflammation of the connective tissue which surrounds these vessels. The inflamed connective tissue is composed of fibrils, between which are found, in certain cases of cirrhosis at the commencement, a rather considerable quantity of migratory round cells, or fusiform cells (fig. 139). When the connective tissue becomes completely organised these fibrils thicken and form fasciculæ, semi-transparent, homogeneous,

and hyaline, and the cells which separate them flatten as in adult connective tissue. All the changes of connective tissue, all the intermediate steps between embryonic tissue and adult or cicatricial tissue, may be observed in cirrhosis. It must not, however, be thought that these changes in the connective tissue are always in direct relation with the period which has been presumed to be the commencement of the disease. Thus in hypertrophic cirrhosis, which may have lasted one or two years, masses of embryonic tissue may be found, whilst in the liver of a man who may have died accidentally of an intercurrent disease, and who had never shown imminent symptoms of cirrhosis, may be found thickened interlobular trabeculæ formed of large fibrous fasciculi interspersed with flat cells. The disease varies in fact according to the sub-

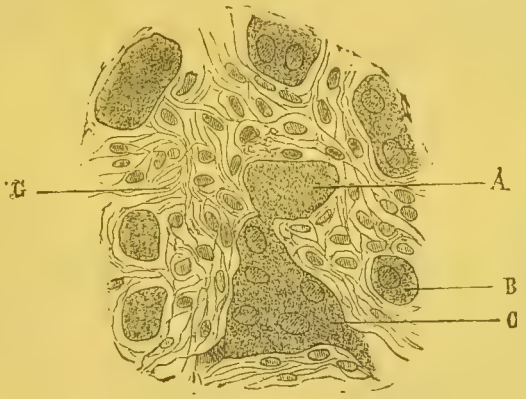

FIG. 139.—DIFFUSED SYPHILITIC INTERSTITIAL HEPATITIS.
A, C, network of hepatic cells in a state of fatty degeneration; B, isolated hepatic cell; G, new connective tissue. Magnified 300 diameters.

jects and the sensitiveness of their tissues to alcoholic intoxication, and according to the continuity or intermittence of the intoxication. It will easily be understood that the connective tissue of the liver may be acutely inflamed in one case or very slightly inflamed in another, so that chronic cirrhosis may be established silently and may increase with extreme slowness in certain individuals. The fibrous tissue of the vessels belonging to the portal veins and the hepatic vein and the bile ducts also undergoes considerable change.

Lesions of Glisson's capsule and of the peritoneum.—We have said that Glisson's capsule is always thickened, adherent, and difficult to detach, and that these changes are particularly well marked at the depressions and grooves which separate the lobules. Cicatrices of the capsule are never so deep or hard and ramified in cirrhosis as those present in gummata. The peritoneum around

the liver is very seldom intact in well-marked hypertrophic or atrophic cirrhosis. Sometimes the perihepatitis being slightly marked, small granulations, hardly visible to the naked eye, or villous filaments, are found on the surface of the liver, particularly in the interlobular depressions. At other times, lamellar fibrous false membranes are found, which float freely on the surface of the liver, or which adhere to the diaphragm or neighbouring organs. At other times, again, these false membranes are covered with fibrin, which floats in the fluid of ascites. More or less acute peritonitis may become general and lead-coloured or black ecchymosis may be produced in the peritoneum. On microscopically examining a section of Glisson's capsule which passes perpendicularly through the vegetations on the peritoneum, the first thing observed is thickening of the capsule. On studying the structure of these vegetations it is seen that they are sometimes sessile and end by an enlargement (see *f*, fig. 140), sometimes long and thin, dividing and subdividing with a free extremity, or attached to neighbouring growths. The growths examined under a high power appear to be composed of fasciculi of connective tissue, separated by flat cells; some of them are more delicate, and are formed by a long and thin fasciculus. Most of the large growths contain vessels; the smaller growths do not always have them. They are all lined by epithelial cells, which may be seen in masses or thick layers on the surface of the growth. The cells are more tumefied, and their protoplasm more considerable and more granular than those of the normal cells of the peritoneum. They resemble the large epithelial cells of an inflamed peritoneum. The vessels of these vegetations are easily injected by way of the portal vein. It may therefore be thought that by becoming the point of departure of adhesions with neighbouring organs they may aid the return of the blood to the heart by collateral channels.

State of the blood vessels and circulation in cirrhosis.—In recent cases of cirrhosis with formation of embryonic tissue, the interlobular branches of the portal vein and the hepatic veins are surrounded by round cells, and the external coat of their walls is infiltrated with similar cells, which are present in rather considerable numbers; in the cirrhotic islet, the connective tissue which accompanies the capillaries is sometimes sprinkled over with the same elements. The capillaries and small blood vessels undergo the same changes as in inflammation. The cells forming their walls tumefy, become embryonic, and the tissue soft and friable. The extra- and intra-lobular portal vessels, and the small branches

of the hepatic artery which are situated in the midst of connective tissue of recent cirrhosis, or in embryonic tissue, may become so

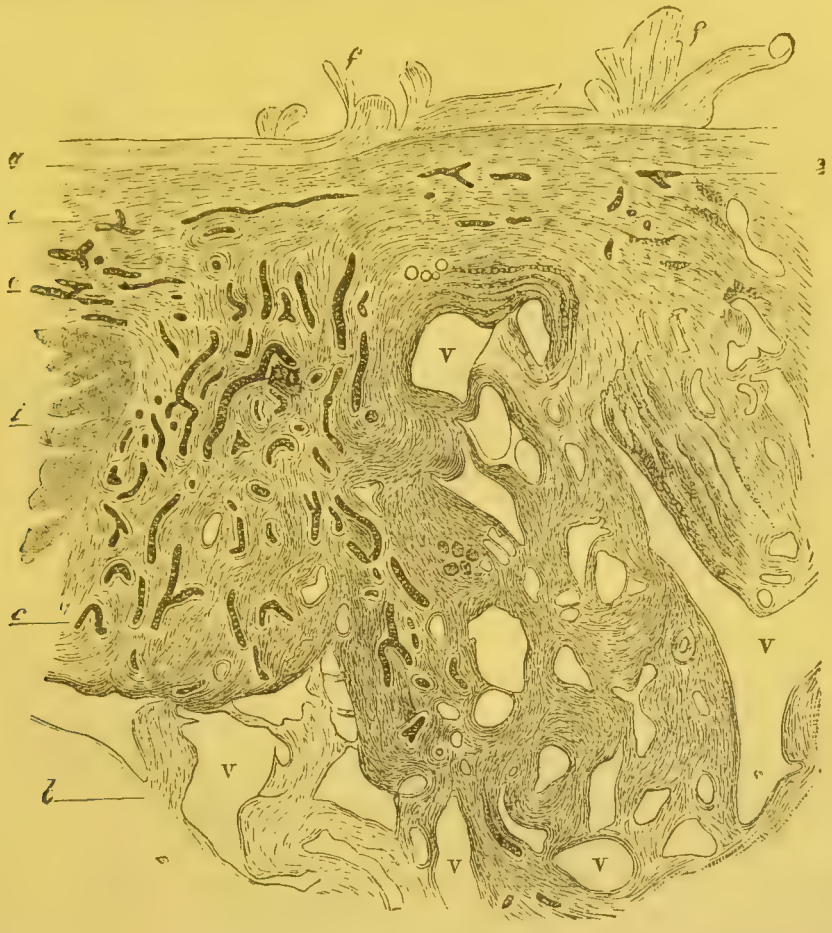

FIG. 140.—HYPERTROPHIC CIRRHOSIS.

f, *f*, growth on the peritoneum, *a*, and Glisson's capsule; *i*, a part of a hepatic lobule. The whole of the figure represents connective tissue intersected by bile ducts, *c*, and capillary vessels enormously dilated, *v*. Magnified 40 diameters.

considerably dilated as to resemble erectile tumours. One of us observed a case of this kind in May 1873 ('Arch. de Phys.,' Nov. 1873) in a subject who died in one of M. Sée's wards. This was a case of hypertrophic cirrhosis, which hypertrophy affected particularly the whole mass of the connective tissue and the newly-formed embryonic tissue. In the sclerosed part of the liver, which was infiltrated with blood, the capillaries were seen to be enormously dilated and anastomosing with one another, and at certain spots an actual cavernous tissue was found, the large irregular lacunæ of which were filled with blood. The walls of these cavities and vessels were simply formed of neighbouring connective tissue, and they

were lined internally by a layer of endothelial cells. The same lesion was found in a certain number of lobules and throughout their whole extent. The capillaries of the lobule, dilated and full of blood, had by pressure induced atrophy of the liver cells, which had become fatty and small. There could be no doubt that the softness of the new embryonic tissue had favoured these dilatations. The branches of the portal vein and the hepatic artery were in fact permeable to blood, while the circulation being impeded in the capillaries of the lobule, the blood pressure had distended the smallest still permeable vessels. Dilatation of the vessels is not uncommon in cirrhosis, but it is rarely carried to such a high degree as in the preceding case. Later on, when the cirrhotic tissue has become dense and resistant, it is still intersected by very numerous blood vessels of large diameter and with walls formed solely of the surrounding connective tissue. These are channels hollowed in the indurated connective tissue, the walls of which, modified at first by inflammation, become blended with the surrounding tissue and one with it. In the walls of the interlobular branches of the portal vein the contractile and elastic elements intended to propel the blood into the capillaries are no longer to be found, nor the soft cellular zone around the vessel which permits of alternate contraction and dilatation; its external as well as its middle coat are wanting, a layer of endothelial cells alone remains lining a channel which is neither elastic nor contractile. While the branches of the portal vein are thus altered, the hepatic veins are not less modified in chronic cirrhosis, particularly in atrophic cirrhosis. Sabourin has, in fact, found that they show many forms of endophlebitis (*vide* fig. 144) and phlebitis.

Sometimes in obliquely dividing a hepatic vein surrounded by fibrous tissue a cicatricial line is seen at the centre, which shows that the lumen of the vessel has disappeared. The internal coat, tumefied and chronically inflamed, has filled up the lumen of the vessel. When long-standing phlebitis has terminated, by positive obliteration, only a round mass of fibrous tissue is seen on transverse section of the veins, and on longitudinal section a fasciculus of the same tissue. Sometimes after phlebitis, which has affected all the coats of the vessel, more particularly the internal coat, the thrombus may become organised, and become later on intersected by a new network of capillaries and lacunæ in which an incomplete circulation is re-established (*vide* figs. 141 and 143). Transverse sections of these vessels show at their periphery a large and rather regular circle, dark-coloured and undulating, in which fibrous

fasciculæ and smooth muscle cells are found. Inside this circle a fibrillar tissue is seen sprinkled over with connective-tissue cells, in the midst of which lacunæ are found lined by endothelial cells and containing normal blood corpuscles. Sometimes large sinuses

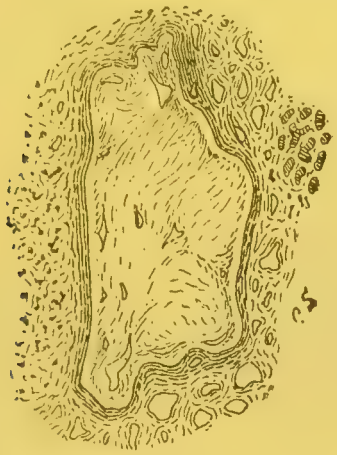

FIG. 141.—SECTION OF A HEPATIC VEIN OBSTRUCTED BY FIBROUS TISSUE IN THE MIDST OF WHICH VERY SMALL VASCULAR LACUNÆ ARE SEEN.

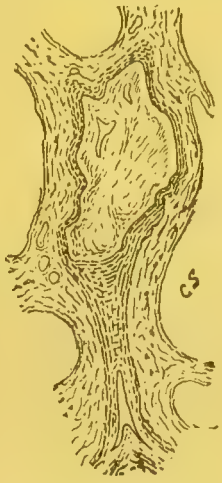

FIG. 142.—SECTION OF A HEPATIC VEIN OBSTRUCTED BY CONNECTIVE TISSUE, IN THE MIDST OF WHICH A TRIANGULAR VASCULAR OPENING IS SEEN.

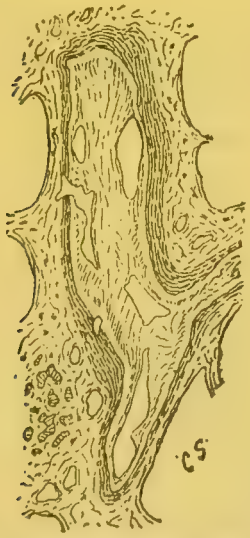

FIG. 143.—OBLIQUE SECTION OF A HEPATIC VEIN, IN WHICH THE ORGANISED FIBROUS THROMBUS SHOWS MANY LARGE-SIZED LACUNÆ IN WHICH THE BLOOD CIRCULATES FREELY.

FIG. 144.—TRANSVERSE SECTION OF A HEPATIC VEIN AFFECTED WITH ENDOPHLEBITIS AND PHLEBITIS.

hollowed in the fibrous tissue and filled with blood are found around these diseased blood vessels. At other places the calibre of the hepatic veins is reduced to a narrow orifice in the midst

of fibrous tissue which has taken the place of the internal coat (fig. 142). Phlebitis and thrombosis of the trunk of the portal vein are sometimes present in cirrhosis. Ch. Leroux has reported cases. Obliteration of this vein and of its branches has also been found. This will be considered when treating of adenoma.

These different lesions of the portal vein, the capillaries, and the hepatic veins illustrate the difficulties of the circulation in the liver. The cardiac impulse and the *vis a tergo* are feeble normally in the veins passing from the intestine and the spleen to form the trunk of the portal vein. In cirrhosis, the interlobular branches having lost their elasticity and contractility, it can be easily understood how the blood passes with difficulty through the capillaries of the lobules. This is what actually takes place during life. The multiple causes of impeded circulation in the portal vein and of ascites are: First, the changes of structure already described in the walls of the branches of the portal vein contained in the cirrhotic tissue; secondly, obliteration of a certain number of lobular capillaries by extension of the cirrhosis to the cellulo-vascular tissue of the lobules; thirdly, obliteration of the hepatic veins; and fourthly, the occasional thrombosis, which may be more or less extensive, of the portal vein.

According to Rindfleisch, the hepatic artery, in which the blood pressure is evidently much higher than in the portal vein, replaces the latter at all points of the sclerosed tissue where it is obstructed, so that the system of blood vessels in the cirrhotic tissue can be supplied by arterial blood, for it is by means of arterial blood that the bile is elaborated. Considering the many injections which we have made of the portal vein we consider this statement too absolute. When injected, the fluid passes very rapidly into the vessels at the periphery of the lobules, and thence into the accessory portal veins, and into the veins in the bands which unite the liver to the diaphragm; often the capillaries of the lobule itself are not affected. In the final stages of cirrhosis, the blood of the portal vein, being unable to penetrate the lobules, flows partly into the vessels which supply the fibrous bands established between the liver and the diaphragm (Kiernan), and into the system of enormously dilated portal veins described by Sappey. Sappey concludes from his researches ('Acad. de Méd.,' March 8, 1859) that in cirrhosis the blood of the portal vein is conducted into the inferior vena cava by much-dilated accessory portal veins, the subcutaneous abdominal, internal mammary, and all other veins with which they may anastomose also becoming distended.

In this process a small vein contained in the suspensory ligament of the liver, and in the obliterated umbilical cord, plays a quite peculiar and important part. It extends from the sinus of the portal vein to the femoral artery, following either the subaponeurotic veins or the subcutaneous abdominal veins. The current passing from above downwards frequently causes a thrill felt by the hand, and a continuous murmur heard by means of the stethoscope (Sappey). The obvious insufficiency of this collateral circulation to relieve the portal system is shown by ascites, which becomes more and more marked notwithstanding the accessory portal veins. In one case of cirrhosis under our observation we noticed large round lymphatics, from 0·2 mm. to 0·5 mm. in diameter, between the lobules, and situated in the midst of the sclerosed tissue; they were filled and distended by lymph cells.

Condition of the interlobular bile ducts and the circulation of the bile in a cirrhotic liver.—At the same time that the blood vessels undergo the changes already described, varying amounts of fibrous tissue appear in bands in the bile ducts (*vide c*, fig. 140). In all cases of cirrhosis, the interlobular bile ducts are found well preserved in the portal spaces, which are enlarged by the new formation of sclerosed tissue. They retain their proper coat, their epithelium of cubic cells, and their lumen. But most frequently, in the thick fibrous zone which accompanies the interlobular portal branches, a network of numerous bile ducts is seen anastomosing together, instead of the single duct corresponding to each of the interlobular branches of the portal vein. In part when a group of liver cells has completely or almost entirely disappeared, the connective tissue is intersected by a similar network of bile ducts, forming delicate meshes and surrounded by much larger ducts. One of us thought therefore that in cirrhosis, at the same time that the liver cells atrophied and became replaced by fibrous tissue, the bile ducts persisted, whence it resulted that they became so distinct in complete atrophy of the cells of the lobule, or in the peripheral fibrous zone of a lobule of which only the centre remained intact. It may be supposed that the bile ducts observed in cirrhosis simply represent the normal interlobular and intralobular ducts which have become more apparent in consequence of atrophy of the parenchyma. These anastomosing bile ducts, which are found in all cases of cirrhosis in the circumportal fibrous trabeculæ, are formed exactly like the normal interlobular bile ducts. They have a hyaline membrane and a lining of small cubic cells, and possess a

central lumen. But they are not found at least in the early stages of cirrhosis, in the fibrous trabeculæ which accompany the hepatic veins, for there are none in this situation normally. In certain cases, however, of chronic hypertrophic cirrhosis, networks of bile ducts may be seen in all the fibrous trabeculæ, in those which are developed along the hepatic veins as well as those which accompany the portal veins. It is thus necessary to ask how and from what elements these canaliculi originate. It must first be noticed that these anastomotic canaliculi are not always of the same diameter: at the centre of a thick band of cirrhosis one or two wide-mouthed ducts may be found free or filled with detached cells derived from their epithelial lining; the diameter of these ducts may vary from 20 μ to 60 μ, which is equal or larger than that of the normal perilobular ducts (see *f*, fig. 145). Besides these, numerous smaller canaliculi are present which are rectilineal or undulating, and form by their anastomoses elongated or polygonal meshes more or less regular.

These canaliculi are completely lined with small cells, which are sometimes cubical, sometimes elongated and flattened in the

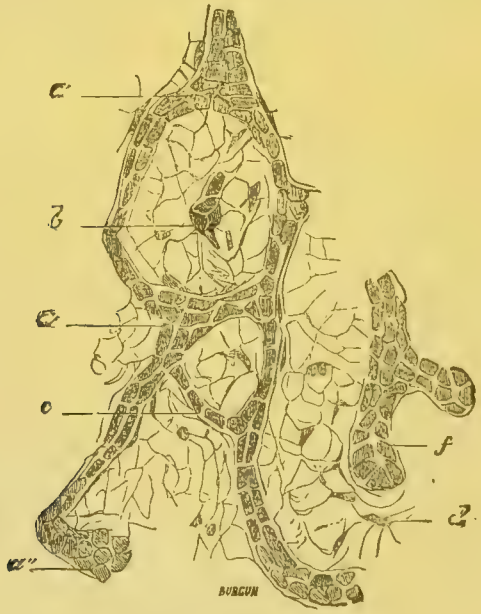

FIG. 145.—NETWORK OF BILE CANALICULI SITUATED IN THE NEW CONNECTIVE TISSUE OF CIRRHOSIS.

f, interlobular bile duct; *c*, very small duct continuous with other canaliculi equally delicate, and containing cells placed end to end. These canaliculi lead into larger ducts, *a*, *a'*, *a''*; *d*, connective-tissue cell. Magnified 300 diameters.

direction of the duct. The ducts are united together by very delicate branches, which also often contain a single row of cells

arranged end to end (see *c*, fig. 145); these cells contain one oval nucleus and they completely fill up the cavity of the canal round which they are moulded. When observing these very delicate canaliculi, which measure from 5 μ to 10 μ in diameter, and which are filled by one or two layers of elongated cells, they might be mistaken for capillaries containing white blood corpuscles. But their continuity, easily recognised, with the larger canals lined with cubical or cylindrical epithelium leaves no doubt as to their true character. The finest of these canaliculi are particularly observed at the edge of the fibrous trabeculæ and the islets of cirrhosis. They are directly continuous, at the periphery of the lobules of the hepatic parenchyma, with the trabeculæ of liver cells, of which they seem simply the transformation. Kelsch, Kiener, and Sabourin seem to us to have plainly demonstrated this continuity of the new canaliculi with the trabeculæ of the liver cells, not only by direct examination of the fibrous trabeculæ of cirrhosis, but also by their knowledge of what passes in the case of adenoma. In adenoma, the hepatic trabeculæ often in fact show in their interior the dilated lumen of the intralobular bile canals, full of small yellow or greenish yellow concretions formed by the bile pigment. The liver cells situated round these dilated canaliculi are flattened around these small biliary concretions, and are transformed into cubical or flat cells, forming a real epithelium to the central duct (see fig. 152). The lumen of the latter is free or filled with small concretions. A trabecula of liver cells is thus transformed into a bile duct, and the liver cells have become the epithelium of the duct. On comparing these facts with what passes in cirrhosis, we are led to admit that the spurious bile ducts of the perilobular fibrous trabeculæ represent trabeculæ of liver cells, which latter, compressed, atrophied, flattened, and changed, have become the epithelium of these spurious ducts. If, according to Eberth and Sabourin, the liver be compared to a gland of composite tubes, of which the hepatic trabeculæ represent the secreting tubes, the hepatic or secreting cells surrounding a fine excretory duct, the pathological changes caused by chronic inflammation are easily explained. The liver cells, after having lost their specific form, return to the embryonic state, and the trabeculæ are changed into tubes composed of indifferent cells. However it may be, if one admits the change of the hepatic trabeculæ into spurious bile ducts, or if one leans to the first explanation given of the changes of the intralobular bile canals, which allow themselves to be penetrated by cells, or if one admits with Charcot a sort of abnormal budding and multiplication

of the interlobular bile ducts, the fact of the existence and even the extreme abundance of these spurious ducts in the fibrous trabeculæ in cirrhosis must be acknowledged. Their large number (see fig. 149), the predominance of fibrous tissue around the bile ducts, and catarrhal inflammation around the latter, has caused this disease to be described as a distinct variety of hypertrophic cirrhosis. The spurious bile ducts are often also seen at points where a localised cirrhosis may exist, from whatever cause. Thus in the fibrous trabeculæ which surround gummata, serous cysts, calculus cysts of the liver, tubercles, &c., are found. What is the functional result of the formation of these spurious ducts? They evidently take the place in cirrhosis of the secreting parts of the liver. They point consequently to a diminution of the secretion of bile. They form a network communicating with one another and with the large bile ducts, which may be shown by injections made from the common duct. It is not certain that they communicate easily with the intralobular canaliculi of those portions of the liver which are still able to secrete bile. The liver cells themselves are moreover always more or less altered in cirrhosis. Hence the secretion of the bile is generally incomplete, as we have already remarked.

State of the liver cells in cirrhosis.—The liver cells present very variable changes, which are probably contemporaneous with the lesions of the connective tissue that accompany them. It, however, seems to us probable that, in most cases, the liver cells undergo lesions before the connective tissue is affected, and on the other hand it is not rare to see the liver cells almost normal, not only at the commencement of cirrhosis, but even in advanced, old, and very marked atrophic cirrhosis. The changes observed in the cells are principally due to alterations of form, atrophy, flattening, and to infiltrations with the colouring matter of the bile, fat, blood pigment, black pigment, and amyloid material. One word on each of these changes. On examining sections of a cirrhotic liver, it will be observed that the islets of cirrhosis are composed of granular nucleated cells, normal in character, but it is none the less true that many of them have disappeared and have been replaced at the periphery of the islets by connective tissue. In the fibrous trabeculæ, in fact, cells may be found isolated or in small groups. Their protoplasm and their nuclei may be normal, but in consequence of the pressure exercised by the interlobular and intralobular connective tissue, they atrophy while still preserving their primary form, and diminishing in every direction. More frequently

the connective tissue isolates them from the trabeculæ of liver cells, and by compressing them transforms them into delicate tubes formed of atrophied cells, which change has been well described by Klebs. In other cases, the pressure being all in one direction, they are flattened the one against the other. The ease with which these cells and lobules flatten is well known. In the round islets of cirrhosis, formed of cells which appear normal, they are still arranged in a quite peculiar manner which distinguishes them from the physiological state. They in no way recall the radiating arrangement of the cellular trabeculæ, but are agglomerated together, the cells being round or polyhedral by reciprocal pressure. When the islets are coloured green, as may be observed in retention of the bile with general icterus, which sometimes accompanies atrophic cirrhosis and frequently hypertrophic cirrhosis, the liver cells are seen to contain bile pigment in the form of small granules, and often in certain cases the protoplasm of the cells is stained a bright yellow. On carefully adding nitric acid to the preparation, the cells become deeper stained and of a yellowish green colour. The same result is obtained with an iodine solution. In these coloured cells, at the same time that there is infiltration of bile, fat globules may accumulate in them and distend them more or less. These globules of fat are not coloured, but the protoplasm arranged around the fat, as in the adipose cells, is stained by the bile. On examining islets of a dark green colour under the microscope, the intralobular bile canals are frequently seen to contain small fragments of a hard refractive yellow or green substance. These are the small microscopic biliary concretions which hardly exceed the ordinary diameter of ducts, measuring from 4 μ to 5 μ. The most frequent change of the cells in cirrhosis is fatty degeneration. The cells then contain small drops of fat or a single large drop which distends them. Their nuclei are often preserved, and pushed to the periphery by the drop of fat, as in the subcutaneous adipose cell. When the cirrhotic islets are formed solely of cells infiltrated with fat, their colour is generally yellowish to the naked eye. Besides the cells filled with fat, cells are also found more or less infiltrated with bile or blood pigment. These lesions give to the entire lobule the yellowish or brown colour which was looked upon by Laennec as characteristic. The red pigment derived from the red blood corpuscles often predominates in the cells. They then contain brown granulations of hæmatin in variable amount, and the lobules appear of a mahogany-brown colour. This state of the liver cells is similar to that observed in the nutmeg liver,

due to the pressure of the blood in the right side of the heart and in the hepatic veins. In cirrhosis, parts may be found spotted with black. The observer must always be on his guard against the changes produced by cadaveric decomposition; under its influence the red pigment is easily changed into black pigment, and certain parts of the liver, more particularly its surface, take a grey or slate tint. But when the autopsy is made in winter twenty-four hours after death, and there are no visible signs of cadaveric decomposition, the black pigment may be attributed to pathological change. Thus many anatomists, and we ourselves, have noticed this black pigment either in the connective tissue or in the liver cells themselves in subjects who have been affected by intermittent fever during life (see fig. 146). The complication of amyloid degeneration of the cells and vessels in cirrhosis is rather rare in the liver. It may be met with in diseases which lead to amyloid degeneration of the viscera, particularly in prolonged suppuration.

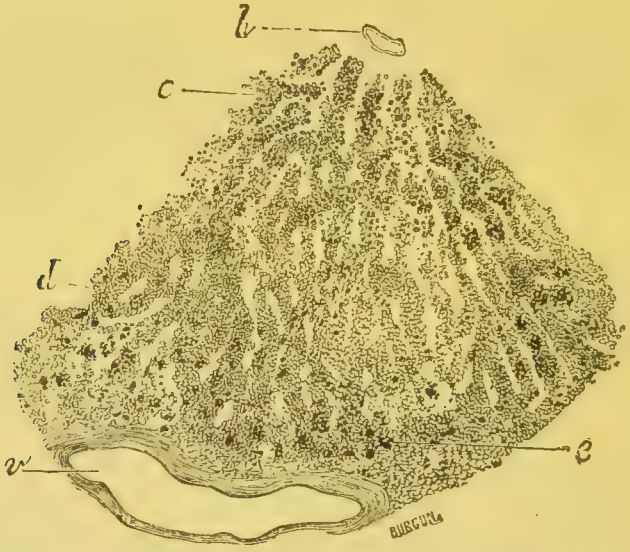

FIG. 146.—SECTION OF THE LIVER IN WHICH THE HEPATIC CELLS ARE PIGMENTED.

h, central vein of the lobule; *c*, trabecula of liver cells; *e*, granulations of black pigment in the cells of the periphery of the lobule; *v*, branch of the portal vein. Magnified 40 diameters.

Concomitant lesions of cirrhosis.—In consequence of chronic inflammation of Glisson's capsule the peritoneum is generally inflamed, and fibrinous false membranes are developed on its surface. Peritonitis, limited to the edge of the liver, with its fibrinous false membranes, ecchymoses, and effusions of blood into the false membranes, is sometimes observed without abdominal punctures having been made to evacuate the ascitic fluid. Almost invariably, the mucous membrane of the digestive tube from the cardia to the anus

is congested, and often shows a very pronounced condition of chronic catarrh. The hæmorrhoidal veins are almost always dilated, in consequence of the hinderance presented by the cirrhotic liver to the portal circulation. The lower part of the rectum is the seat of piles. The œsophageal veins are equally varicose. The spleen is generally hypertrophied in cirrhosis; sometimes even it may be indurated and the seat of chronic inflammation, affecting particularly the connective tissue of the trabeculæ and the capsule.

Varieties of cirrhosis.—We have hitherto described cirrhosis considered generally, and all the lesions observed in the various parts composing the liver, viz. the connective tissue, blood vessels, bile ducts, and liver cells. But every case of cirrhosis does not show all these alterations. There are, on the contrary, forms of cirrhosis which are distinguished by a special localisation, or by a collection of lesions comparable with one another. These forms of cirrhosis may be considered as varieties.

a. **Cirrhosis observed in the course of intermittent fevers.**—We have had the opportunity of examining many specimens of cirrhosis in children affected with malarial cachexia, and in whom alcoholism could not be suspected. We have observed transportation by the portal veins of leucocytes impregnated with black pigment, diapedesis of these cells into the circumportal connective tissue, thickening of the connective tissue, and at the same time black pigmentation of the liver cells. In recent years, Kelsch and Kiener have studied malarial poisoning in the hospitals of Algeria. They have observed in the liver of persons who have died from pernicious fever that not only are the portal vessels and capillaries of the lobules crowded with pigmented leucocytes, but that the epithelial cells of these vessels also contain black pigment. In the veins of persons who have succumbed to intermittent fever of long duration, or from malarial cachexia, these observers have noticed different forms of cirrhosis, generally with hypertrophy of the liver, nodular parenchymatous hepatitis of the affected lobules, deposits of adenoma, simultaneously with more or less marked pigmentation of the newly formed connective tissue, and of the liver cells.

b. **Cardiac cirrhosis.**—We have already described chronic congestion with dilatation of the capillary vessels and atrophy of the liver cells, so often observed in patients affected with chronic cardiac disease (see p. 324). But under these conditions, a quite special form of cirrhosis may sometimes be observed, affecting principally the tissue round the hepatic veins. This is what is

properly called cardiac cirrhosis. It is unnecessary to say that subjects affected with cardiac disease may also show general cirrhosis. In the first edition of this manual we described cardiac cirrhosis, and insisted on the new formation of embryonic or fibrous connective tissue along the subhepatic veins and around the central veins of the lobules. Later, Talamon and Wickham Legg declared that they had never seen in cardiac affections the production of connective tissue around the central veins of the lobules. Sabourin has recently treated this question ('Revue de Médecine,' July 10, 1883), and has confirmed our view. The following is a summary of his opinions:—In diseases of the heart, the capillaries which immediately follow the branches of the subhepatic veins are generally dilated. These veins and capillaries form bands, which end by surrounding portions of the hepatic lobules having the same arrangement as the trabeculæ of fibrous tissue which accompany the hepatic veins in uni- and multilobular cirrhosis. In these trabeculæ, composed of dilated veins and capillaries, the wall of the capillaries is thickened; round cells are seen around the wall of the veins and of the capillaries. The trabeculæ of liver cells, interposed between the thickened capillaries, atrophy, and the liver cells, the protoplasm of which is diminished, preserve their nuclei. All the tissue between the

FIG. 147.—GENERAL VIEW OF THE HEPATIC LOBULES IN CARDIAC CIRRHOSIS. (After Sabourin.)

The trabeculæ of fibrous tissue, T, accompany the hepatic veins, S H, limiting the lobules in the midst of which may be found the portal veins with the accompanying bile ducts. The peripheral zone of these lobules shows a network of dilated capillaries, V.

capillaries is compressed, and finally becomes fibrous (see fig. 148, T).

In the sclerosed connective tissue the capillaries remain in the condition of slits or lacunæ, varying in size and filled with blood. Here we see cirrhosis having for its seat the region of the hepatic veins, and accompanied by lesions of the capillaries adjoining these veins.

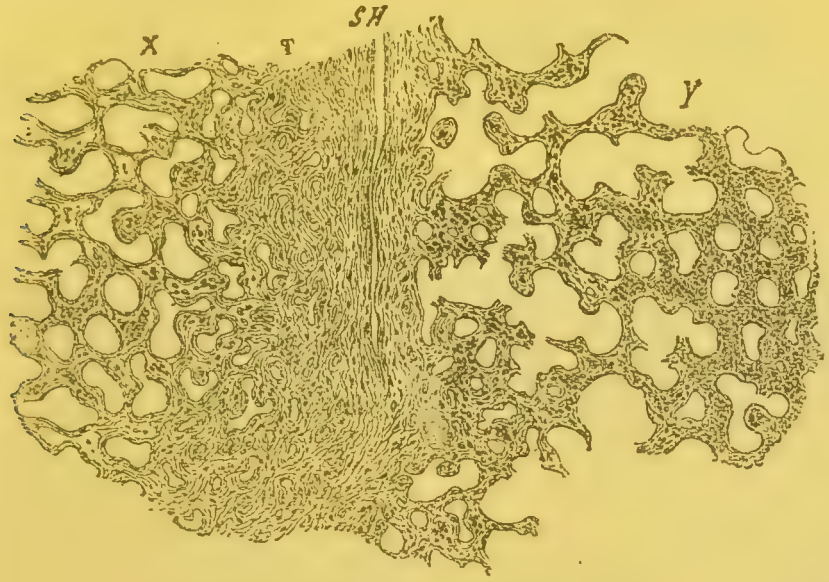

FIG. 148.—EVOLUTION OF CARDIAC CIRRHOSIS.
(After Sabourin.)

S H, hepatic vein cut obliquely; at X the capillaries of the hepatic lobule are dilated, and the trabeculæ and liver cells atrophied; condensation of the connective tissue is produced at T at the same time that the capillaries are less dilated; to the right of the vein at Y the capillaries are much more dilated. Magnified 40 diameters.

c. **Hypertrophic cirrhosis.**—Hypertrophic cirrhosis does not always show the same aspect and the same structure. Therefore we are obliged to divide this group into many types.

1. **Biliary cirrhosis.**—Many years ago, when examining cases of hypertrophic cirrhosis, we showed that the connective tissue of the cirrhotic trabeculæ presented a large number of bile ducts, and when later Wickham Legg, Charcot, and Gombaut succeeded in producing cirrhosis by ligature of the ductus choledochus, it was asked whether there were not a direct relation between icterus, retention of the bile, chronic inflammation of the bile ducts, new formation of canaliculi, and development of the connective tissue. Hanot, on studying the lesions of the interlobular bile ducts in hypertrophic cirrhosis, found that the interlobular ducts of a certain size were surrounded by a zone of thickened embryonic connective tissue, forming a complete sheath around them. These ducts contain a normal or proliferated and thickened epithelium, and

in their lumen are found free round cells or detached epithelial cells. Hanot concluded from these facts that there was catarrh of

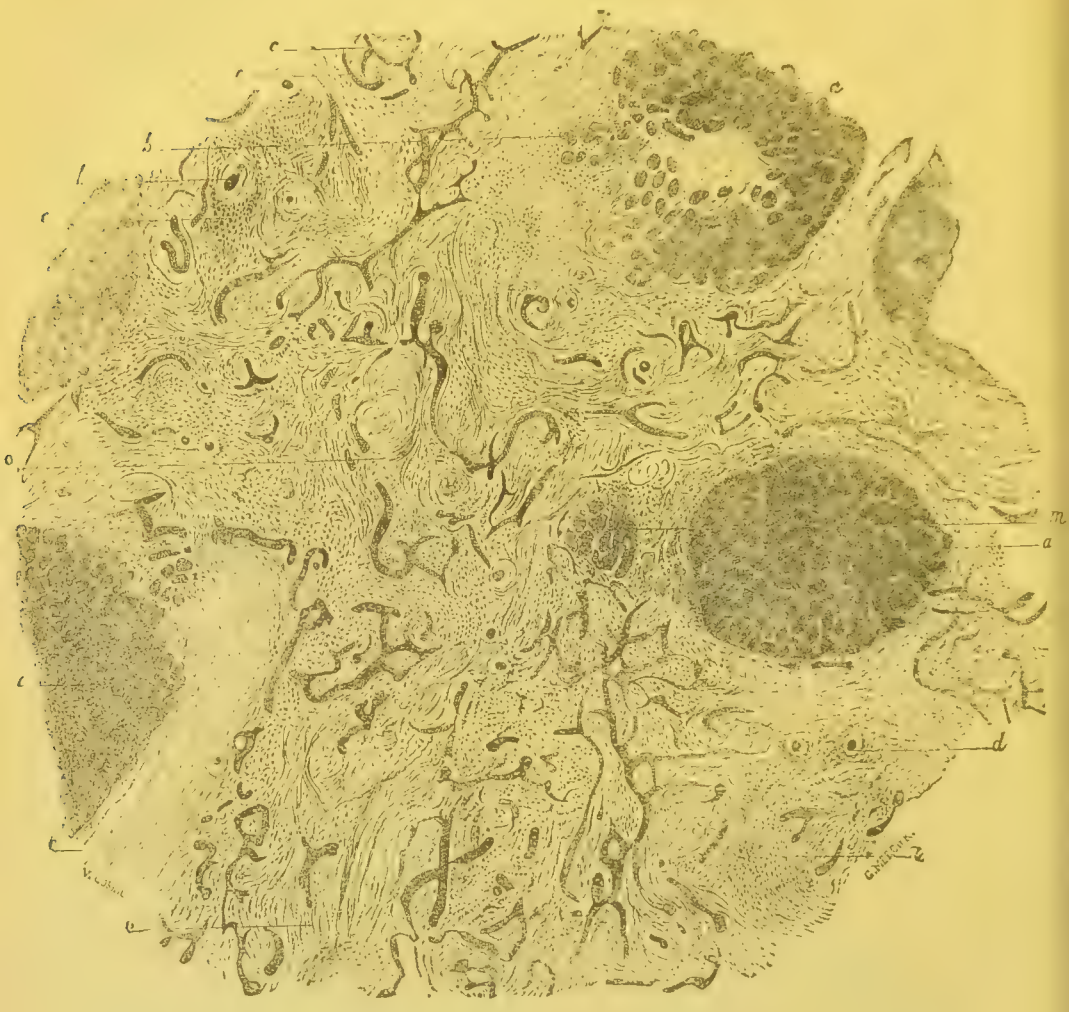

FIG. 149.—SECTION OF THE LIVER FROM A CASE OF HYPERTROPHIC CIRRHOSIS.

a, *a*, *a*, hepatic lobules; *b*, *m*, groups of isolated liver cells in the midst of a sclerosed tissue; *c*, *c*, bile ducts of new formation intersecting the fibrous tissue in every direction; *n*, *m*, islet of embryonic tissue. Magnified 80 diameters.

the bile ducts and chronic inflammation of the connective tissue surrounding them. A similar lesion seems to have hindered the normal course of the bile up to a certain point. Taking into consideration the experiment of the ligature of the common bile duct and the new formation of bile canaliculi, this variety of cirrhosis and the icterus which is its principal symptom are partially explained. It is thus that that special variety, biliary cirrhosis, was constituted of which Charcot has given a classic description. Its symptoms are icterus, usually absence of ascites, and a rather rapid course:

pathologically it shows a hypertrophied liver containing thickened trabeculæ, composed of embryonic or fibrous tissue, rich in new canaliculi. These trabeculæ, instead of showing a regular annular arrangement around the hepatic lobules, often show knots and projections which penetrate into the parenchyma; finally, the embryonic or fibrous tissue which often surrounds the bile canaliculi is frequently affected with catarrhal inflammation. This description applies, in fact, to a considerable number of cases of hypertrophic cirrhosis, and hence we have given biliary cirrhosis as one of its distinct varieties. Some objection must, however, be made to its name, in so far as it expresses an essential characteristic, for icterus is found in many other varieties of hypertrophic or atrophic cirrhosis. New canaliculi are also found in most cases of cirrhosis; and finally the pathological cases, in which the hepatic ducts visible to the naked eye are filled with calculi, obliterated in places, a condition homologous to ligature of the common duct, do not agree with the experiments of Wickham Legg, Charcot, and Gombaut. In fact, in cases of obliteration of the large ducts of the liver a fibrous thickening is found around these ducts, which are obliterated or dilated in places, but an actual hypertrophic cirrhosis is never observed here.

2. **Fatty hypertrophic cirrhosis.**—The name of biliary cirrhosis was for many years regarded as synonymous with hypertrophic cirrhosis; but another form has been recently described, simultaneously by Hutinel[1] and Sabourin.[2] The cases published by these authors and those recorded since have established the reality of this variety, which is characterised as follows:—

Icterus is the constant symptom; it is observed rather frequently in phthisical patients; the liver is large and is generally smooth on the surface; the colour of the parenchyma is yellow, or greenish yellow, which fact is due to the complete fatty degeneration of all the liver cells. On section, the liver is seen to be smooth and not granular. In large microscopic sections, examined under a low power, the thickened trabeculæ forming complete circles around the cirrhosed lobules are not recognised. The connective tissue of the portal spaces is the initial seat of the cirrhosis. This tissue sends into the lobules a series of irregular tracts, which penetrating them, subdivide and separate them into little groups of cells. The bile canaliculi which are found

[1] 'Étude sur quelques cas de Cirrhose avec Stéatose du Foie,' *Soc. Clin. de Paris*, Mars 1881.

[2] 'Cirrhose Hypertrophique Graisseuse,' *Arch. de Phys.*, 1881, p. 584.

here in rather considerable numbers are surrounded by dense, thick fibrous zones. This penetration and ramification of fibrous tissue within the hepatic lobules is scarcely observed in any but this variety of cirrhosis. But its chief characteristic lies in the fatty degeneration of all the liver cells. These are filled and distended by one or more drops of fat surrounded by protoplasm. The nucleus, pushed to the periphery, is well preserved. These spherical cells are all bordered by fibrils of connective tissue, and by a layer of small round or oval cells. Seen in section and stained by carmine they resemble the cells of inflamed connective tissue. The hepatic lobules are then completely invaded throughout their whole extent by a growth of embryonic connective tissue. In the bands around the lobules a few liver cells are also found, united in groups or isolated, all of which are fatty. The hepatic veins are sometimes obliterated.

3. **Hypertrophic cirrhosis of diabetes.**—It was quite natural to seek for the explanation of diabetes in the liver, and Wilks and Stockvis have found increase of weight of the organ and interstitial hepatitis. Diabetic patients sometimes succumb from true hypertrophic cirrhosis. Lecorché thinks that the disorder of the glycogenic function of the liver, observed in this disease, is related to the organic changes of cirrhosis. It must be acknowledged, however, that the lesions peculiar to diabetes are far from being understood at the present time; on the other hand, it must be allowed that to alcoholism must be attributed much of the cirrhosis developed in diabetics who have been too faithful observers of the alcoholic treatment of the disease. However this may be, Hanot and Charcot have reported two autopsies of diabetic patients who had not been addicted to alcohol, but in both of whom a very marked melanodermia had been observed during life. At the autopsy, pulmonary tubercles were found, and hypertrophic cirrhosis, in which the fibrous trabeculæ had originated around the portal and the hepatic veins; also infiltration of the liver cells and the newly-formed tissue, with black pigment granules, was present. While recording these facts they call for fresh observations. It must not be thought that all cases of hypertrophic cirrhosis may be included among one of the three categories here sketched. It is not so; for example, hypertrophic cirrhosis may be seen without icterus, but with marked ascites. In every case of hypertrophic or atrophic cirrhosis, variations may be seen which upset all classifications hitherto made.

d. **Atrophic cirrhosis.**—This is a typical form of cirrhosis, and

was described by Laennec for the first time. The liver is abnormally small, shrunken, granular, lobulated, and irregular on its surface. On dividing it, its surface is seen to be also granular; the

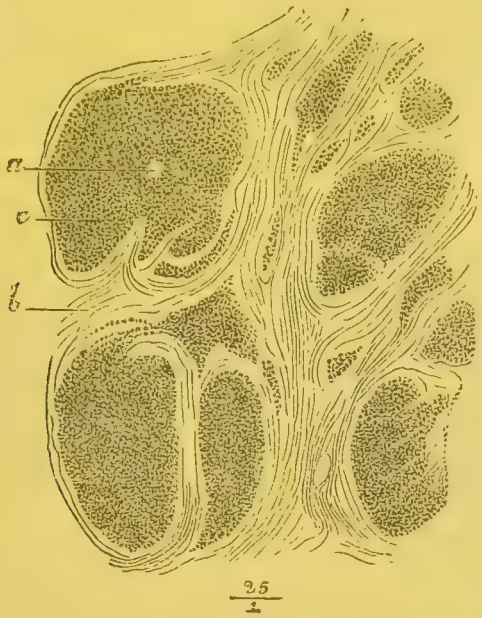

FIG. 150.—CIRRHOSIS OF ALCOHOLIC ORIGIN.

b, much-thickened interlobular connective tissue; *c*, hepatic lobule; *a*, central vein of the lobule. Magnified 25 diameters.

granulations project on the divided surface, and on attempting to tear the liver, which is difficult, for it is elastic and resistant, they seem to be spherical. They vary in colour, being grey, russet-coloured, reddish yellow, red, green, &c. According to the lesions of the liver cells already known to us, they are separated by thick and generally regular bands of almost semi-transparent and sclerosed fibrous tissue. In a large section the granulations are seen to be small, sometimes large, as in multilobular cirrhosis, sometimes unequal, sometimes exactly circular, surrounded by regular and thick bands of fibrous tissue. This is typical annular cirrhosis. In this form, lesions of vessels are observed, particularly obliterating phlebitis of the hepatic veins, of which the description has been already given. Here, also, ascites is the rule. Icterus is not generally present. From all these characters it may be inferred that atrophic cirrhosis is a slow disease essentially chronic. They are, however, exceptions to this pathological and symptomatic grouping. For example, Hanot has published a series of cases of atrophic cirrhosis accompanied

by icterus and rapid in its growth. The cells showed then a destructive fatty degeneration comparable to that of poisoning by phosphorus.

Pathologists have asked if a liver affected with cirrhosis may not necessarily show various lesions during the slow process of this disease, so that, for example, hypertrophic cirrhosis may become changed into atrophic cirrhosis. The symptoms observed during life do not give any positive indications, and the autopsy, showing nothing but the lesions at the moment of death, yields no further explanation. Hence one is obliged, in order to reply to the question, to formulate more or less rational hypotheses, based on the generalisations gathered from the course of the lesions. It is certain that the cicatricial fibrous tissue has the power of contracting, and it is impossible to deny that it does so in atrophic cirrhosis, in which disease the liver passes from its normal size to one greatly reduced. But it is, however, not less true that in hypertrophic cirrhosis, in which the trabeculæ of new formation are not less thick and less fibrous than in atrophic cirrhosis, the liver progressively increases in size during the first two or three years, and attains considerable dimensions at the time of the autopsy. Probably this increase in size is due to the fact that the connective tissue increases throughout the evolution of the disease, at the same time that fat accumulates in the liver cells, and that lobules of adenoma are formed. Then, in the present state of science, without denying the contractile properties of fibrous tissue, may we not admit the transformation of one variety of cirrhosis into another, and particularly the change of hypertrophic cirrhosis into the atrophic variety?

The complications of hepatic cirrhosis.—We will now describe the complication of cirrhosis with adenoma, and will only indicate its complication with tubercle and cancer.

Complication of cirrhosis with adenoma.—We place adenoma of the liver immediately after cirrhosis, for, according to recent researches on the subject, it is intimately related to the cirrhotic process, and does not seem to be a simple complication. The more or less numerous and voluminous nodules of adenoma consist essentially in an hypertrophy and hyperplasia of the cells of the hepatic trabeculæ, which have become larger, moniliform, and contain microscopic bile canaliculi, and which finally undergo granulo-fatty degeneration. The new formation of a tissue of liver cells may, moreover, be demonstrated in the interior of the

portal veins, and adenoma then becomes infectious. At the publication of the first edition of this manual we did not think the cases of Lancereaux,[1] Griesinger, and Rindfleisch sufficiently succinct to merit a special description; but since then the excellent researches of Eberth,[2] of Kelsch and Kiener,[3] and of Sabourin[4] have brought to light new cases, and have completely cleared up the history of this lesion. In a section of a cirrhotic liver, whether atrophic or hypertrophic, the isolated nodules of adenoma are seen with the naked eye in the form of lobulated, encysted masses, varying in size, attaining sometimes to that of a nut or larger, of a grey-yellowish colour, friable, and often the seat of hæmorrhages. When the adenoma is general, the liver is large, tumefied as in secondary cancer. It is affected with cirrhosis, and in the midst of the sclerosed tissue encysted adenomatous tumours are found, of a golden yellow colour, and caseous, often softened and blood-stained. Beyond these tumours, a certain number of hepatic lobules are found degenerated in the same manner. The trunk of the portal vein, near the hilum, or one of its branches only, often contains a pinkish-grey coagulum, which is hard or softened in places, and which extends into its finest ramifications. Preparations of adenoma of the liver, obtained by dissociation, show the liver cells isolated or grouped without order and epithelial cylinders. These cylinders, deprived of their proper wall, generally contain large prismatic cells; these contain a granular protoplasm and one or more nuclei, and often fat granules; they stain with picro-carminate like the liver cells. Some of the cylinders show internally a rudiment of a central canal, which contains here and there small refractile round or ovoid blocks; these are biliary concretions (*vide* fig. 152). A large number of these cylinders which contain these calculi are moniliform with numerous and large swellings. The cells lining these swellings are modified and are formed of a single layer of small cubical cells.

Microscopic sections are more instructive. In the parts of the liver which are least diseased, all the anatomical signs of cirrhosis are recognised, with annular fibrous trabeculæ containing pseudo-bile ducts in more or less considerable number. In the islets of hepatic parenchyma varicose cellular trabeculæ are often observed with the small biliary concretions in the midst of a distinct central

[1] 'Contribution à l'Étude de l'Hépato-adénome,' *Soc. Méd.*, 1868.

[2] 'Das Adenom der Leber,' *Virchow's Archiv*, vol. xliii.

[3] 'Contribution à l'Étude de l'Adénome du Foie,' *Archiv. de Phys.*, 1876.

[4] 'Contribution à l'Étude des Lésions du Parenchyme hépatique dans la Cirrhose,' *Thèse de Paris*, 1881.

canal, and that peculiar arrangement of the cells described by Kelsch and Kiener under the name of nodular evolution. In the section of the cirrhotic islets which become changed into adenoma appear the round masses of hypertrophied hepatic trabeculæ, the cells of which are highly granular and contain one or more voluminous nuclei. At a more advanced stage these trabeculæ, much thicker, become imbricated and form a distinct nodule, and are directly continuous with the surrounding trabeculæ (*vide a*, fig.

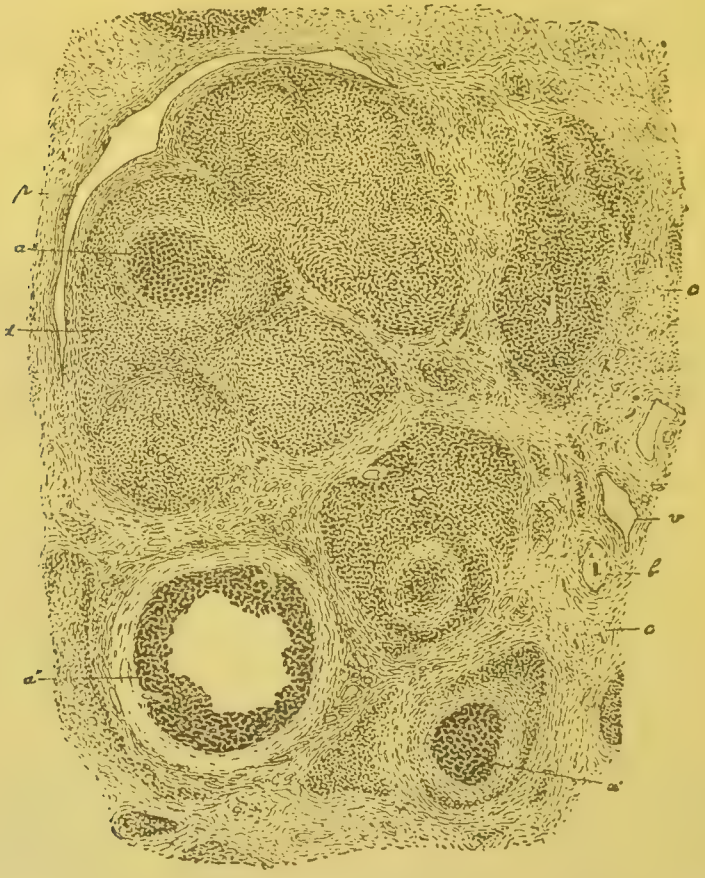

FIG. 151.—SECTION OF A CIRRHOTIC LIVER SHOWING LOBULES OF ADENOMA IN DIFFERENT STATES.
(From Sabourin.)

a, nucleus of adenoma originating in a lobule; *a'*, a little larger nodule; *a''*, nodule of adenoma the large cells of which are partly disintegrated; *c*, connective tissue; *v*, blood vessels; *b*, bile ducts.

151). As this nodule increases in size, the trabeculæ surrounding it flatten, atrophy, and form imbricated lamellæ like the leaves of an onion. Finally the nodule becomes isolated from the rest of the lobule by a zone of flattened liver cells, which are ultimately replaced by fibrous tissue encysting the nodule of adenoma. This

encysting, described by Sabourin, constitutes a kind of secondary cirrhosis around the nodules of adenoma. The trabeculæ of

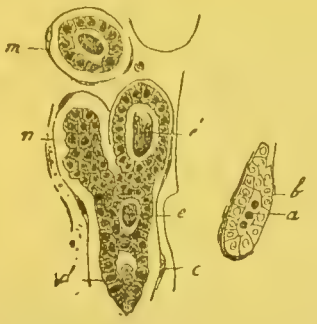

FIG. 152.—TRABECULÆ OF LIVER CELLS WHICH HAVE BECOME EMBRYONIC, TESSELATED, OR CYLINDRICAL, AND SHOWING CENTRALLY A CANAL WITH MICROSCOPIC BILE DUCTS.

(After Sabourin.)

m, connective tissue; *n*, small tesselated or cubical cells; *e*, *e'*, calculi.

adenomatous nodules show a variable structure; instead of being very large, the cells composing them are generally normal in size or even smaller. These trabeculæ have no proper membrane, and are separated from one another by capillary vessels, the wall of which may be thickened, and around which a fibrillar connective tissue is often formed. The cylinders full of adenoma may become true canaliculi, and in section show at their centre a lumen which may be transverse, oblique, or longitudinal, according to the direction of the section; this lumen contains, in places, microscopic biliary calculi. These calculi, when they become larger, are surrounded by a layer of epithelial cells, which may become here cubical or even cylindrical (*vide* fig. 152). The lobules of adenoma are often invaded throughout by fatty degeneration, which affects the epithelial cells of the solid or hollow cylinders. When this granular or fatty-granular melting is very marked, the cells fragment in irregular blocks, forming a magma in which it is difficult to recognise the primary elements. These lobules also sometimes become sclerosed, in consequence of the formation of connective tissue around the walls of the capillaries; the epithelial cylinders are then isolated from one another and compressed, and the cells finally undergo atrophy. An islet of adenoma is thus changed into a lobule of cirrhosis. Rather frequently, the lobules of adenoma are the seat of hæmorrhages, which are the consequence of the dilatation of vessels and the friability of the tissue. The adenomatous lobule is then dissociated by the blood which is

extravasated into its interior, and even sometimes only a blood clot is found in its place, in the midst of which are found the débris of liver cells and epithelial cylinders. At other times the blood infiltrates the entire lobule, the blood corpuscles penetrating everywhere, even between the epithelial cells, without the structure of the lobule being immediately disorganised. Adenomata of the liver have one singular peculiarity; the branches of the portal vein, and more rarely the hepatic veins, contain clots formed of hepatic cells and even epithelial cylinders similar to those just described. These clots extend into the branches of the vessels. Hitherto no satisfactory explanation has been given of these facts.

Complication of cirrhosis by tubercle.—We have of late frequently observed cirrhotic livers, generally those which were hypertrophied, in the midst of which semi-transparent miliary tubercles were detected; the granulations had an opaque and perfectly distinct centre, and formed either small greyish spots, scarcely visible to the naked eye, or were recognised by the microscope as very small tubercular follicles with giant cells. These tubercles are rarely numerous, and they are generally seated in the midst of the trabeculæ of connective tissue. Sometimes old-standing tuberculosis of the lung with cavities will be found at the same time; but in other cases the lungs are intact, and the tuberculosis occurs in a liver primarily cirrhotic, and is accompanied by an irruption of miliary tubercles localised to the perihepatic and diaphragmatic peritoneum, or generalised to all the serous membranes. It is probable that the localisation of tubercles in the liver results from this organ being already affected with chronic inflammation. Perhaps also the patients affected with cirrhosis by staying too long in hospital in the company of phthisical patients may contract tuberculosis by contagion.

Coincidence of cirrhosis with carcinoma.—All tumours cause, as we have already said, a partial cirrhosis around themselves. Primary carcinoma of the liver, whether in a single mass or in nodules disseminated in numerous nodules throughout the organ, is accompanied by trabeculæ of sclerotic connective tissue, which surround the hepatic lobules and which contain new canaliculi like the connective tissue of new formation in cirrhosis.

Degeneration of the liver.—We have already described fatty degeneration and amyloid degeneration of the liver cells. We must now consider the topography of these forms of degeneration and the concomitant lesions of the other elements constituting the liver.

Fatty degeneration.—The accumulation of fat in the liver is not due to the development of subcutaneous fat nor to polysarca,

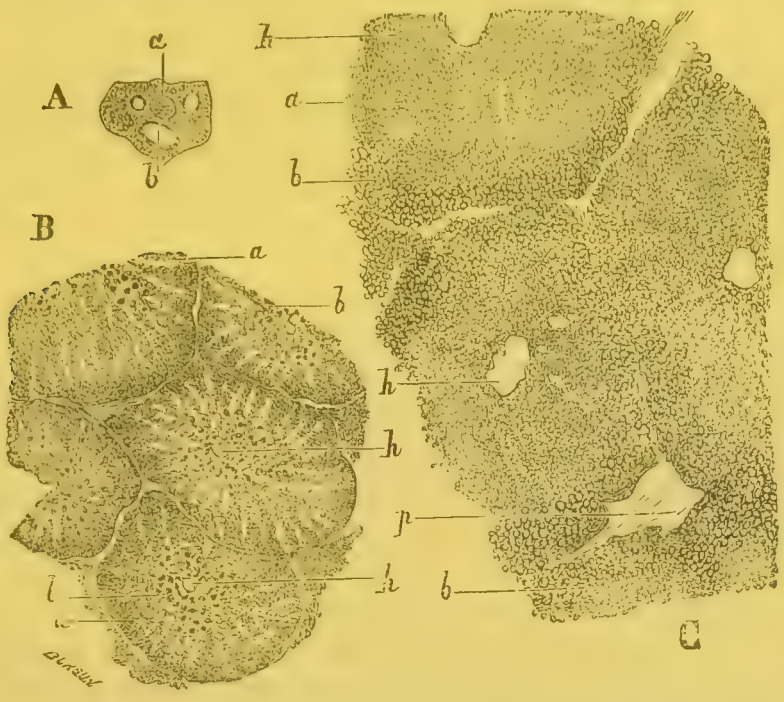

FIG. 153.—FATTY INFILTRATION OF THE LIVER.
(Drawing made by M. Sinéty.)

A. A liver cell showing many drops of fat, *b*, and granules of the same kind ; *a*, nucleus of the cell. Magnified 300 diameters.

B. Liver of a dog suckling her young ; section made after hardening in osmic acid. The cells at the centre of the lobule are filled with drops of fat, *b*, stained black by osmic acid ; *h*, the central vein of the lobules. Magnified 40 diameters.

C. Liver during the digestion of fatty foods ; *h*, central vein ; *p*, portal vein ; *b*, cells at the periphery of the lobules charged with droplets of fat. Magnified 40 diameters.

at least when drunkards are not considered ; on the contrary, the persons in whom at the autopsy fatty degeneration of the liver is found, are generally emaciated by a long chronic disease, such as pulmonary phthisis, suppuration of the bones, scrofula, or they are the victims of a cardiac disease. We shall see, in fact, that hinderance to the circulation and diseases of the chest exercise a great influence in the production of fatty degeneration of the liver, and that when the fat is stored up in the liver this indicates, not an excess in the economy, but, on the contrary, its powerlessness to burn up the hydrocarbonaceous materials furnished by digestion. There is, however, an exception to this rule, in the physiological accumulation of fat in the liver before and during lactation in all mammalian females ; in woman particularly, at the moment when lactation begins and during all the time that it lasts, the liver cells at the centre of the lobules are filled with large drops of

fat. The cells of the half of the lobule which surrounds the central vein are charged with fat, though they still preserve their nuclei and protoplasm, while the cells of the periphery (*vide* fig. 153) contain very little. This considerable quantity of fat is evidently held in reserve for the fabrication of the milk, fat lobules forming a considerable part in the formation of milk, where they are free or surrounded by an albuminoid envelope. The fatty substance destined for use in lactation is arranged in the hepatic lobule around the hepatic veins, that is to say, the nearest possible to the vessels from whence it is carried into the blood. In most other cases of partial fatty degeneration the fat is usually seated, on the contrary, at the periphery of the lobule. Thus during the physiological work of digestion, in animals who have recently ingested milk or some other fatty food, the fat passes into the blood of the portal vein, and the liver cells retain some small drops. But only the cells nearest the periphery of the lobule, for a very narrow circular area, show fat granules in their interior. In all pathological cases fatty degeneration is secondary, and it generally occupies a more or less extended peripheral zone or the whole of the lobule. Thus, for example, in the external half of the lobule a complete distension may be observed of the cells by one, two, or three fat globules. These cells, instead of having their normal polyhedral form, have become spherical and large; their nucleus, which is preserved, is pushed towards the periphery of the element, and the protoplasm completely surrounds the fat. These altered cells greatly resemble a fat cell of the subcutaneous cellular tissue, and sections obtained after hardening of the fatty liver might be mistaken for a preparation of cellulo-adipose tissue. The periphery of this degenerated lobule appears at the autopsy to be anæmic, grey or yellowish, and opaque. In the centre of the lobule, on the contrary, the hepatic tissue has preserved its brown or pink colour, and the cells are normal or contain only a few fat granules or pigment granules. It is this condition of the liver which induced observers at the commencement of this century to admit the existence of two different substances in the liver, one red, the other grey. The grey or fatty substance is in relation with the interlobular branches of the portal vein and with the nearest capillaries. This distribution of the lesion is caused by the hinderance to the circulation in the liver, by stasis of blood in the portal capillaries, and simultaneously by insufficient hæmatosis. Pulmonary and cardiac affections also cause arrest of the fatty matters in the liver brought hither by the blood during digestion. If the

pulmonary circulation be incomplete, or the blood have any difficulty in passing through a valve of the heart, pressure increases in the right auricle and is transmitted to the hepatic vein, and the portal circulation is consequently slowed. In the liver observed in cardiac diseases a new element is added in the dilatation of the hepatic vein and its capillaries with pigmentary infiltration of the liver cells. In chronic pulmonary diseases, and particularly in phthisis, the entire hepatic lobule is generally in a state of fatty degeneration. The same condition is observed in cachexia with chronic suppuration. Hence it follows that the distribution of fat in degeneration affects a certain relation with the hepatic lobules, and that the cells of the periphery are generally diseased in a uniform manner. However, in a series of cases of complete fatty degeneration observed in phthisical patients, Sabourin [1] has seen the primary lobules dissociated as in cirrhosis, islets of cells charged with fat immediately surrounding the branches of the portal vein, while the ramifications of the hepatic vein passed to the periphery of the lobules thus composed. Whence it results that in place of a normal lobule many segments of islets were seen, forming by their union lobules of spherical form, having a branch of the portal vein in their centre.

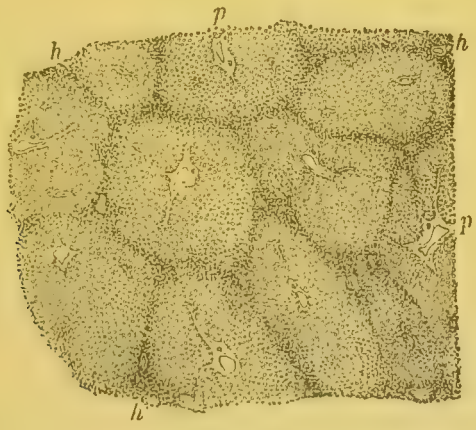

FIG. 154.—SECTION OF A FATTY LIVER.
(After Sabourin.)

p, *p*, portal vein situated at the centre of the adipose lobules ; *h*, *h*, hepatic veins.

When the liver is affected throughout its entire extent by fatty degeneration, it is hypertrophied, for all the cells have increased in size in consequence of the accumulation of fat within them. Its colour is uniformly grey or yellowish; its edges, instead of being sharp and well defined, are obtuse ; it is soft in consist-

[1] 'La Glande Biliaire et l'Évolution Nodulaire du Foie,' *Rev. de Méd.*, Mai 1883.

ence, for it contains a large quantity of oily fluid, and Glisson's capsule is tense and shining. It greases paper, and on scraping

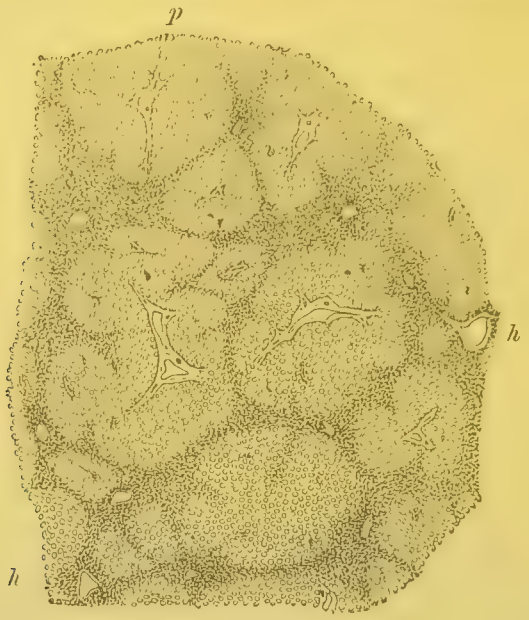

FIG. 155.—SECTION OF THE LIVER IN FATTY DEGENERATION. (After Sabourin.)

p, portal vein; *h*, *h*, hepatic veins.

the divided surface drops of oil may be seen with the naked eye. Nothing is easier than to make the diagnosis at first sight. Circulation still takes place in these large fatty livers, but it is probably embarrassed in the capillaries by the pressure of the hypertrophied cells. The secretion of bile is frequently vitiated, as Frerichs has observed. The liver cells are not, in fact, in the normal condition for secreting bile. Thus large bile ducts may be found empty or containing only mucus, and the gall bladder filled with mucous and decolourised bile. In this decolourised bile the colouring matters are wanting, though the bile acids are still present. Finally, in these large hypertrophied fatty livers sacciform dilatations of the bile ducts are found, and a catarrhal condition of their mucous membrane. In cases of fatty liver observed moreover in the course of chronic cachectic disorders, particularly in tuberculosis and cardiac diseases, we have also observed another series of hepatic lesions which terminate by fatty degeneration, namely those of parenchymatous hepatitis following infectious diseases or certain poisonings, and the degeneration consecutive to nodular hepatitis and adenoma; only here the cells are filled with fine proteic or fatty granulations, and have a tendency to

disintegrate and become destroyed. We have already insisted on these points in distinguishing between fatty infiltration which does not kill the cell, and granulo-fatty necrobiosis which ends in the death of the element. Among cases of parenchymatous hepatitis, that which follows poisoning by phosphorus, arsenic, and antimony is characterised by a considerable fatty infiltration of all the liver cells, which cells are quite filled with oily globules. The organ is normal in size or slightly tumefied, grey and opaque on section, frequently congested, and of a pasty softness. The kidneys are almost always at the same time in a state of complete fatty degeneration.

Amyloid degeneration.—Amyloid degeneration of the liver cells (*vide* p. 320) consists in their infiltration by a refractile, translucid, peculiar substance, which possesses the property of fixing iodine and staining mahogany-brown by a weak iodised solution. This staining of a dark mahogany-brown is frequently modified by sulphuric acid, which causes successively a change to green, blue, violet, or red, or to only one of these colours. The liver cells are changed in this disease into small vitreous blocks with blunt angles or they are spherical. These altered cells conglomerate and form masses in which irregular fissures are often seen; they no longer show any of their normal structure, neither nucleus, granulations, nor drops of fat, pigment granules nor glycogen. This amyloid degeneration commences in the liver from the hepatic arteries and the capillaries of the lobules. The interlobular branches of the hepatic artery penetrate, as we know, to the periphery of the lobule, and there are broken up into capillaries which anastomose with those of the portal vein. The amyloid degeneration of these arterioles transforms them into channels with hard and refractile walls, composed of the endothelial and muscular elements infiltrated by the amyloid substance. The nearest liver cells are the first affected; whence it results that the lesion is first limited to an intermediate zone between the peripheral zone of the lobule and its centre, always nearer the periphery than the centre. At this stage of the change, the lobule is divided into three zones, one very narrow at the periphery in which the cells are in a state of fatty degeneration, an intermediate in a state of amyloid degeneration, and a central zone in which the cells are either granulo-fatty, or normal, or infiltrated with a yellow or red pigment. When the lesion is older and more marked, the entire lobule is degenerated; but it is very rare for the whole of the liver

to be amyloid; there are always parts of lobules, or entire lobules, which are simply in a state of fatty degeneration. The lesion is sometimes propagated by the hepatic veins, and to the branches of the portal vein when the entire lobule is affected. The degeneration may affect only or almost only the vessels. We have ourselves observed a case in a patient affected with splenic leucocythæmia, in which the capillaries of the hepatic lobules were alone affected with amyloid degeneration. The thickened walls of these capillaries formed a complete and elegant network, while the portal and hepatic veins were normal. The liver cells showed no amyloid lesion; they were only a little atrophied in consequence of the thickening of the walls of the capillaries. In spite of the amyloid thickening of the walls of the capillaries, the endothelial cells were preserved and red blood corpuscles were still found within them.[1] These researches had better be made with anilin staining fluids, such as methyl-violet, safranine, &c., which define the degenerated parts and permit of well-preserved and characteristic preparations being made.[2]

To the naked eye, the amyloid liver has very nearly the same appearance as the fatty liver; it is of a pasty consistence, is bloodless, grey or yellowish grey, and is sometimes quite waxy in places. Its edges are blunt, and its size is normal or slightly increased. On making a large thin section and on examining it in a slide by transmitted light, transparent vitreous parts are observed,

[1] In the cases where the degeneration is more advanced, the capillaries of the diseased lobules are completely changed. Their walls are so much thickened that the lumen of the vessel is entirely obstructed, or only visible as a point or slit in transverse sections. The circulation of the blood is impossible, and a trace of endothelium is no longer to be seen. The liver cells are then either in the state of fatty or amyloid degeneration. In a case recently brought before the Société Anatomique by M. Thibierge, a large portion of the liver, particularly its anterior border and inferior surface, was quite bloodless and transparent like wax. In the lobule in sections of these parts the capillaries were seen to be thickened, changed into amyloid trabeculæ, only separated from one another by rows of fine fat granules representing the final vestiges of the hepatic trabeculæ. The interlobular branches of the portal vein were thrombosed and surrounded by a fibrous tissue of new formation. This is the most complete example of amyloid degeneration that we have observed. The rest of the liver, which was much hypertrophied, had undergone less marked amyloid change, and cirrhosis, with many new bile canaliculi, was also present.

[2] The method of determining the presence of amyloid substance by means of Paris violet was described in vol. i. p. 70. With safranine the parts which have undergone amyloid degeneration are stained yellow, while the normal elements are coloured red. The preparations made with this reagent are very striking, and they have the advantage of being suited for mounting and preserving in Canada balsam.

varying in size. Moreover, in pouring tincture of iodine or a feebly iodised solution on the divided surface of the liver, parts of lobules or entire lobules are seen to assume the characteristic brown colour. This reaction, practised on the post-mortem table, immediately demonstrates the nature of the lesion. Generally when the liver is affected the spleen and kidneys are equally altered; if the kidneys be not amyloid they almost always show a granulo-fatty degeneration of the epithelial cells of the tubuli.

The etiology of amyloid degeneration of the liver shows many points of contact with that of fatty degeneration. Amyloid degeneration is present in all cachectic diseases with chronic suppuration, in tuberculosis, scrofula, syphilis, sometimes in cancer, leucocythæmia, leprosy, &c. In syphilis, and in the tuberculosis of drunkards, this form of degeneration often complicates cirrhosis. We have also once seen amyloid degeneration with cirrhosis in leprosy. In this case, the bacilli of leprosy were found in the elements of the newly formed fibrous tissue (*vide* fig. 132, p. 338). Amyloid degeneration offers this point of contact with simple fatty degeneration, that denutrition, emaciation, in which the lesions of the liver take some part, are the sole symptoms. The local symptoms do not indicate any lesion of the liver; there is no pain, no icterus, no ascites; at the most, in certain cases, but not in all, a slight hypertrophy of the organ is noted, the lower edge of which seems blunt and soft to the finger, instead of being hard and sharp.

Tumours of the liver.—We have already spoken of the tumefaction of the organ caused by acute suppurative inflammation, by chronic inflammation (hypertrophic cirrhosis), by adenoma, which frequently complicates cirrhosis, and by certain forms of degeneration which cause a limited or complete hypertrophy; these are sometimes clinically grouped under the name of tumours. We do not intend here to make a symptomatic study of tumours, but it is well to be forewarned against rather frequent error in diagnosis, caused by the normal depressions of the anterior border of the liver, and by the equally normal projection made sometimes by the gall bladder. When the liver is slightly lowered or hypertrophied, and its free border can be followed by palpation, the notch-like depression caused by the longitudinal groove and the projection made by the gall bladder sometimes simulate a hepatic tumour.

Angioma.—Cavernous angioma is rather frequent in the liver;

it is most frequently seen at a point on the surface of the liver in the form of a small, round, dark red tumour. When incised, blood flows out and it collapses, and an areolar cavernous tissue is then seen, the cavities of which, formerly filled with blood, are then empty; these blood tumours are often multiple; exceptionally they become very large. We have recently seen a form of diffused angioma, very remarkable from its extent and its distribution under Glisson's capsule, and along the branches of the portal vein. In order to study angiomata, they should be first placed, without opening them, in a fluid which coagulates blood, alcohol for example. On cutting sections the cavities are seen filled with

FIG. 156.—CAVERNOUS ANGIOMA OF THE LIVER (SECTION MADE AFTER HARDENING IN ALCOHOL).

a, the cavernous spaces filled with blood; *b*, the fibrous trabeculæ limiting the cavernous spaces.

blood, and separated from one another by delicate septa. These septa are formed of a dense fibrous tissue and a layer of endothelial cells lining them. The entire tumour is surrounded by a zone of embryonic connective tissue, which is intersected by the dilated vessels which are distributed to the lacunæ of the tumour. These lacunæ communicate irregularly with one another; they are developed from the capillaries situated in the embryonic tissue, which tissue permits their enlargement. These tumours can be injected from the hepatic artery.

Tubercle.—Tubercular granulations are common in the liver, and are often very numerous in patients who have succumbed to acute miliary tuberculosis. They are so small that they are per-

ceived with difficulty by the naked eye. The liver is then anæmic and yellowish, for it is generally in a state of fatty degeneration, and it is only by looking carefully in a good light that the small

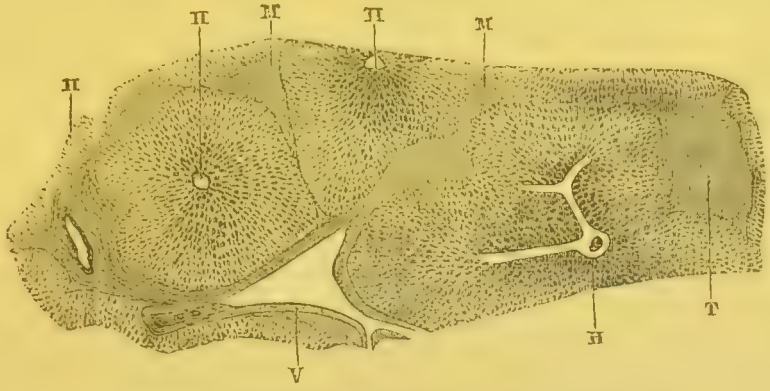

FIG. 157.—TUBERCULAR GRANULATIONS IN THE LIVER.

H, H, central veins of the lobules from which the cells radiate in lines; M, M, thickened interlobular connective tissue which has become embryonic; a tubercular granulation, T, has developed in this tissue; V, section of a branch of the portal vein. Magnified 20 diameters.

semi-transparent granulations are seen between the lobules. The granulations of the capsule and the peritoneum are more easily recognised, for they make marked elevations, and their colour is more pronounced on the surface of the organ. Tubercles of the liver itself are almost always located in the connective tissue which accompanies the portal vessels. Sections of these vessels show them generally either in the centre of the granulations or near them. They are accompanied by a new formation of embryonic tissue, which is continuous with them, and from which they cannot be distinguished when quite recent. They are consequently surrounded by interstitial hepatitis. In this zone of partial cirrhosis the spurious bile ducts are often seen in more or less considerable numbers. Sometimes the new growth is developed between the trabeculæ of liver cells, which are then separated by a tissue composed of small round cells. Later, when the older granulations show at their centre atrophied cellular elements, they are easily distinguished from the peripheral tissue. The superficial granulations are situated at the same time in Glisson's capsule, in the prolongations of this membrane between the lobules, and in the lobules themselves. Tubercles of the liver have the same structure as tubercle of other organs. They almost invariably, even the smallest, contain giant cells. Julius Arnold has seen these cells develop in the midst of the bile ducts, at the expense of the epithelial cells. We have verified this fact. With

regard to the distribution of the bacilli peculiar to tuberculosis, they are seated in varying numbers in the tubercular nodules, and in the giant cells as in every other tubercle. In the rabbit and guinea pig tubercles of the liver are very easily produced by injecting tubercular products into the peritoneum. The bacilli, free at first in the peritoneum, seem to penetrate directly into the liver by traversing the perihepatic peritoneum and Glisson's capsule, to finally become distributed throughout the organ. In fact, in examining sections from the surface of the liver at the level of superficial tubercles, thickening and hyaline degeneration of the peritoneum and Glisson's capsule are observed, and the bacilli are present at this spot (Baber and Cornil, 'Journal de l'Anat.,' 1883, p. 456). Large tubercles of the liver, having a diameter of from 1 to 10 mm., are occasionally seen in the liver. The latter are formed by the conglomeration of many tubercular granulations, and are soft and caseous. They sometimes accompany peritoneal tuberculosis in children.

Syphilis and gummata of the liver.—We have already in vol. i. (p. 189) given a general outline of the nature and development of syphilitic lesions of the liver, hence we have here only to complete this important subject. We said that syphilis sometimes causes actual interstitial hepatitis or cirrhosis and precedes the formation of gummatous tumours. Syphilitic interstitial hepatitis in new-born children and in adults differs slightly in character.

Syphilitic interstitial hepatitis is rather frequently found in the fœtus or new-born child dead from hereditary syphilis. Gubler has given a good description of the naked-eye appearances of this lesion. The surface of the liver is smooth, its colour uniform, yellowish and partly semi-transparent, of a flint-like appearance. On dividing it across, small opaque, yellow or greyish granules are sometimes seen. The hepatic parenchyma is rather firm and elastic; on letting a morsel of the liver fall on the post-mortem table it rebounds by its elasticity; on indenting it with the finger-nail it is not, however, as resistant as a cirrhotic liver, which is due to the fact that there is no completely organised fibrous tissue; in fact embryonic tissue formed of small round or oval cells predominates in the portal spaces or between the trabeculæ of liver cells. It must not, however, be concluded that embryonic tissue found in the liver of the fœtus at six or nine months or of new-born children is always an indication of syphilis, for at this age the liver contains embryonic fibrous tissue and not adult connective tissue;

but in syphilitic interstitial hepatitis it is more abundant than normally. In the portal spaces, moreover, round islets of embryonic tissue occur which represent actual small gummata. In the adult,

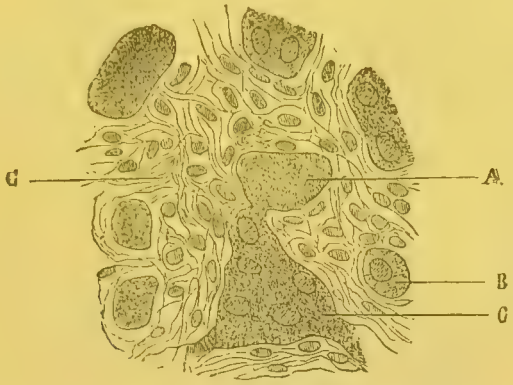

FIG. 158.—DIFFUSE INTERSTITIAL HEPATITIS.
A, C, network of liver cells in a condition of fatty degeneration; B, isolated cells; G, new connective tissue. Magnified 300 diameters.

in subjects who have died of an intercurrent disease, a similar syphilitic cirrhosis may be accidentally discovered, which simultaneously affects the connective tissue around the acini and the inter-trabecular connective tissue in the lobules. This localised or general interstitial hepatitis usually precedes the formation of gummata. It may be complicated with amyloid degeneration.

Syphilitic gummata.—During the tertiary period of syphilis the liver is often the seat of gummata. They are composed of the union of two, three, or more small tumours the size of a millet seed or a small pea or larger; these tumours are angular, yellowish in colour, and very hard; they are surrounded by a thick zone of dense and hardened connective tissue which forms a common envelope; whence results a large mass usually seated at the bottom of a cicatricial depression on the surface of the liver. Many groups of these gummata surrounded by their fibrous envelope may be found in the same liver. At the cicatricial depressions thickening of Glisson's capsule is noticed, and also generally fibrous adhesions which, springing from the liver, unite this organ to neighbouring parts. On dividing the liver so that the section passes through one of these cicatrices and the group of gummata lying beneath, it will be seen that the pink or grey fibrous tissue which surrounds the central caseous growths is continuous around the neighbouring hepatic lobules. The chief gross appearances of gummata, and which differentiate them from anything else, are their dryness, their yellow caseous condition, and their great hardness. This elastic resistance found on indenting them with the finger-nail

distinguishes them from caseous tubercles which are soft, and their hardness differentiates them from other forms of tumours, sarcoma, scirrhus, &c., which yield a large quantity of fluid on scraping. A liver affected with gummata is generally found at the autopsy to be much diminished in size, for the lesions being of old standing, the peri-hepatitis and cicatricial shrinking around them soon induce atrophy. But it may be quite otherwise at the commencement of hepatic syphilis. The liver may be even hypertrophied in the acute congested and inflammatory periods of tertiary syphilis. According to Lancereaux, Klebs, and other authors, gummata of the liver may be re-absorbed, leaving cicatricial depressions in their

FIG. 159.—GUMMATA OF THE LIVER SEEN IN SECTION OF THE ORGAN. IN THE CENTRE OF THE FIGURE IS A COLLECTION OF GUMMATA SITUATED BETWEEN THE RIGHT AND LEFT LOBE.
(Figure borrowed from Virchow's 'Pathology of Tumours.')

place. It is not doubted but that caseous nodules may be partly absorbed. In vol. i., p. 197, we described lacunæ filled with fat granules situated around the caseous centre of gummata, which lacunæ we look upon as lymph channels (fig. 161), aiding in this process of re-absorption; but it is difficult to believe that these tumours may entirely disappear. In the central caseous part of old gummata small cellular elements are found which are close

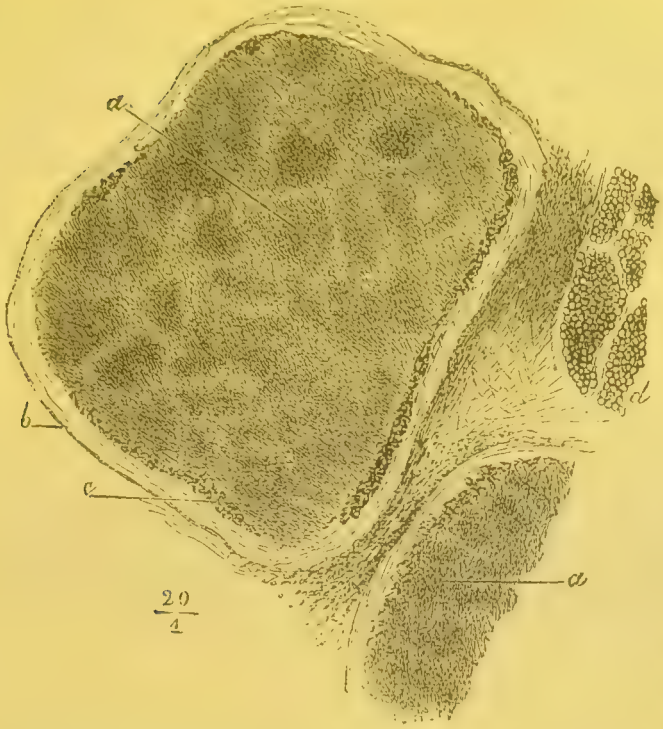

FIG. 160.—SECTION OF OLD GUMMA OF THE LIVER MADE AFTER HARDENING THE TUMOUR IN CHROMIC ACID.

a, angular masses enveloped in the fibrous tissue, *b* ; *e*, dark zone in which spaces are seen filled with fatty granules ; *d*, hepatic lobule. Magnified 20 diameters.

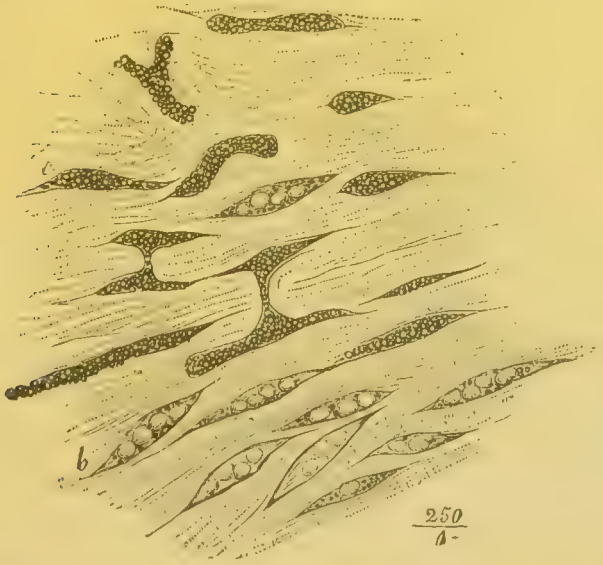

FIG. 161.—FIBROUS TISSUE FORMING THE ENVELOPE OF A GUMMA UNDERGOING ABSORPTION.

b, spaces containing cells and fat granules ; *c*, the same spaces containing only fat. Magnified 250 diameters.

together, filled with fine granules, and in a state of granulo-fatty degeneration. The blood vessels are here obliterated, and in the peripheral fibrous zone very dense connective tissue is found intersected by sclerosed vessels and containing between its fibres either round or flattened cells. More recent gummata of the liver

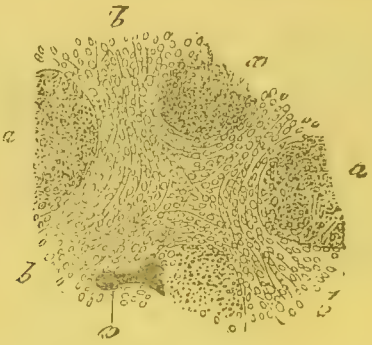

FIG. 162.—SYPHILITIC GUMMA OF THE LIVER.

a, centre of the nodules in which the cells have become granular; *b*, periphery of these nodules; *v*, vessels. Magnified 100 diameters.

(*vide* vol. i. p. 195) are composed of small microscopic nodules (*a*, fig. 162), the centre of which has already undergone atrophy and granular degeneration, while the round cells of the periphery blend with the neighbouring embryonic tissue. A large gumma is composed of a great number of these nodules. Giant cells are sometimes found in recent gummata or at the periphery of old

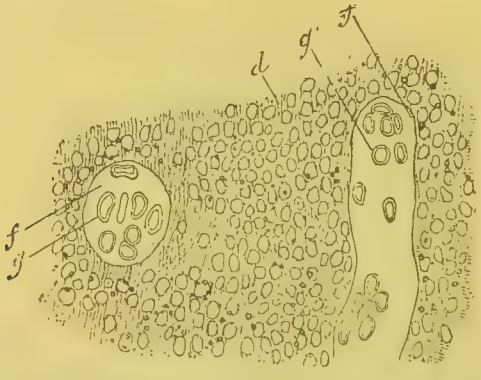

FIG. 163.—THE SAME PREPARATION SEEN UNDER A POWER OF 400 DIAMETERS.

d, elements of the gumma; lumen of the blood vessels in which red blood corpuscles, *g*, are seen.

gummata, but they are much rarer than in tubercle. Since Klebs described the bacilli peculiar to syphilitic growths, and many observers have verified this discovery, we have searched for these rods in recent syphilomata and gummata, particularly in those of the liver, but we have not found anything characteristic.

Leucæmic Tumours.—The liver of subjects who have succumbed to leucocythæmia presents many kinds of lesions. It is generally very large, and may weigh from 8 to 10 lbs. Small extravasations of leucocytes are first met with (described in vol. i.); further, in ganglionic or splenic leucocythæmia and in generalised lymphadenoma new formations of reticulated lymphatic tissue are often observed; these are actual tumours in the histological sense, and they coincide with considerable congestion of the organ. In the case of amyloid liver, these lymphadenomata may exist in considerable numbers. These neoplasms of retiform tissue are found between the lobules, around the interlobular vessels, and particularly along the course of the branches of the portal vein.

Sarcoma.—Sarcoma is rare in the liver. The melanotic variety is most frequent, for primary tumours other than melanotic are rarely found in the organs whence spring the radicles of the portal vein.

Carcinoma.—Carcinomatous and epithelial tumours are rarely primary in the liver; they are generally secondary to tumours of the same nature in the stomach, intestine, rectum, peritoneum, lymph glands, uterus, testicles, breast, &c., or of the gall bladder. In fact, the gall bladder and the bile ducts may be the seat of primary cancer which extends to the whole liver. Often, however, the cancerous nodules of the liver are so large, and the lesion of the vesicle so inconsiderable, that an inexperienced observer might conclude that the affection was primary in the liver, while the contrary is the fact. Secondary carcinomata of the liver have this characteristic: they are of considerable size, the liver being infiltrated, for example, by morbid masses weighing 4 or 6 lbs. or more, while the primary tumour, seated, for instance, in the stomach, and consisting of an ulcerated encephaloid, is hardly larger than the hollow of the hand. It cannot, however, be doubted that the lesion of the stomach is the primary one, considering the previous suffering in the region of this organ, and how the signs by means of which such a cancer is recognised date back one or two years, while the hypertrophy of the liver has only been developed at the end of the illness and under the eye of the physician. Of all the organs of the body the liver is the one in which secondary carcinomatous growths are most frequent. As it is a law that secondary growths have the same structure as the primary tumours, it results that all the known varieties of

carcinoma are found in the liver. The primary carcinoma consists of a homogeneous mass without a vestige of hepatic tissue at its centre, which is formed of cancerous tissue, more or less old, often yellow and opaque, and uniformly degenerated. At the edge of the tumour the nodules of secondary infection are observed. All these tumours yield a milky fluid on section and show under the microscope the typical structure of carcinoma, that is to say, septa of connective tissue forming a reticulum and limiting spaces which intercommunicate. These spaces are filled with large polyhedral cells, varying in form, racket-shaped, elongated, oval, or spherical, clear in appearance and containing one or more nuclei furnished themselves with large refractile nucleoli. The septa which correspond to the cellulo-vascular reticulum of the liver are intersected by capillary vessels. In secondary carcinoma, instead of finding a considerable mass infiltrating an extensive surface of the liver, as in the preceding case, a large number of islets are observed which are nearly all of the same age and spread pretty uniformly throughout the entire organ. These round secondary nodules vary in size from that of a millet seed to a small nut. It is thus understood how, if the primary carcinoma be very near to the liver, as, for example, in the stomach or the gall bladder, the part of the liver nearest to the primary tumour would be the first to undergo change. The nodules developed on the surface of the liver form hemispherical projections, one half of the tumour lifting up Glisson's capsule, while the other half is seated in the parenchyma of the organ. The centre of these projections is generally depressed in a cup-shaped manner, which depression is caused by the fatty degeneration and atrophy of the cells. A liver affected with primary or secondary carcinoma is generally greatly enlarged, particularly when the tumour is encephaloid. It often reaches far below the lower edge of the ribs, and by palpation the inequalities of its convex surface and its anterior border may be felt below the false ribs. The presence of these tumours on the branches or the main trunk of the portal vein causes ascites, which does not, however, prevent the diagnosis being made by palpation. When, in fact, the abdominal wall is only moderately distended by the effusion, it can be depressed by pressing the finger directly downwards, and the cancerous nodules can then be easily felt when they are present in the anterior border of the liver.

It is unnecessary to describe here in detail the histological characters of the varieties of hepatic carcinoma, for that would be to give a complete account of carcinoma, but we will describe the

peculiarities due to its seat in the liver and its mode of development here. A very remarkable feature in hepatic cancer is the invasion and repletion of the afferent branches, the trunk and divisions of the portal vein, by the morbid tissue. We have often observed, as the result of hematoic or telangiectatic carcinoma of the stomach, similar cancerous formation in the portal vein. In this form of cancer, networks of dilated capillaries and small aneurisms are very easily recognised with the naked eye as sinuous lines or red isolated spots. In the case we examined, sinuous cords were observed about the size of goose quills on the peritoneal surface of the ulcerated gastric tumour which was seated near the pylorus; these cords were nothing else than the afferent branches of the portal vein, and were easily followed to the parent trunk. On incising these veins, they were found to be full of a soft carcinomatous tissue resembling the primary tumour, and in its semi-fluid and whitish tissue dilated capillaries were seen similar to those on the tumour in the stomach. These capillaries were budding from the internal surface of the veins and were often very long, lying in the direction of the blood current. The wall of the vein, which could still be recognised on the peritoneal surface of the stomach, though infiltrated with new elements, was blended on the ulcerated side of the stomach with the carcinomatous tissue, and this wall was entirely changed into alveoli filled with cells. The morbid change did not stop here; the trunk of the portal vein and all its hepatic branches were filled with the same elements, cancerous tissue and dilated vessels springing from the altered wall of the veins, or derived from a lower point and growing into the cavity of the vessels situated above; whence on section of the liver the divided interlobular portal veins were seen around the lobules, and they were filled with cancerous juice which could be squeezed out. In another series of cases carcinomata of the lymph glands, either primary or secondary, or tumours of organs adjacent to the portal vein, are propagated to the walls of this vein and determine the formation of cancerous fleshy granulations floating in the lumen of the vessel. We have frequently observed such cases; a cancerous and much hypertrophied lymph gland touches the wall of a vein at a certain point; a close adhesion is affected over a considerable surface; the wall of the vein thickens at this spot, and the connective tissue of the external coat is changed into a carcinomatous tissue; the middle coat, then the internal, undergoes change in the same manner, so that a limited swelling due to the

neoplasm projects into the lumen of the vessel. The vascular endothelium proliferates at this spot; later, the cancerous tissue bud becomes more and more prominent, softens, and disintegrates under the influence of the blood current; fragments are thus carried away which, arrested in an interlobular branch, form true cancerous emboli, which in their turn become the point of departure of secondary tumours. Later, the neoplasm on the portal vein ulcerates, whence results a loss of substance of the coats of the vein, so that adjacent carcinomatous tissue constitutes its wall. The method of production of carcinomata of the portal vein is easily understood. They are often described in a manner which is not absolutely correct; it is said that the carcinoma adjacent to the portal vein has perforated its coats and penetrated its cavity. The contrary may however be said, for the wall of the vein has become, by propagation of the neighbouring tumour, the point of departure of a carcinomatous bud which finally ulcerates. The perforation of the vein is in consequence of the infiltration of its coats with the cancerous granulation, and of their subsequent softening.

Many cases of **melanotic carcinoma** of the liver reported by German authors show that the capillaries of the hepatic lobule are then filled with the cellular elements of the tumour. The radiating direction of these capillaries and the pigmentation of the cells have given this variety of carcinoma the name of the radiating pigmented cancer (Rindfleisch). We have had occasion to examine a case of secondary melanotic carcinoma of the liver, in which the neoplasm seemed at first sight to have irregularly infiltrated the whole of the organ. In microscopic sections, the diameter of most of the portal vessels was much larger than normally, and they were round in form. Their walls were infiltrated with large cells, and on their internal coats were fleshy granulations of connective tissue infiltrated with large cells. These granulations either filled up the entire calibre of the vessel, or a central lumen was left containing free cells and blood. The cellular elements were more or less pigmented brown. Almost all the vessels were altered in the same way. The arterioles of the liver were not the seat of such an acute carcinomatous endarteritis, but in their internal surface were seen layers of endothelial cells, some of which were pigmented. Some of the lobules of the liver were entirely changed into carcinomatous islets; the circular form of the lobules was preserved; their interlobular portal branches were recognisable, though affected with endophlebitis, described above.

The central vein and the radiating capillaries of the lobule were *in situ*, and almost normal; but the network of liver cells was replaced by nests of cells with nuclei containing large nucleoli, and the protoplasm of most of these cells was pigmented. The thickened connective tissue which accompanied the vessels formed the stroma of the carcinomatous alveoli. The interlobular bile ducts were also easily recognised by their direction and their seat; but their small cubical cells were replaced by large cells, with large nuclei and refractile nucleoli, and their size was increased. It would be difficult to see a more beautiful example of the participation of all the parts of the liver in the development of a tumour. It must not, however, be thought that cancerous degeneration of the walls of the veins, and their filling up with cancerous tissue, and the consecutive venous and capillary emboli, constitute the usual mode of the development of secondary carcinoma. On the contrary, miliary and recent nodules are seated most frequently in the interlobular connective tissue, around the small divisions of the portal vein, and they owe their origin to the new formation of cells between the fasciculi of connective tissue. Inflammation of the veins is then characterised by the formation of numerous endothelial cells on their internal surface. This latter lesion may, however, be also regarded as the result of the development of a cancerous nodule in the connective tissue, as well as its cause. Rindfleisch attributes the chief part in the genesis of carcinoma of the liver to proliferation of the hepatic cells. We, however, do not consider this mode of formation to be so common, but it is none the less true that if we now understand a few facts concerning the development of carcinoma in the liver, there still remain others to unravel, and in particular the part played by the lymphatics at the commencement of these tumours. It has been said that the cells of hepatic carcinoma reproduce the structure and form of the normal cells of the liver; we have never observed this analogy. The cells of hepatic carcinoma are, as elsewhere, clear, contain very large oval nuclei, brilliant nucleoli, &c.; they do not resemble liver cells in anything, and do not contain the granules met with in the protoplasm of the latter.

Cylindrical-celled epithelioma is rather frequently observed in the liver, secondary to similar tumours developed primarily in the stomach, small intestine, rectum, and gall bladder. The naked-eye appearances of these tumours are the same as those of

encephaloid, that is to say they consist of nodules varying in size, and of a soft consistency, yielding a quantity of milky juice. They may also assume the appearance of colloid cancer in consequence of either partial or total colloid change in the cells, an appearance which the primary tumour then also presents. To determine the nature of the tumour, it must be hardened in absolute alcohol, or in Müller's fluid, gum, and alcohol; if the examination be limited to scraping, the tubular form of the neoplasm cannot be discovered. In hardened sections the tubes may be seen divided across longitudinally or transversely, or they appear as ovoid cavities lined with a layer of cubical or cylindrical cells. The arrangement of these elements exactly reproduces the structure of the primary tumour. It is impossible to demonstrate the existence of a separate membrane around these tubular growths; they are simply limited by the neighbouring connective tissue. In the centre of the tubes a distinct lumen or cavity is seen. In the colloid parts of the tumour there are the same tubes, and the

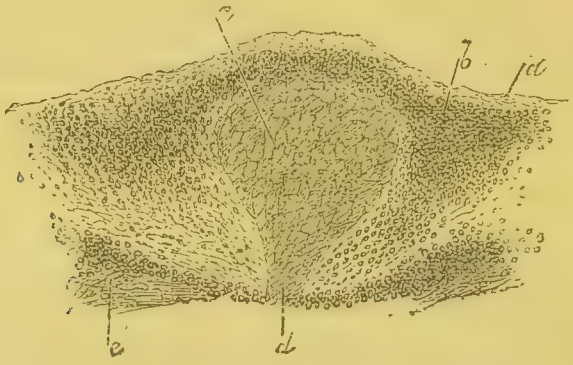

FIG. 164.—GRANULATION PROJECTING ON THE SURFACE OF THE LIVER AND FORMED BY A HEPATIC LOBULE.
(From a new-born infant.)

a, Glisson's capsule; *c*, lobule of liver cells surrounded by embryonic connective tissue, *b*. Magnified 150 diameters.

same cavities lined with a layer of cells which have undergone colloid degeneration.

Adenoma.—We have already (p. 380) given a full description of adenoma of the liver, considered particularly as a complication of cirrhosis. Those nodules which project under Glisson's capsule (fig. 164) and reproduce the structure of a lobule of the liver are less adenomata, showing a tendency to grow, than faults of development and formation dating back to intra-uterine life, and they have only a teratological interest.

Serous cysts.—Advanced putrefaction of the liver and the development of vacuoles containing gases and fluids under Glisson's capsule, or in the substance of the liver, might at first sight be mistaken for serous cysts. The cavities also frequently met with in the midst of carcinomatous or sarcomatous nodules must not be mistaken for cysts. Serous cysts of the liver are very rare. They are generally seen in the form of small round or oval vesicles the size of a pin's head or of a pea, seated under Glisson's capsule or in the substance of the organ, in the trabeculæ which accompany the portal veins. They rarely attain the size of a small nut. They are generally grouped together, have a delicate fibrous wall, and contain a clear transparent fluid. Sometimes they intercommunicate, forming thus a multilocular cyst. The development of these cysts is easily followed, particularly when they are small and multiple. In fact, in sections, dilated interlobular bile ducts are seen in certain of the portal spaces, surrounded by a zone of connective tissue which finally isolates them. These cysts are nothing else than isolated and distended bile ducts in the midst of a fibrous tissue. They are lined internally by a layer of cubical or flat epithelial cells.

Biliary cysts.—Cysts are rather frequently found on the surface of the liver containing biliary sand. They are lined by a single layer of flat epithelial cells. The connective tissue surrounding them is continuous with that at the periphery of the lobules, and constitutes a local cirrhosis. In the sclerosed tissue, the bile ducts show the same lesion as in general cirrhosis.

Hydatid cysts.—Echinococci cysts, which are rather common in the liver, form large and prominent tumours, which generally project either on the upper part of the convex surface of the liver under the diaphragm, on its anterior surface, or in its substance. We find in these tumours from without inwards, first, a thick fibrous envelope or adventitious membrane, the structure of which is that of fibrous tissue with parallel lamellæ and flat cells. This fibrous membrane is continuous with the thickened connective tissue which surrounds the lobules, forming a peripheral cirrhosis to the tumour; the neighbouring lobules are flattened by pressure. Secondly, within is the perfect hydatid membrane, spherical and tense in recent growths; withered, crumbled, and torn in old cysts. This membrane is characterised by its parallel and regular lamellæ formed of an hyaline substance without the interposition of any cellular element. Within this membrane, of which the sharp fracture, its arrangement in lamellæ, and its vitreous appear-

ance are quite characteristic, small vesicles are found surrounded by a membrane similar to the parent membrane, though generally thinner. These vesicles, the volume of which varies between that of a pin's head and a fowl's egg, are uniformly spherical. They

FIG. 165.—TRANSVERSE SECTION OF A HYDATID MEMBRANE WITH ITS LAMELLÆ, *a*, *b*.

contain a serous fluid without albumen, and small granules which are nothing else than echinococci. Often echinococci are not found, when the cyst is said to be sterile; the echinococci are small cyst worms formed by a vesicle adhering to the germinal membrane, and in the midst of which is found the head of the animal, characterised by a proboscis, a double row of hooks, and four suckers. The echinococci are the cyst worms of the *Tænia echinococcus*, which has its habitat in the intestine of the dog. The egg of this tænia liberated in the fæces of the dog, and ingested with water or the food, loses in the stomach of man its enveloping membrane, and the liberated embryo perforates the coats of the stomach to become lodged in neighbouring or distant organs, there to undergo the second phase of its development. When the hydatid cysts, having reached their highest development in the liver, still remain *in situ*, they shrink, and the hydatid membranes rupture or break up; they are then contained in an opaque, thick fluid, rich in salts and chalk, which is rendered yellowish or red by the presence of the colouring matters of the bile and blood. The echinococci are destroyed or broken up; often only their hooklets remain. Sometimes old hydatid cysts are found in which the fibrous membrane has undergone calcareous infiltration or even partial ossification. Another variety of hydatid tumours of the liver has been described by Friedreich, Virchow, &c., under the name of *multilocular hydatid*

tumour. M. Carrière has given a description of it in his thesis (1868), from a case which we also examined. These tumours are composed of small hydatid cysts arranged in a fibrous stroma. Each cyst is formed of a membrane characterised by parallel hyaline lamellæ; complete echinococci may here be met with or simply hooklets. These tumours have a slight resemblance to colloid carcinoma; but microscopic examination immediately removes all doubts. Hydatid cysts which continue growing may attain such a size as to cause accidents necessitating surgical interference. At other times they may be the cause of limited peritonitis and adhesions between the liver and the diaphragm, the walls of the abdomen, the large intestine, the duodenum, &c. They may also open into the pleura or lung, the intestine, the gall bladder, or the bile ducts. Cases have even been cited of perforation of the portal vein. When the opening takes place into the peritoneum, fatal peritonitis ensues.

The Bile Ducts and the Gall Bladder.

Inflammation.—Catarrhal inflammation of the gall bladder is chiefly caused by the irritation produced by calculi; these may, however, frequently fill the gall bladder without causing any lesion, as may be seen at the autopsies of old women at the Salpêtrière, in whom calculi are frequent. Sometimes the mucous membrane is injected, and the gall bladder contains a decolourised, mucous, stringy bile, containing pus cells. The mucous membrane is then thickened, crumpled, and œdematous, instead of showing its usual delicacy and fine velvety surface. At a more advanced stage, one or more ulcers are found in the mucous membrane, particularly at the lower part of the gall bladder. These ulcers, when rapidly formed in the acute stage, in consequence of puriform infiltration of the connective tissue of the mucous membrane extending into the muscular layers, may cause perforation and the escape of the calculi into the sac of the peritoneum. This accident is extremely rare; ulcers when present are simply marked by local irritation of the peritoneum which covers the exterior of the gall bladder at the affected part. False fibrinous membranes are produced, or fibrous thickening of the serous membrane and adhesions. Peritonitis circumscribed by adhesions permits of communication of the gall bladder with the duodenum or colon. The escape of calculi may take place by these various channels, and even by means of biliary fistulæ communicating with the exterior

through the abdominal walls. The inflammation which is then propagated to the cystic, hepatic, and common bile ducts induces very marked icterus. This inflammation of the gall bladder, and of the neighbouring peritoneum, may cause a limited tumefaction at its level, perceptible by palpation of the abdomen during life. General ascites or peritonitis may be the consequence. Though calculi rarely cause these serious accidents, they often cause thickening of the mucous membrane, connective tissue, and muscular tissue, comparable to the hypertrophy of the bladder which is the result of calculi. The tumefied fasciculi of muscular tissue may be then felt, separated by depressions. Louis, Andral, and Rokitanksy have described infiltration of the mucous membrane and gangrenous ulceration in cholera, typhoid fever, and purulent infection. Catarrhal inflammation of the common cystic and hepatic ducts, which is rather frequent, either occurring spontaneously or as the result of duodenitis, produces catarrhal or simple icterus. At other times it is due to the presence of biliary calculi derived from the gall bladder, or found *in situ* in the ducts of the liver. Biliary sand or a soft mass formed of small fragments of calculi are the most active causes of this form of inflammation. All degrees may be observed from catarrh of the mucous membrane of the common duct, limited to its orifice or to its tract in the duodenal walls, to acute suppurative inflammation. It is thus easily understood how œdematous swelling of the mucous membrane of the duct and of its orifice and the secreted mucus may arrest the flow of the bile, and produce icterus just in the same way as coryza hinders respiration by the nasal fossæ in consequence of swelling of the mucous membrane. It is true that there have been few autopsies in which this lesion has been clearly demonstrated in simple jaundice, but the cases reported by Virchow and Vulpian have been enough to induce conviction on this point. With congestion, mucoid exudation and a mucous plug are simultaneously observed. More acute inflammation, due to the presence of biliary sand, extends to most of the bile ducts in the liver. The mucous membrane of these ducts is covered by a mucus which is transparent, or more or less cloudy by the presence of desquamated epithelial cells and pus cells. The ducts are dilated, and their mucous membrane is thickened, as well as the connective tissue which covers them; it is under these circumstances that pouch-like dilatations are observed lined by mucous membrane, and filled either with a mucous or puriform fluid. These dilatations greatly resemble

small abscesses disseminated throughout the liver; they are lined by a delicate membrane composed of cylindrical cells, and contain many of these cells mixed with lymph cells, blood pigment, and granules of bile pigment. Some of these cavities only contain pus, and are hollowed in the midst of the liver tissue without any limiting membrane, but it is rare for them not to contain cylindrical cells mixed with pus cells. These are then biliary abscesses (*vide* p. 345). In more acute inflammation, the much-dilated bile ducts are filled with mucoid, opaque, whitish, and slightly viscous pus, and its amount is so considerable that on dividing the liver it might at first sight be thought that an abscess was opened. It contains a considerable quantity of cylindrical epithelial cells and lymph cells. All acute inflammation of the bile ducts causes a more or less serious intermittent and febrile condition during life. It may be complicated with inflamed portal vein, peritonitis, &c. Narrowing and even complete obliteration of the hepatic and common bile ducts may be the result of acute inflammation of these ducts, and they may become changed into fibrous cords, as has been recorded by Andral. Sometimes, though rarely, papillary excrescences grow on the mucous membrane of the ducts, as the result of inflammation.

When a large calculus passes into the cystic duct, and thence into the common duct, it may be arrested in the narrow duodenal portion of the latter. If any difficulty be experienced in passing it, its presence alone, or the contraction of the ducts and gall bladder, may give rise to symptoms of hepatic colic; but still more serious inflammatory accidents may occur if it be impacted at a spot in the duct which it blocks. The bile can no longer flow, hence icterus follows, and the inflammation of the mucous membrane and of the submucous tissue, which it sets up by contact, is propagated to the neighbouring organs, notably to the peritoneum, resulting in limited suppurative or necrotic inflammation which leads to perforation. If the calculus be arrested near the duodenum, mortification of a part of the mucous membrane of the wall enables it to pass into the intestine, a satisfactory result, but if it perforates the peritoneum, fatal peritonitis will ensue. After a prolonged arrest of calculi, too large to be expelled by the common or hepatic ducts, complete retention of bile, and dilatation of the ducts situated behind the obstacle will follow. If this condition continues, the dilated ducts thicken and become surrounded with a thick layer of fibrous tissue. In the serous mucus they contain, which may be discoloured or

still stained by the colouring matter of the bile, biliary concretions, varying in size, are often found. The largest of the bile ducts situated immediately behind the obstacle are often those which alone undergo these lesions, for they do not invariably extend to all the bile ducts. Cysts, however, containing a more or less discoloured bile may be found in various parts of the liver. The fibrous thickening observed around the dilated ducts remains local, and this partial cirrhosis does not extend to the whole of the fibrous tissue of the portal spaces, nor of the sublobular veins. The lobules of the liver are all, however, more or less infiltrated with bile, and their cells are stained with bile pigment. But this retention of bile, though complete, and these lesions of the ducts, which are like those in ligature of the common duct, do not cause general cirrhosis. The interlobular bile ducts, which are invisible to the naked eye, are changed in most diseases of the liver, in cirrhosis, acute yellow atrophy, cancer, phosphorus poisoning (O. Wyss), parenchymatous hepatitis, and still more in suppurative hepatitis. In the parenchymatous hepatitis of puerperal fever, variola, &c., we have seen that there is infiltration of the perivascular connective tissue with lymph cells, simultaneously with catarrh of the small ducts contained in the inflamed tissue. These inflammatory lesions of the bile ducts, causing an abundant mucous secretion and the formation of cells which choke them, have certainly the effect of preventing the bile secreted in the liver cells from reaching the common duct, whence retention of bile results. In tumours of the liver, the desiccation, flattening, and compression of the bile canals also play a part in the production of icterus by retention of the bile. Another rather rare accident in inflammation of the bile ducts is hæmorrhage into their mucous membrane. This may occur either in cirrhosis, cancer of the liver, or simple inflammation ('Quinquaud,' thesis by Ferray). Accidental hæmorrhage may also occur in consequence of abscess of the liver; in a case recorded by Lebert it was caused by rupture of an aneurism of the hepatic artery into the gall bladder.

Tumours of the gall bladder.—According to Rokitansky, adipose tissue is sometimes, in polysarca, deposited in the sub-peritoneal tissue of the gall bladder. Carcinoma and cylindrical-celled epithelioma are developed in the mucous membrane of the gall bladder. Cases of carcinoma of the gall bladder have only been recently described; it is, however, not a vary rare affection. It may be primary or secondary; if the latter, it follows carcinoma of the liver,

stomach, intestine, or neighbouring glands. Primary carcinoma of the gall bladder is generally colloid in character; sometimes it is encephaloid and more rarely scirrhous. Generally, though not always (14 in 15 cases of carcinoma and epithelioma analysed in L. Bertrand's thesis, 1870), the gall bladder contains one or more calculi; the larger they are, the less numerous. The bile is sometimes decolourised, at others thick and brown; it may contain fragments detached from the tumour. The surface of the gall bladder is at the diseased spot uneven and granulating, for new growths take the villous form in the gall bladder as they do in the urinary bladder. The tumour invades either a part or the whole of the mucous membrane, which is increased in thickness, and on section it appears as a colloid tissue, or a white substance infiltrated with a milky juice, according to the character of the tumour. The lesion of the mucous membrane and the submucous tissue may be propagated to the muscular tissue, which is always more or less hypertrophied and œdematous. The calibre of the gall bladder is generally increased, sometimes it is diminished. The tumour is often continuous into the cystic and common ducts, the mucous membrane of which is degenerated, granulating, and lessened in calibre; hence retention of bile in the hepatic and in the interlobular bile ducts. Icterus and biliary cysts may be the result. Generally the tissue of the liver itself is invaded by carcinoma at spots near the diseased gall bladder, and throughout the whole liver are distributed nodules, the structure of which resembles the primary tumour in the gall-bladder. The cancerous masses in the liver are often so large, and the lesion of the gall bladder so small, that it is difficult to believe that the latter is primary; the rapid and considerable extension of carcinoma of the liver secondary to that of the stomach enables us to understand the relation existing between the nodules in the liver and the ulcer in the gall bladder. The neighbouring lymph glands are always changed and diseased; the duodenum, colon, and even the stomach may become invaded by carcinoma which has commenced in the gall bladder. These various organs are then united by fibrous and cancerous adhesions; the patches in the stomach and intestine are smaller and more recent than the ulcer in the gall bladder. It is doubtful whether the cancer preceded the formation of the calculi, or if the latter existed previously, and should count among the causes of the tumour by the irritation they set up. We are, however, inclined to the first hypothesis. The non-ulcerated superficial granulations of a gall bladder affected by cancer are lined by

cylindrical cells and are generally formed of a simple embryonic tissue which is highly vascular. Sometimes, however, they show the alveolar structure of scirrhous, encephaloid, and colloid carcinoma. The ulcerated part of the tumour is deprived of all epithelial lining. The alveolar structure of carcinoma is very marked in the submucous tissue. In the muscular tissue, an infiltration of embryonic cells is first noticed, then actual cancerous tissue.

Cylindrical-celled epithelioma of the gall bladder does not differ in its naked-eye appearances from encephaloid carcinoma. The histological characters of the tumour are absolutely identical with those described in cylindrical-celled epithelioma of the liver. Primary epithelioma of the gall bladder also gives origin to secondary nodules in the liver, and it has the same complications and the same gravity as carcinoma. In the cases of epithelioma which have been published, calculi in the gall bladder have also been present.

CHAPTER VIII.

THE PERITONEUM.

The description we have already given of experimental inflammation of the peritoneum (vol. i. p. 88) and of the diseases of the serous membranes (vol. i. p. 423) enables us to dispense with any detailed account of the pathological histology of the peritoneum.

Peritonitis.—Peritonitis may be acute or chronic, general or partial. Acute peritonitis, very rarely primary, is almost always the result of an injury, or a lesion of one of the organs contained in the peritoneal sac, such as perforation of the intestine or stomach, abscess opening into the peritoneum, superficial inflammation of organs covered by this serous membrane, lymphangitis and phlebitis of the uterus and its appendages, metastatic abscess of the liver, &c.

In **acute general peritonitis** the vascular injection is very marked, and is accompanied from the beginning by a more or less abundant fibrino-purulent effusion between the meshes of the great omentum, into the connective tissue of the peritoneum and between the layers on its surface. The parietal peritoneum is affected as well as the different layers of the omentum and the mesentery, and fibrinous adhesions are produced very rapidly between the parietal and visceral serous membranes, and between the different organs contained in the abdomen. Thus, in puerperal peritonitis, when the patient dies two or three days after the commencement of the illness, the parietal layer of the peritoneum is found thickened and infiltrated with pus, of a grey and opaque colour, united in places either with the omentum or with the intestines by soft fibrinous false membranes, which are impregnated with pus. The pus effused into the abdominal cavity collects at certain dependent spots, such as surround the uterine appendages in the pelvis, suppurative inflammation of which is often the point of departure of peritonitis, the lower surface

of the liver, &c. The highly vascular and thickened great omentum is sometimes spread over and adherent to the surface of the intestines, sometimes twisted on itself and crumpled up, forming a red irregular fleshy mass covered with pus. When the great omentum is extended, it adheres to the intestines, particularly to the loops of the small intestine, from which it is difficult to detach it; its free edge is also almost always united to the abdominal wall at several points. Beneath the great omentum, the intestinal loops, which are swollen and distended by gas, are united together by fibrin impregnated with pus, which forms either a thick layer, or a grey or yellowish grey mass filling up the grooves or divisions between the loops. This thick semi-solid exudation is more or less abundant. It is difficult to separate the segments of the intestine thus agglutinated together without rupturing the wall of one of them, for the intestinal walls are themselves infiltrated with fluid, and are pale and softened. The mucous membrane

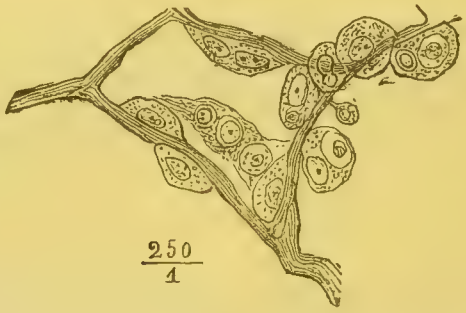

FIG. 166.—OMENTUM ARTIFICIALLY INFLAMED, STAINED WITH NITRATE OF SILVER. THE TUMEFIED EPITHELIAL CELLS ARE UNDERGOING PROLIFERATION AND ARE BECOMING DETACHED FROM THE TRABECULÆ. THE PUS CELLS ARE ENCLOSED IN FIBRIN AND THUS REMAIN ADHERENT TO THE FIBROUS TRABECULÆ.

is also infiltrated in the same manner; it is sometimes anæmic, sometimes congested, and always covered by a puriform mucus. The surface of the liver and spleen also give evidence of acute superficial inflammation; their peritoneum is infiltrated with pus, and their proper capsules are thickened and opaque. The uterine appendages, the liver or other organs are affected with lymphangitis, phlebitis, or superficial abscesses, which are the points of departure of purulent peritonitis. Intra-abdominal peritonitis may be sero-purulent or quite serous; in either case it contains flakes of fibrin. In the great omentum the lesions we have already described in experimental peritonitis are found, that is to say, fibrin, lymph cells, and tumefied granular cells containing one or more nuclei. Lymph cells and fibrin are found between

the connective-tissue fasciculi of all the membranes, which appear thick and opaque to the naked eye. The lymph cells accumulate, particularly around the vessels. The liver and kidneys are seen to be pale on section, and their cells are generally granulo-fatty. The fluid exudation in the peritoneum may contain blood as well as serum and pus; the sub-peritoneal cellular tissue is then the seat of ecchymoses. But this hæmorrhagic form of peritonitis is rarely simple; it is almost always complicated with neoplasms, such as cancer or tubercle, or it may be related to hepatic cirrhosis. The termination of acute peritonitis varies much. When it does not prove rapidly fatal, the exudation is reabsorbed at the same time that embryonic connective tissue is formed on the surface of the peritoneum and penetrates into the fibrinous false membranes with the newly-formed blood vessels, which themselves have embryonic walls. These organised false membranes establish fibrous adhesions between the inflamed parts, whence generally results a series of digestive troubles, due to the fact that the intestines are narrowed, immobilised, or fixed in an abnormal position. The cellular bands extending from the great omentum to the parietal peritoneum or to the small intestine, or the filamentous membranes established between the visceral and parietal peritoneum, may become the cause of internal strangulation. In other cases, acute purulent peritonitis may terminate, after the reabsorption of the pus, by a kind of caseation of the pus, which may become collected at one or more points in the peritoneum, encysted in false membranes, and finally caseous. At other times limited foci of suppuration, being seated either in the lower pelvis, behind the rectum, between the layers of the mesentery, or on the lower surface of the liver, may cause perforation of the intestine from without inwards, or even of the abdominal walls. When perforation both of the intestine and the skin occurs simultaneously, a fæcal fistula is produced.

Acute localised peritonitis is traumatic, or, what is more usual, follows inflammation of an organ contained in the peritoneum. It is easily understood how, if inflammation be propagated to the surface of one of these organs, the peritoneum itself infallibly becomes inflamed; and it is thus that localised peritonitis is developed at the level of the liver, gall bladder, spleen, uterus and its appendages, bladder, &c., whenever they are the seat of inflammation, tubercle, or tumours, which extend to the surface. The most frequent form of localised peritonitis is that of the pelvis, in consequence of phlebitis or lymphangitis of the uterus and

its appendages, or of the broad ligaments, metritis, parturition or abortion, peri-uterine hæmatocele, &c. At the cæcum, acute peritonitis rather frequently follows simple or ulcerative inflammation, or perforation of the vermiform appendix. If, however, the appendix be adherent to the posterior wall of the cæcum, as may sometimes occur, it is found surrounded by retro-cæcal cellular tissue, and is consequently outside of the peritoneum ; its inflammation or perforation then causes simple or plegmonous inflammation of the neighbouring cellular tissue. Ulceration of the cæcum causes the same accidents.

Chronic general peritonitis either follows acute peritonitis or occurs spontaneously. In the latter case it is very rare for it not to be related to some chronic affection, peritoneal or intestinal tuberculosis, cancer of one of the abdominal organs, cardiac disease, malarial cachexia, &c. In cancerous peritonitis, the new growths developed on the surface of the peritoneum throw into the serous cavity large cells containing voluminous nuclei and enormous nucleoli ; these are mixed with lymph cells and the fluid exudation. Thus, as has occurred to us many times, we have been enabled to diagnose cancerous peritonitis by microscopical examination of the fluid withdrawn by an exploratory puncture. The chronic peritonitis which follows acute peritonitis, leads to adhesions between the intestinal loops, and between these and the abdominal walls ; the bands are composed of filamentous or lamellar tissue, which varies in suppleness and abundance. Complete obliteration of the cavity of the peritoneum may be produced. If the new connective tissue is soft and cellular enough to allow of the movement of the intestines, life may still be possible, as is proved by the autopsies of aged persons who have certainly suffered such lesions for a number of years. In cardiac disease, as well as in hepatic cirrhosis and malarial cachexia with hypertrophy of the spleen, it is not properly true peritonitis which is present, but serous effusion or ascites. However, even in simple ascitic effusion some lesions are always present, which may be referred to chronic inflammation. These lesions consist in thickening of the capsules and of the peritoneal investment of the liver and spleen, and in budding or granular growths on the surface of the liver in cirrhosis, and from the circumsplenic peritoneum in malarial cachexia. Further, the parietal peritoneum is thickened, and the omentum and intestines often present adhesions or thick vascular fringes. In cirrhosis of the liver, a more marked form of peritonitis is frequently added to this condition, and is characterised by the

presence of flakes in the serous or sero-sanguineous fluid. Puncture of the abdomen does not seem to be always free of the charge of producing or aggravating this inflammatory condition of the peritoneum.

Chronic or sub-acute hæmorrhagic peritonitis, such as is observed in hypertrophic cirrhosis, articular rheumatism, tuberculosis, Bright's disease, &c., is characterised by vascular new membranes, which in structure resemble those of pachymeningitis. The new membranes cover a part or the whole of the parietal peritoneum, and the peritoneal surface of the intestines and mesentery; the whole of the peritoneal surface of the upper and lower pelvis may be covered by them. They are simple and delicate, formed of a single layer, or they may be composed of superimposed layers separated by effused blood; the embryonic tissue composing them may also be infiltrated with red blood corpuscles. When they are thick and ecchymotic the fluid effused into the abdomen always contains blood in rather considerable quantity. Blood is also sometimes extravasated into the connective tissue near the new membranes. This form of peritonitis is remarkable in that the whole of the surface of the peritoneum is always of a blackish-brown colour, as well as the effused fluid. Hæmatomata of the peritoneum sometimes localise themselves, in the retro-uterine cul-de-sac for example, where they form a variety of peri-uterine hæmatocele.

Tubercle of the peritoneum and tubercular peritonitis.—Nothing varies more than the distribution and sequelæ of tubercles of the peritoneum. They may be discrete, as is seen in some tubercular patients, in whom only a few very small semi-transparent granulations are present on the intestinal layer of the peritoneum, at the level of the tubercular ulcerations of the mucous membrane. The lymphatics which ramify under the peritoneum are then inflamed and tubercular (*vide* vol. ii. p. 302), and in their stratum, traces of peritonitis are sometimes found, fibrinous false membranes and soft bands. But the aspect changes when the peritoneum or a considerable part of the serous membrane is covered by miliary granulations, which cause a peritonitis characterised chiefly, if not solely, by considerable ascites; the effused fluid is citron-coloured, transparent, and sometimes contains fibrinous flakes. The latter is observed when the granulations are small and are seated on the surface of the serous membrane. In other cases the peritonitis is more acute, particularly when the granulations are found in the deep connective tissue of the peritoneum and in its folds. The mesentery, great omentum, and

mesocolon are then considerably thickened, for the granulations are surrounded by an embryonic tissue with which they are continuous without line of demarcation. The great omentum and the mesentery may attain the thickness of a centimetre or even of a centimetre and a half. The great omentum shrinks and becomes adherent to the arch of the colon. The mesentery also approaches its fixed point, to which it draws the small intestine. The effused fluid varies much in this form of tubercular peritonitis; citron-coloured at first, it may become purulent and contain flakes of fibrin at the same time that fibrinous false membranes are developed on the surface of the serous membrane. It is often partly or entirely absorbed, and the abdomen diminishes in size without losing its resonance. The effused pus is sometimes collected at one or more spots at the dependent parts, where it remains encysted by false membranes and finally becomes caseous.

Tubercular peritonitis is sometimes limited above by the adhesion of the large omentum to the wall of the abdomen. Thus the sac of the peritoneum may be found quite normal above the umbilicus, while lower down it contains serous or thick pus, and is covered by false membranes which spring from a serous membrane infiltrated with tubercle. If in these cases the peritonitis be limited to the lower portion of the abdomen, this is due to the fact that the tuberculosis has its origin in the small intestine, the mucous membrane of which is ulcerated. In some cases of tubercular peritonitis, the intra-abdominal effusion is sanguineous. Around the tubercles in these cases, ecchymoses and vascular new membranes are often observed which are themselves the seat of granulations. In children and more rarely in adults, tubercles of the peritoneum may acquire the size of a small pea or even nut; these are produced by the union of many granulations and are caseous. The lymph glands situated either in the mesentery and at its insertion or above the lesser curve of the stomach, and the lumbar glands always participate more or less in tuberculosis. They show either granulations or caseous infiltration. When these glands are very large and caseous the lesion is called *tabes mesenterica*. This disease is seen particularly in scrofulous children. It is unnecessary for us to describe again the structure of tubercle of the peritoneum and of the lymph glands (*vide* vol. i. pp. 432, 555). We will only add that the bacilli of tuberculosis are met with here as well as in all other growths of this kind. In the glands, the bacilli are, like the tubercular islets, seated in the cortical substance and most often in the follicles. In the connective tissue

around the tubercular glands, tubercular follicles are also present, and diffused infiltration with bacilli exists.

Chronic partial peritonitis is generally caused by chronic inflammation of an organ covered by the peritoneum; thus perityphlitis leaves behind adhesions of the vermiform appendix; inflammation of the uterus causes adhesion of the Fallopian tubes to the uterus, and the formation of fibrous tissue in the ligaments of the Fallopian tubes and the ovaries, &c. Foreign bodies fallen into the peritoneal sac from the digestive track after perforation bounded by adhesions; fibrous uterine polypi projecting into the abdomen; lipomata and papillomata of the appendices epiploicæ—which may be pedunculated or detached, or which, properly speaking, have fallen into the cavity of the peritoneum—extra-uterine gestation, all these may be the cause of chronic localised peritonitis, which is particularly characterised by the formation of fibrous pseudo-membranes. Tubercle, if developed only at a spot in the peritoneum, may also give rise to localised peritonitis. Such is primary tuberculosis of the Fallopian tubes, which is generally accompanied with tubercle of the peritoneum covering the uterus and its appendages and the cavity of the lower pelvis.

Primary carcinoma of the peritoneum and cancerous peritonitis.—Primary carcinoma of the peritoneum generally begins in the omentum. It may be of the encephaloid or scirrhous variety, but it is most generally colloid; when the latter, it often forms tumours of considerable size, implicating the whole of the peritoneum; the tumour may be so large as to fill the abdomen and may be mistaken for a very large ovarian cyst. In structure these colloid carcinomata present nothing peculiar (*vide* vol. i. p. 182). The oldest parts are formed of large alveoli filled with large round transparent cells; in the most recently formed parts there is a great deal of fibrous tissue composed of extremely fine fibres, between which is a colloid substance with or without cells.

Secondary carcinoma of the peritoneum is developed in consequence of tumours of the same character in the stomach, intestine, liver, uterus and its appendages, &c. It is shown first in the form of a diffused or nodular thickening of the connective tissue of the peritoneum in relation with the diseased organ. Thus in cancer of the stomach, either cancerous nodules or an infiltration of the same character are found in the peritoneal layer of this organ, and veins or lymphatics will almost always be discovered ramifying under the peritoneum, which are derived from the gastric

tumour and directed towards the liver or neighbouring lymph glands. These early manifestations of peritoneal carcinoma are followed by infiltration of the entire serous membrane, which becomes covered by granulations or small tumours varying in size from that of a millet seed to a small pea, or larger. The smallest of these granulations greatly resemble tubercles to the naked eye, particularly when the primary carcinoma is scirrhus. Microscopical examination leaves, however, no doubt on the question, for all these new growths exactly reproduce the structure of the primary tumour. Not, however, to allow of any doubt on the subject, a microscopical examination should always be made. It is not very rare to see an eruption of tubercles over the whole peritoneum supervene after cancer of the uterus or stomach. Secondary carcinoma of the peritoneum is always accompanied by more or less acute peritonitis characterised by a more or less abundant citron-coloured effusion into the abdomen, and sometimes by fibrinous exudation. At other times, cancerous growths in the peritoneum are accompanied with vascularised new membranes and hæmorrhagic exudation. These new connective-tissue growths cause filamentous adhesions between the organs, which by extension of the cancer also finally undergo cancerous change. Acute purulent peritonitis may be caused when a segment of intestine affected by cancer opens into the peritoneum, or when putrefactive softening and destruction of the cancerous tumour cause the formation of an abscess situated very near the surface of the peritoneum; this is chiefly observed in cancer of the uterus and its appendages. Nothing is more frequent than the termination of this form of carcinoma by subacute, acute, or purulent peritonitis; either the free and degenerated Fallopian tube pours its cancerous juice into the peritoneum, or the putrefactive destruction of the neck or part of the fundus of the uterus implicates the peritoneum of the pelvis and leads to acute peritonitis by contact. Primary carcinoma of the great omentum sometimes also causes abscesses of the deep connective tissue of the anterior wall of the abdomen; they are situated between the muscular planes, and may extend as far as the subcutaneous adipose tissue.

Other growths or tumours of the peritoneum are very rare; they are **lipomata**, which originate in the adipose tissue which lines the parietal layer or in the appendices epiploicæ, and various forms of **cysts**. We have had the opportunity of examining a large proliferous cyst of the peritoneum removed by M. Maisonneuve, and many dermoid cysts containing fat, hair, bones, teeth, &c.

At the autopsy of an aged female in the Salpêtrière one of us once observed **the corpuscles of Pacini** in the diaphragmatic peritoneum. These corpuscles were from 1 to 3 mm. in length; several of them sprang from a common pedicle; they showed the concentric layers and the central nervous filament exactly as in the corpuscles of Pacini of the fingers. **Hydatid cysts** containing echinococci are sometimes found in the peritoneum; they are produced by the spontaneous opening of a cyst of the liver into the abdomen, or they are developed primarily in the large omentum or some other part of the serous membrane.

CHAPTER IX.

THE PANCREAS.

The pancreas is formed of small glands or acini, which pour their secreted juice, the pancreatic juice, by means of the canal of Wirsung, into the second part of the duodenum. There is generally also a second duct, which passes from the head of the pancreas, and which opens near the first (Verneuil, Cl. Bernard, Sappey, &c.) The acini or glandular culs-de-sac measure from 45 to 90 μ in diameter. They are lined by a very delicate proper membrane, and contain prismatic-shaped cells, the apex of which corresponds to the lumen of the vesicle. The excretory ducts, the delicate wall of which is solely composed of connective tissue and elastic fibres, are lined by a single layer of small cylindrical cells. These ducts may be injected with soluble Prussian blue under a slight continuous pressure. The colouring matter first penetrates into the central lumen of the cul-de-sac, then into a system of ducts forming a complete network around the glandular cells (Langerhans, Saviotti, Gianuzzi). This network of canaliculi resembles that of the intralobular biliary canaliculi. The acini of the gland are surrounded by adipose tissue, which serves also to support the blood vessels and nerves. The blood vessels and lymphatics have the same arrangement as in the salivary glands. The nerves, derived from the sympathetic system, are composed of fine fibres, and accompany the blood vessels. The pancreatic juice is clear, limpid, a little viscous, alkaline, contains albuminous substances, and possesses the property of emulsifying fat (Eberle, Cl. Bernard). It acts, moreover, in the same manner as the saliva in completing the transformation of starch into sugar (Bouchardat and Sandras); finally, it also aids the digestion of nitrogenous matter (L. Corvisart). The pancreas is thus one of the glands most necessary to intestinal digestion, if it be not absolutely indispensable to life. When the pancreatic juice is no longer poured into the intestine, fat is incompletely digested, and is found in the fæces, which are then generally fluid (fatty diarrhœa).

Pathological Anatomy of the Pancreas.

The pathological anatomy of the pancreas has been hitherto little studied, particularly as the pathological changes of the glandular cells, and the connective tissue of the gland, do not produce any changes appreciated by the naked eye. Thus in treatises on pathology little precise information is given as to the histological lesions of this organ.

Parenchymatous inflammation.—According to C. E. E. Hoffmann ('Lesions of the Organs in Typhoid Fever,' 1859), the pancreas is constantly changed in typhoid fever in the same way as the liver. In the first week of the illness very acute hyperæmia of the connective tissue of the pancreas is observed, while the glandular cells appear to be hypertrophied. In the second week, the cells become multinucleated, their protoplasm becomes granular and filled with fat granules, so as to hide the nuclei, and the outline of the cells is slightly more marked. The hypertrophy of the acini resulting from this lesion produces compression of the blood vessels and anæmia of the interstitial connective tissue. It is probable that a similar lesion is present in other infective processes.

Suppurative inflammation of the pancreas is extremely rare; but there have been cases of disseminated metastatic abscesses, of diffuse suppuration of the gland, or of inflammation propagated to the whole of the surrounding connective tissue and to the lymph glands. Thus the pancreas (Gendrin) has been seen bathed in an abscess formed around itself, which abscess may open into the peritoneum, duodenum, or stomach. These abscesses must not be confounded with cysts containing a whitish mass.

Interstitial inflammation of the connective tissue of the pancreas may also occur. According to the few cases which have been published, the head of the pancreas becomes immersed in the chronic inflammatory thickening of the connective tissue which surrounds it and the duodenum. This may be seen, for example, when a biliary calculus, arrested in the common duct near the duodenum, sets up chronic inflammation of all the neighbouring connective tissue. This is what occurs in tumours of this region consecutive to simple ulcer of the pylorus or duodenum, &c. The pancreatic duct is then either normal or contracted.

Induration of the pancreas.—We have frequently had brought to us for examination a hard grey-coloured pancreas, in which the

glandular acini were well marked. This condition is generally taken for scirrhus. We have examined these organs without discovering any appreciable lesion. But it may be asked with Klebs if we have not here either parenchymatous inflammation similar to that present in typhoid fever, or a new formation of acini or adenoma, as Vulpian thinks, or thickening of the connective tissue of the organ.

Fatty degeneration.—Fatty degeneration of the epithelial cells of the glandular acini must be clearly distinguished from the deposit of fat in the cellular tissue around the pancreas. These are two conditions which have nothing in common. Granulo-fatty degeneration of the epithelial cells of the acini is rather rare, and the conditions under which it is observed have been well defined; we have seen a case of this kind in senile marasmus, and it is probable that it may be found in many states of cachexia. When there is an obstacle to the excretion of the pancreatic juice, the glandular acini atrophy and their cells become filled with fatty granules. Atrophy of the pancreas is the consequence, and fatty degeneration of its acini. A deposit of the tissue which forms a covering to the pancreas and which penetrates between the lobules accompanying the vessels is a rather frequent lesion. When in cases of alcoholism, chronic cardiac disease, diabetes, arrest or difficulty in the flow of the pancreatic juice, the glandular parenchyma disappears either wholly or partly, it may be replaced by a cellular adipose tissue which is developed in the fibrous framework of the pancreas around its vessels and ducts. The new adipose tissue reproduces more or less exactly the form of the gland, and at the autopsy a mass of adipose tissue may be found having the dimensions, size, and shape of the pancreas, bisected centrally by Wirsung's duct, without a single normal or preserved acinus being present.

Atrophy of the pancreas may be brought about in different ways: (1) from without by pressure on the gland by neighbouring organs; (2) from within by cystic distension of, and concretions in, the excretory ducts of the gland; (3) by granulo-fatty degeneration of the epithelial cells of the acini; (4) by interstitial inflammation, and particularly, according to Klebs, by stasis of the blood in the gland in consequence of chronic disease of the heart, liver, and lungs. Ph. Munk and Sylver have each published cases of atrophy of the pancreas in diabetes. Sometimes the atrophied acini are replaced by adipose connective tissue which is produced around them; at other times, without adipose tissue being pro-

duced in their place, the atrophied acini are located in the midst of a loose connective tissue, and the pancreas is then considerably diminished in size. This state is often complicated with calcareous concretions or with a whitish mass contained in the ducts.

Amyloid degeneration.—According to Rokitansky the cells of the acini may undergo amyloid degeneration. This is however generally doubted, and in any case it is very rare. The blood vessels of the pancreas have been several times observed to be in a state of amyloid degeneration at the same time as those of the liver and spleen.

Tumours of the pancreas.—Tubercle of the pancreas is so rare that Cruveilhier doubted its existence, and thought that in all cases looked upon as tubercular the glands near the pancreas had become caseous. Tubercular granulations may be, however, developed in the connective tissue separating the acini, and even in a case cited by Aran ('Archiv. Gén. de Méd.,' 1846) there was a caseous tubercular mass in the gland itself. Tuberculosis of the pancreas is always secondary to that of the lung or peritoneum.

Syphilitic gummata are also equally exceptional. Cases can hardly be quoted. Klebs observed a case of gummata of the pancreas in a six months fœtus, in which were also present syphilitic lesion of the lung, liver, and kidney.

In a case of **lymphadenoma** of the stomach and pre-vertebral lymph glands, reported by M. Lépine, the right half of the pancreas was increased in size and was contained in, but was not confounded with, the tumour formed by the glands. In the place of the normal pancreatic tissue, a soft, whitish, encephaloid tissue was present. The mucous membrane of the pyloric part of the stomach, the liver, diaphragm, and right lung were invaded, as well as the pancreas and glands, by an encephaloid infiltration. The morbid tissue in the stomach as well as in the liver and pancreas were exclusively formed of retiform connective tissue.

Carcinoma.—Carcinoma of the pancreas is rare; it may be primary or secondary. In 467 cases of carcinoma collected by Williglk, there were nine cases of the pancreas, most of which were secondary. Primary carcinoma of the pancreas is most frequently developed in the head of this organ, very rarely in its left extremity, or in its middle. As primary carcinoma of the pancreas extends very rapidly from its head to the parts nearest to it, that is to say, to the duodenum, the lymph glands, the common duct, &c., it is difficult to know exactly which is the primary seat

of development of a tumour which implicates all these organs. Primary carcinoma of the pancreas is sometimes scirrhous, sometimes encephaloid or colloid. When it commences by one or more tumours which unite, the carcinoma rapidly affects a more or less considerable part of the gland, which soon becomes changed into a uniform cancerous mass. When the tumour is seated solely at the head of the pancreas, Wirsung's duct is contracted; at the level of the duodenum it passes into an indurated tissue which strangles it, and the secretion of pancreatic juice is arrested. If the left half of the pancreas is respected and continues to secrete a more or less modified secretion, the excretory ducts dilate in this part of the gland and form cysts. The subserous connective tissue, the muscular layers, and the submucous connective tissue of the duodenum soon become equally affected, as well as the papilla at the common orifice of the bile and pancreatic ducts, whence result narrowing of the duodenum—which may become very marked—icterus, &c. The propagation of carcinoma to the lymph glands would have the effect of compressing the portal vein; the degeneration of the sub-peritoneal connective tissue would cause compression and narrowing of the aorta. It is very rare for the stomach to be attacked secondarily. In a case of primary colloid carcinoma of the pancreas, Klebs and Lücke observed secondary hydropic and cystic dilatation of the great omentum, which had pushed the transverse colon from above downwards. This tumour had been punctured during life. Secondary carcinoma of the pancreas is propagated to the neighbouring organs—the stomach, liver, duodenum, lymph glands, &c. It is rarely seen in the form of well-isolated nodules, at least when not of a melanic character; most frequently the new growth in the pancreas is directly continuous with the primary cancerous mass. The head of the pancreas is almost always the first to be invaded, and it is rare for the whole organ to become involved.

Cylindrical-celled epithelioma of the pancreas has been once observed by E. Wagner. It is probable that it was secondary to epithelioma of the duodenal mucous membrane.

Sarcoma is only seen in the pancreas in the melanic form.

Cysts.—The sole cysts of the pancreas are those which result from the dilatation of the excretory ducts of the gland. When a tumour, such as cancer of the head of the pancreas or of the duodenum, or a biliary calculus, obstructs the duodenal orifice of the pancreatic duct, or when pancreatic concretions block that duct, one or more dilatations are produced behind the obstacle.

These dilatations, which are more or less regular in form, reach to the surface of the gland. In the left or middle lobe of the pancreas, cysts may be found quite spherical, and which seem to be bounded by a limiting membrane. But on opening them they are found to communicate with the principal duct by a more or less narrow opening. These cysts, as well as the irregular and moniliform duct of Wirsung, contain a mucus which is rendered opaque by containing salts and concretions which are generally white and friable. These cysts and calculi are not very rare. One of us has seen two cases. In one of these cases the large dilated excretory ducts contained an opaque, thick, white, soft mass, as well as white, irregular, friable calculi composed of phosphate and carbonate of chalk. The internal surfaces of these ducts were lined with a single layer of delicate flat cells with irregular edges. Their wall was thick, formed of superimposed layers of lamellar connective tissue, separated from one another by flat nucleated cells. These modifications of structure in the wall, and the form of the epithelial cells, were evidently due to the pressure exercised by the concretions. In this case no trace of the glandular acini was to be seen. The secreting tissue of the pancreas was replaced by a cellulo-adipose tissue. Under the microscope, small unaltered excretory ducts, containing their cubical epithelial cells, were only observed in the fibrous septa of this tissue. The size of these pancreatic concretions varies greatly; Recklinghausen has found them 4 cm. long and 1 cm. wide. Generally they are much smaller. They may cause acute inflammation, and even the formation of abscess.

Section III.—The Hæmato-Poietic Glands.

CHAPTER I.

THE SPLEEN.

I. Normal Histology of the Spleen.

The spleen, an asymmetrical vascular gland, is composed of a fibrous envelope covered by the peritoneum, of a soft parenchyma red in colour and containing peculiar white bodies called the Malpighian corpuscles, and of vessels and nerves. The corpuscles and the splenic pulp are composed of a retiform connective tissue. The fibrous membrane of the spleen is very resistant and varies in thickness; it is formed of bundles of connective tissue and of elastic fibres, between which flat cells are found. In most of the mammalia muscle fibres are also present. From its under surface spring septa which divide up the splenic tissue. The membrane is reflected over the blood vessels which penetrate the spleen, forming a fibrous sheath to them. The septa or trabeculæ of the spleen contain smooth muscle fibres in those animals in which they are also found in the capsule. In man, the presence of smooth muscle fibres is affirmed by certain histologists (Meisner, Frey), and denied by others (Kölliker, Gerlach, Henle). The splenic artery and vein enter at the hilus of the spleen, and, as we have already said, are surrounded by a fibrous sheath derived from the capsule. This sheath is finer than the wall of the artery and thicker than the vein. Each of the principal branches of the splenic artery divides into a tuft of branches, which do not anastomose with those of neighbouring branches. When these branches are not more than 0·2 to 0·4 mm. in diameter, they become separated from the veins, continue to subdivide, and on their ramifications are found the corpuscles of Malpighi. These corpuscles, either round or oval, are arranged around the small arteries, which generally occupy their centre; their normal diameter varies from 0·2 to 0·7 mm.

The arteriole which crosses them, or which is in intimate connection with them by a point on their surface, sends arterioles into their interior and gives origin to a capillary network. The Malpighian corpuscles are formed of a retiform tissue exactly similar to that of the closed follicles of the intestine. The trabeculæ of this tissue are inserted into the sheath of the arteries and capillaries; at the periphery of the follicle the meshes of the reticulum become narrower, the fibres are closer together, but there is not a positive membrane between the corpuscles and the splenic pulp. The reticulated tissue of the latter is continuous with the retiform tissue of the follicle. The cellular elements contained in the meshes of the retiform tissue are lymph cells, the largest of which contain pigment granules and even blood corpuscles. The Malpighian corpuscles do not contain veins, while the splenic pulp is, on the contrary, intersected by a close and highly developed network of veins. In sections of the splenic pulp, small veins are seen divided, having a diameter of 20 μ to 40 μ; they are very close together and are separated by a retiform tissue the meshes of which are very fine (the intervascular cords of Billroth). The walls of these veins are formed of condensed retiform tissue, and they are lined with large endothelial cells. The cells contained in the meshes of the reticulum of the splenic pulp are similar to those of the retiform tissue of the Malpighian corpuscles. After what we have said it will be easy to identify these cells with those of the closed follicles of the intestine and the lymph glands, and the whole spleen may be compared to a lymph gland in which the medullary tissue has been replaced by a cavernous tissue, the veins replacing in the spleen the peri-follicular spaces and lymph channels of the glands. There is little doubt that the lymph cells can pass from the retiform tissue into the blood current and *vice versâ*. We have no accurate knowledge as to the connection between the arterioles of the corpuscles with the venous network of the pulp. Histologists are not agreed on this point, some thinking that the arterioles are continuous with the veins (Billroth, Sweigger-Seidel), others admitting the existence of the intermediate capillary system (Axel Key); and finally others again, among whom may be numbered W. Müller, think that the communication is made by means of the spaces which are limited by the fibrous network of the splenic pulp.

The blood of the splenic vein contains a much larger number of blood corpuscles than the artery (Malassez); consequently the essential function of the spleen must be the formation of red

blood corpuscles, particularly as the blood pigment found in the lymph cells indicates the destruction of a certain number of these elements; the spleen deserves therefore the name of an hæmatopoietic gland. The lymphatics of the spleen in the human subject are not numerous; some are seated in the capsule, others in the depth of the organ where they accompany the arteries. It is probable that the lymphatics which accompany the arteries penetrate as far as the Malpighian corpuscles; their relation with the reticulated splenic tissue is unknown. The nerves of the spleen, composed of a few large tubes, and numerous fibres of Remak, are derived from the splenic plexus, and they enter the organ in company with the arteries. They may be traced as far as the tuft of arterioles in the glomeruli; according to Ecker they terminate by free extremities.

II. The Pathological Anatomy and Histology of the Spleen.

Atrophy of the spleen is frequently observed in old persons; it generally coincides with a more or less marked thickening of the capsule. The splenic parenchyma may also become indurated, but it more often preserves its normal consistency. It is generally pale and anæmic, at least if there has been any cardiac complication during life which has caused some impediment to the circulation. Thickening of the capsule of the spleen is caused, as in every other similar case, by the formation of layers of connective tissue separated by flat cells. This tissue shows a remarkable hardness and consistency; it is often cartilaginous and infiltrated with calcareous salts. Chronic inflammation of the peritoneum is then generally observed on the surface of the capsule, and new growths may be observed in the form of tough non-vascular fleshy granulations, or patches, or floating shreds.

Hyperæmia of the spleen.—Congestion of the spleen occurs in a number of morbid conditions which differ widely from one another, and it constitutes also the first stage of most of the diseases of the spleen. No organ is more liable to congestion, which condition is, in a certain sense, physiological during digestion; but by reason of the structure of its trabeculæ and capsule, which contain elastic fibres and muscular fasciculi, it contracts easily and expels the blood which it contains. In the pathological condition, when the cause of the congestion is frequently repeated or is constant, it is no longer the same. The congested spleen is always

increased at the same time in size. Congestion may be acute or chronic. An acute though temporary condition of congestion is observed in all febrile infectious diseases, such as the eruptive fevers, pyæmia, cholera, erysipelas, &c., and in a certain number of pyrexial states.

In all infectious diseases, tumefaction of the spleen seems to be related to the presence in the blood of bacteria peculiar to these various diseases. The blood is arrested for a certain time in the spleen and there undergoes changes in its composition; the bacteria are also arrested in this organ and cause more or less marked irritative lesions. Typical accumulation of bacteria in the spleen is seen in anthrax, both in animals and men. The blood vessels, particularly the veins of the pulp, are filled with *bacillus anthracis* lying in the direction of the blood current. The disorders caused by bacteria in the spleen are not sufficiently well known for us to describe them. The splenic congestion observed in febrile diseases does not solely consist in the plugging of the blood vessels, particularly of the veins of the pulp. It also obviously affects the proper function of the spleen, that is to say the destruction and formation of blood corpuscles. We have no knowledge at present of the minute changes of the blood in the spleen as the result of each infectious febrile disease. This is an important subject for future research. In most of the conditions of acute hypertrophic congestion observed in infectious diseases, the spleen is soft and rather tense, its pulp is not of a dark red colour, but pink, which is due to the large number of leucocytes which the blood contains.

In **intermittent fever,** the spleen may be tumefied from the beginning of the attack. This hyperæmia passes away during the period of apyrexia to return at each attack, and soon the tumefaction becomes persistent. In these fevers, splenic congestion is always accompanied with destruction of the red blood corpuscles in the spleen, and pigmentation of the splenic tissue. When the illness has lasted some time, and a condition of malarial cachexia is produced, the spleen is not only congested, it is also indurated and becomes in a way cirrhotic with pigmentation. This condition will be described later.

Typhoid fever is one of the infectious diseases which most frequently affects the spleen. It is then almost always hypertrophied, often becoming more than double its normal size. In the adult this increase in size is less marked than in children, for in the latter the capsule is less dense and thick, and consequently

more extensible. The capsule is stretched and thin. On section, therefore, it is found to be infiltrated with blood, and of a brown, or, more frequently, of a pink colour. The Malpighian corpuscles are sometimes very apparent and large, at other times they are invisible; this may be due to cadaveric softening. The spleen is generally less firm than in health. On examining the cellular elements of the splenic pulp under the microscope, between the tenth and fifteenth day of the illness, in the fresh state, though stained with picrocarminate, tumefied lymph cells will be found in the midst of the blood corpuscles; these cells are soft and granular and are often multinucleated, and many of them contain one or more red blood corpuscles in their protoplasm; in fact, two, three, four, or even eight or ten red blood corpuscles may be counted in a single lymph cell. The nucleus or nuclei of these large cells are quite visible. The red blood corpuscles contained in the protoplasm are sometimes normal in size and easily recognisable by their contour, colour, and the homogeneous appearance of their mass; sometimes they are small, measuring not more than 3 μ or 4 μ in diameter; at other times, again, they are granular, and are only recognised by the yellow colour of the granules which they contain. The large endothelial cells of the veins have always appeared to us to be normal. Billroth has, however, observed proliferation of their nuclei in typhoid fever. The number of the lymph cells which contain red blood corpuscles is so considerable in typhoid fever, that in a drop of the pulp, obtained by scraping, a hundred may be counted. In sections made after hardening in Müller's fluid, gum and alcohol, it can be easily ascertained that the large cells containing red blood corpuscles are seated in the interior of the veins of the pulp. Towards the end of the disease, the spleen diminishes in size; its surface is seen on section to be of a brown colour and less rich in blood. On microscopic examination, the cells can no longer be found in a state of proliferation, but the lymph cells contain fat granules (Fœrster) and red pigment, and pigment granules are found free in the pulp.

From what precedes it is seen that the lesion of the spleen in typhoid fever is neither a simple congestion nor inflammation. Under the influence of the special bacteria of typhoid fever, or owing to changes in the composition of the blood caused by these microbes, congestion is produced with accumulation of the white corpuscles, and simultaneous destruction of the red corpuscles, which are then devoured by the white cells. In acute con-

gestion in connection with intermittent fever and enteric fever, foci of actual blood effusions may be found, and in a rather considerable number of cases rupture of the spleen has been observed. Typhoid fever is sometimes accompanied with splenic infarctions. Chronic congestion of the spleen is always observed in diseases of the liver, accompanied with hinderance to the circulation in the portal vein, and in cardiac diseases with impeded circulation of the venous system. The blood pressure in the splenic vein is increased, whence results stasis with hypertrophic congestion of the spleen. Cardiac diseases, however, are a less frequent cause of hypertrophy of the spleen than chronic disease of the liver, cirrhosis in particular. It is rare for chronic congestion not to be accompanied by a certain degree of interstitial splenitis with induration and thickening of the capsule, with or without pigmentation of the elements of the splenic tissue.

In **chronic cardiac diseases** the capsule of the spleen is almost always hard and thick, and on its surface small growths are found, or fibrous plates, cartilaginous in appearance. The volume of the spleen is normal or increased. On dividing the tissue, it is seen to be of the colour of venous blood, and it reddens on exposure to the air by the blood becoming oxygenated. The surface of the section is smooth and the tissue does not collapse; on scraping it yields but a small amount of fluid, and it has a certain feel of firmness; it can nevertheless be torn with the finger-nail. On closely examining the surface of the section, fibrous trabeculæ and blood vessels, which are much more apparent than in the normal condition, appear prominently on the red background. These trabeculæ are, in fact, thickened, and are very rich in connective-tissue fibres. The small splenic arteries are hard, and their walls are thickened. Their interior is frequently the seat of endarteritis, particularly when atheromatous lesions of the aorta are present, and the external coat is equally increased in thickness. The finely retiform tissue of the pulp and the corpuscles does not generally show any marked alteration. The splenic capillaries and veins are distended with blood.

In **hepatic cirrhosis**, and in all diseases which impede the portal circulation, the spleen is very much hypertrophied, being at least double its normal size and having a thickened capsule; the growths on its peritoneal surface are generally very numerous. This peri-splenitis is related to ascites and subacute peritoneal inflammation, which so often accompanies cirrhosis. On dividing the spleen, it is seen to be of the colour of venous blood, and its

fibrous septa are generally thickened. In the splenic pulp lymph cells are found with brown or red pigment in the protoplasm around their nuclei. The endothelial cells of the veins often contain pigment granules. The veins, examined in section, are generally seen to be abnormally large. The connective-tissue trabeculæ which spring from the capsule, and those forming the retiform tissue of the pulp, are normal, at least they are only slightly thickened. The splenic hypertrophy is thus seen to be due particularly to distension of the veins, but slightly to thickening of the fibrous trabeculæ. The lymph cells are not more numerous than in the normal condition.

Interstitial splenitis.—Chronic congestion of the spleen ends, as we have already seen in the previous cases, in the formation of new connective tissue which may be regarded as the sign of slow irritation or inflammation similar to cirrhosis of the liver or interstitial pneumonia. In no disease is this lesion so marked and so acute as in malarial cachexia. The appearance of the spleen in patients suffering from this disease varies greatly. Sometimes on section it is red or pink, sometimes of a slaty brown colour. The septa as well as the pulp may be of a blackish brown colour. These differences of colour are due to the greater or smaller amount of pigment contained in the connective tissue and in the leucocytes of the blood in the spleen. There is one lesion that is almost always constant in all cases of intermittent fever which has lasted a certain time, namely, fibrous thickening and induration of the capsule, which is at the same time covered superficially with inflammatory growths. These latter may either consist of projecting fleshy granulations, which are very hard and often cartilaginous in appearance, or of villous growths or floating false membranes of which we have already spoken. These false membranes are vascular, while the flat growths which form small lamellar fibromata (*vide* vol. i. p. 163 and fig. 82) contain very few or no vessels at all. The spleen is almost always much hypertrophied; when it is pigmented it is not unusual for its long axis to measure 20 to 25 centimetres. At the same time it may be highly pigmented when not measuring more than 15 centimetres. It is then indurated and cannot be indented or torn with the finger-nail. In the pulp obtained by scraping a spleen the surface of which is red or pink, lymph cells are found containing black or brown pigment granules; in indurated and pigmented spleens a very large number of lymph cells are found infiltrated with these granules. They are brown and

brilliant in appearance, if small and examined under a high power; sometimes they are larger, blackish or quite black. They are contained in the lymph cells, but they are also sometimes free in the liquor sanguinis. These cells have generally only one nucleus. The large endothelial cells of the internal coat of the veins also contain brown or blackish pigment, but in the form of fine granules, not large grains. When a spleen is thus hardened, the fibrous trabeculæ extending from the capsule to the centre are seen in microscopic sections to be enlarged to a variable degree. New fibres of connective tissue are also formed. The Malpighian corpuscles are as a rule plainly visible. The retiform tissues of the corpuscles and the tissue of the pulp undergo similar changes, which consist essentially in pigmentation of the lymph cells contained in the meshes of the reticulum. Those, however, of the Malpighian corpuscles are less pigmented than those of the pulp. The veins of the pulp in which the endothelial cells are normal or slightly pigmented, also contain a large number of strongly pigmented lymph cells in the midst of the red blood corpuscles. These veins are dilated if the morbid process be recent, and if the spleen be only slightly indurated. Their diameter is normal or even diminished if the lesion be old and the spleen much indurated. The tracts of retiform tissue which separate the veins of the pulp are deeply pigmented and appear on section as the black parts of the preparation. On examining under a high power, it may be seen that this colour is due to lymph cells included in the reticulum. In certain cases these cells are almost completely black. On freeing the retiform tissue of these elements, it will be seen that the filaments comprising the reticulum do not seem to be much thickened. On their surface, very fine pigment granules are observed. In spleens, however, which are highly sclerosed, these filaments are two or three times thicker than normally, but they are always composed of single fibres, and do not show nuclei at their points of intersection, which fact can be ascertained in very delicate sections which have been cleaned by brushing out the free cells. The larger arterioles, arteries, and large veins of the spleen are thickened and indurated, and infiltrated with pigment, particularly in the peripheral zone. The connective tissue of the large fibrous septa also contains much black pigment, situated in and around the cells. The researches of Klebs and Tommasi-Crudeli on the etiology of malarial fever lead one to believe that all the lesions of the blood or spleen which accompany it are caused by a ferment produced by bacilli derived from the soil.

These authors found bacilli in the blood at the commencement of the access of malarial fever. Laveran has, on the other hand, described rods or rather mobile filaments in the blood under the same conditions. Though the descriptions given by these authors vary greatly, the drawings given by Tommasi-Crudeli and by Laveran somewhat resemble each other. It must, however, be allowed that the etiology of intermittent fever is far from being satisfactorily elucidated.

The destruction of the red blood corpuscles in the spleen is not peculiar to malarial fever, since we have seen absorption of the red corpuscles by the white take place in other febrile infectious diseases; for example, in typhoid fever; on the other hand, chronic congestion of the spleen, cirrhosis in particular, ends in induration of its tissue and pigmentation of its cells. But still it is to be recollected that exaggerated pigmentation is produced especially in malarial cachexia, and that it is here a constant phenomenon. In all cases of repeated congestion of the spleen, and more especially in all cases of interstitial splenitis, there is, as we have already seen, thickening of the capsule and the formation of new connective tissue on its peritoneal surface. The folds of the peritoneum, which form the gastro-splenic omentum and the phreno- and pancreatico-splenic ligaments, are at the same time more or less inflamed, and hence it results that the spleen is closely united to all the neighbouring organs by false membranes which become organised into connective tissue. These adhesions may become so firm and close as to perfectly immobilise the spleen. This *fibrous peri-splenitis* is frequently the consequence of primary changes in the spleen, but it may also be the manifestation of a generalised or local peritonitis, whatever may be its cause. It has been particularly studied by Léon Collin in intermittent fever, in which disease it is a constant symptom, varying in severity.

Suppurative splenitis.—Large abscesses caused by cirrhosis, fractures of the ribs, &c., are observed, though very rarely, in the spleen. In a small number of cases, it is not known to what cause to attribute the splenic abscesses observed at the autopsy, and which have given origin during life to acute febrile attacks. In other equally rare cases (Frerichs, Lancereaux), abscesses of the spleen have been observed in persons debilitated with fever, and who have lived in malarial countries. Cases reported formerly as those of abscess of the spleen are open to criticism, for abscess was not then sufficiently distinguished from infarction due to embolism or arterial thrombosis.

Suppurative splenitis is seen under three forms—

1. As a diffuse infiltration, in which a considerable part or the whole of the splenic parenchyma is softened, of a white, greyish, or pink colour. It is then reduced to a soft or purulent mass, in which the blood and the detritus of the proper tissue of the organ are mixed. These cases are described under the name of *splenic gangrene.*

2. Cases in which one or more large abscesses are formed in the splenic tissue. These abscesses, which are caused by traumatism, phlebitis of the splenic vein, purulent infection, or acute fevers (typhoid fever in particular), unite and sometimes form large purulent foci separated from the normal tissue of the spleen by a pyogenic membrane. Abscesses of this kind have been described of considerable size, one weighing thirty pounds (L'Hermite, 'Acad. des Sc.,' 1753). These abscesses generally become encysted, and their pyogenic membrane fibrous. If they be superficial the capsule of the spleen thickens at their level; in other cases, on the contrary, the fibrous capsule being itself invaded by suppuration, and fibrinous or fibrous adhesions being established between itself and neighbouring organs, an abscess of the spleen may open into the stomach or into the pleura or lung across the diaphragm (Vidal, 'Soc. Anat.,' 1853); or it may ulcerate through the abdominal wall or between the ribs. In other cases, the abscess may communicate with the splenic vein (Carswel, Frerichs), and it may finally burrow in the sub-peritoneal cellular tissue into the pelvis, to open into the vagina. Two such cases have been reported by M. Besnier (article 'Rate' in the 'Dict. Encyc. des Sc. Méd.')

3. Metastatic abscesses, rarer in the spleen than in most other organs, are sometimes met with, however, in similar conditions, in pyæmia, puerperal fever, acute endocarditis, phlebitis, &c. They are generally seated towards the periphery of the spleen, their bases being turned outwards. Their number is generally very limited; in volume they vary from that of a millet seed to that of a small nut or larger. They commence in a little islet of dark red colour, like an apoplectic focus in the lung; soon pus is seen in the centre of the mass, which gradually softens, becomes liquid and forms a small abscess. As in the liver, abscess of the spleen is caused by the transmission by the blood of the microbes of pyæmia and their arrest in the organ. The pathogenic condition of the formation of these metastatic abscesses often causes simultaneous suppurative peri-splenitis or even general peritonitis.

Infarctus of the spleen.—The spleen is the organ in which infarctus is most frequent. This is explained by the origin of the splenic artery, and by the absence of anastomoses between its branches. Also when the aorta is atheromatous, and fragments of fibrin penetrate into one of the branches of the splenic artery, the part of the spleen corresponding to the obstructed artery becomes necessarily the seat of infarctus. It is in fact impossible for the circulation to be re-established by collateral vessels. These infarctuses must be carefully distinguished from metastatic abscesses, with which they have nothing in common from a pathological or from an etiological point of view. Splenic infarctuses are the result of atheroma of the aorta, of the aortic valves, and of the splenic artery, &c. The size and the number of these foci vary. The spleen may be invaded almost throughout, or there may be only one, two, or three small infarctuses in its interior. Their form is characteristic. They are always conical, with the base turned towards the surface of the spleen, and the apex towards the hilum. The splenic artery itself, or many of its branches, are completely obstructed by an adherent clot when a considerable mass of the spleen is invaded. The arteriole which is distributed to a small infarctus is always obstructed in the same way. When the infarctuses are recent, their surface on section is seen to be of a dark red, almost black colour, for the blood coagulates in all the small veins and in the arteries, communicating to the part the colour of venous blood. Later, when the fibrin is coagulated and the blood corpuscles are changed into a granulo-fatty substance, the colour of the section becomes greyish, yellowish, or opaque. At first the infarctus is much firmer to the feel than the normal spleen; later, it softens and becomes pasty, semi-fluid, and yellow. The fluid accumulated in the centre of the focus bathes the incompletely detached necrosed parts, and the infarctus may be compared to certain large cavities of the lung in process of formation; around it the spleen is congested and inflamed, but shows no tendency to suppuration. From what precedes, the complete obstruction of the arteries, the coagulation of the blood in all the vessels of the morbid focus, and its subsequent necrotic softening, may be compared to gangrene. It is in fact an arrest of the blood, causing mortification of the tissues. But here, as in the liver and spleen, the mortification taking place without there being any communication with the external air, there is no putrefaction, and no gangrenous odour. The spleen may show anatomical lesions comparable to those of putrid gangrene, but only

in those cases in which a mortified part of its tissue is bathed in the pus of peri-splenitis. Colin has related cases.

Microscopic examination of sections of recent infarctuses simply show blood vessels distended by coagulated blood and containing a reticulum of fibrin. Soon the lymph cells entangled in the reticulum become granulo-fatty. The fat breaks up and balls of crystals of fatty acids are produced, which might at first sight be mistaken for granular bodies. These balls appear here and there as opaque bodies when the preparation is examined under a low power. The lymph cells imprisoned in the retiform tissue of the spleen undergo caseous fatty degeneration, while the red blood corpuscles contained in the vessels pass through the series of changes already described. The trabeculæ of the retiform tissue ultimately undergo molecular disintegration, as well as the lymph cells, whence partial or complete softening of the infarctus results, in which case a fluid containing granular cells, proteic and free fat granules is produced. The infarctus, which was at first tumefied, now flattens, and finally a depression is produced in the surface of the spleen. The capsule of the spleen is almost always altered during the periods of infarctus; it is at first congested, then villi and growths are produced, and it thickens, becoming more dense. It may even become calcified. As the infarctus softens, the fluid parts are taken up and absorbed by the healthy parts of the peripheral splenic tissue. The loss of substance is supplied partly by newly formed connective tissue of the capsule, which is pushed inwards at this point, and partly by fibrous thickening similar to that of the neighbouring splenic tissue; in fact, a fibrous cicatrix finally replaces the infarctus. In those cicatrices of the spleen which are marked on the surface by depression with thickening of the capsule, the latter is generally calcified. On examining the calcified tissue, true osteoblasts with their canaliculi are not seen. In sections, which have been decalcified by the action of chromic or picric acid, small lacunæ are seen, which simply represent interstices in which are found the cells of the previous connective tissue. In infarctuses generally, but also in most cases of sclerosed spleens, either in cirrhosis or in cardiac disease, the splenic arteries are found to be indurated, and there is considerable thickening of their walls, due to end-arteritis or peri-arteritis, with or without calcareous incrustation.

Rupture of the spleen.—Rupture of the spleen, either traumatic or spontaneous, is sometimes observed. When this accident takes place, the spleen is in a condition of congestive or inflamma-

tory tumefaction, which condition is almost always present in intermittent fever, typhus, cholera, and syphilis. All the known cases of rupture of the spleen have been collected and published by Besnier, and from this summary it may be seen that the cases are not very rare. Simple fissures, or cracks, either superficial or deep, are produced, and vary both as to dimensions and appearance. They may be seated anywhere on the surface, but chiefly on its external surface and in the longitudinal fissure. A blood clot is found at the solution of continuity. This clot is sometimes continuous with a mass of blood which surrounds the entire organ. A more or less abundant effusion of blood takes place sometimes into the peritoneal sac; death occurs suddenly if the effusion be considerable, or it sets up peritonitis if the effusion take place slowly in the course of a few days.

Amyloid degeneration of the spleen.—There are two degrees of amyloid degeneration of the spleen; in one it is limited to the Malpighian corpuscles, and in the other the amyloid infiltration is diffused. In these two types of the lesion, the spleen is hypertrophied more or less, globular and of a grumous consistency; its capsule is tense, often thickened by new growths of connective tissue on its surface, and its edges are thickened and blunt. In the first state, the Malpighian corpuscles are seen on section to be increased in size, being 1 to 2 mm. in diameter or even more; these bodies are semi-transparent, formed of a hyaline substance, which becomes stained a mahogany brown on the application of an iodised solution of iodine. The appearance of these large and semi-transparent bodies very near to one another has been likened to cooked sago, whence the name of *sago spleen* (*Sagomilz*), which has been given to this lesion by German anatomists. When a spleen thus altered is examined in sections, either in the fresh state, or after hardening in alcohol, and on being treated with iodine, the formerly colourless corpuscles become stained of a mahogany brown. Under a low power, it is easily seen that the diseased islets are attached to arteries or arranged around these vessels, which they surround like a collar. The addition of sulphuric acid after the iodine staining often stains the diseased parts green, blue, violet, and then reddish brown. In order to ascertain the seat of this degeneration and the minute changes produced, we have made use of Paris violet and safranine (*vide* vol. ii. p. 390, note). The wall of the arteries which pass in the midst, or on the surface, of the diseased corpuscles is itself either

infiltrated or intact. In fact, we have ascertained in many cases that the wall of the central artery of the glomerulus may be intact, while the walls of the arterioles and capillaries, and most of the elements of the splenic corpuscles, the lymph cells, and the retiform tissue, were infiltrated with amyloid matter. The degeneration of the lymph cells may be easily recognised by dissociating the elements of the Malpighian corpuscles taken from a delicate section cut in the fresh state; it is then seen that the cells have become vitreous, that they are globular or changed into small irregular blocks, or are agglutinated together; that they have lost their nuclei, and stain a reddish violet with methylaniline violet. On examining delicate stained sections under a high power, it is seen that in the diseased part of the corpuscle most of the fibrils of the reticulum are infiltrated with amyloid substance, and it is the same with the walls of the capillaries. As all these lymph cells, the reticulum, and the capillaries tend to meet together, and as they stain the same colour, they appear as homogeneous masses, which are grooved by narrow slits, constituting a network; these slits are formed by the capillaries, recognised by their lumen, which is more or less well preserved; their endothelial cells and the blood corpuscles are generally intact and stain blue-violet. The diseased Malpighian bodies are considerably enlarged, and at certain points they are almost in contact with one another. They are only separated by delicate bands of the tissue of the splenic pulp, which is either normal or diseased at this point. The walls of the neighbouring veins are also slightly thickened and diseased. The endothelial cells of these veins are generally normal, their calibre is not modified; the retiform tissue which surrounds them and the lymph cells of the reticulum of the pulp are generally intact.

In the most advanced stages of amyloid degeneration, the spleen is the seat of complete and diffuse infiltration; it is very much hypertrophied and appears on section to be homogeneous, and more or less vitreous according as the infiltration is more or less marked. When the lesion is at its height, large masses of the spleen are pale, deprived of blood, and quite wax-like. Nevertheless the circulation, which is very much impeded, is not entirely suspended, and there may be even foci of suppuration in the spleen in cases of advanced amyloid degeneration. We have observed this at the autopsy of a case of purulent infection consecutive to chronic disease of the bones. In complete amyloid degeneration, all the vessels are altered in a very marked degree,

though some of them are still permeable to blood. The capsule and the trabeculæ of the spleen are thickened and their connective tissue is normal, though intersected by a few diseased capillaries. The Malpighian corpuscles are small and sometimes incompletely degenerated, so that a zone of normal lymph cells is generally found at the centre of the corpuscle around the artery. All the veins of the pulp are affected, their walls are thickened in a marked degree and degenerated, though their calibre remains the same; in their interior the endothelium and a few red blood corpuscles are often distinctly recognised. The retiform tissue which unites the veins of the pulp is sometimes normal, sometimes partly amyloid. Its fibrils are then thickened, and they show, as well as the cells which are continuous with them, the characteristic reactions. In this diffuse degeneration, the splenic pulp, and notably the walls of the small veins of the pulp, seem to be the essential seat of the degeneration. The two degrees of degeneration which we have described are not always well marked, and in each case considered separately variations may be observed both as regards acuteness and distribution.

Tumours of the Spleen.

Leucocythæmia.—In most of the cases of leucocythæmia and adenia,[1] the spleen is infiltrated with leucocytes, and it is hypertrophied in a marked manner. This hypertrophy is most marked in splenic leucocythæmia, when the spleen may measure from 25 to 30 cm. in diameter. As already described (vol. i. p. 249) this hypertrophy principally affects the Malpighian corpuscles, which may acquire the size of a small nut or larger. On section of the organ they are seen as so many grey or whitish nodules, sometimes yellowish in colour towards the centre: they yield juice on scraping. These nodules, formed of a homogeneous tissue, are separated from one another by red zones, which are sometimes so thin that the nodules seem to touch one another. The cellular elements obtained by scraping the grey parts are lymph cells, which are generally uni-nucleated; some of the cells when isolated are seen to be large, measuring from 15 μ to 20 μ in diameter; they are granular and contain many round or oval nuclei. On examining a large and delicate section under a low power, it will be seen that these white nodules correspond to the Malpighian corpuscles, and that the delicate red zones which separate them are nothing

[1] See vol. i. p. 245, *note*.

else than the tissue of the pulp. The hypertrophied Malpighian bodies are composed of retiform tissue, the fine meshes of which are filled with lymph cells and the large proliferating cells described above. In the walls of the arterioles which are distributed to these corpuscles, a large number of leucocytes is found, so that in a transverse section they appear in the midst of the circular islet of small cells. The trabeculæ of the adenoid tissue of the hypertrophied follicles are as a rule abnormally thick. In the centre of the corpuscles, which is yellow and opaque to the naked eye, the lymph cells are seen to have undergone granulo-fatty degeneration. At the periphery of the hypertrophied corpuscles, in the red zone which separates them from one another, may be observed the network of small veins which characterises the tissue of the splenic pulp. This part of the spleen is visibly atrophied by the presence in it of the Malpighian corpuscles. The veins are not large, although they are filled with leucocytes, and their endothelium is normal. A very small number of lymph cells contain brown pigment.

Tubercle.—Tubercle of the spleen is rather frequent in children; it is rarer in adults. It shows itself with all its usual characteristics, sometimes in the form of miliary granules disseminated in the splenic parenchyma, sometimes in large masses, the size, for example, of a small pea; these are produced by the union of many caseous granulations. Tuberculosis of the spleen is never primary. According to Billroth and Virchow, the miliary granulations commence in the reticulated connective tissue of the pulp. The tracts of tissue which separate the veins become thickened, and the seat of new elements; at the same time the nuclei of the cells of the endothelium of the veins proliferate. Fœrster, however, declares to having seen granulations develop in the fibrous tissue of which the large tracts are composed, which radiate from the capsule into the interior of the organ, and he has also met with them in the Malpighian bodies. The difficulty of diagnosing tubercular granulations, both with the naked eye and the microscope, arises from the fact that in form and size, and from the lymph cells they contain, they resemble the Malpighian corpuscles. But in tubercle the centre becomes caseous, and the cells infiltrate with fine granules, at the same time that they atrophy. The small vessels and capillaries which pass into the granulation are filled with granular fibrin, lymph cells, and large endothelial cells, and become obliterated. Moreover, perfectly characteristic

giant cells are formed in the centre of tubercular nodules in the spleen. In preparations treated by Ehrlich's method, the bacilli of tuberculosis may generally be demonstrated. In a recent case of miliary splenic tuberculosis, we found one or two bacilli [1] in each of the giant cells situated at the centre of the tubercular granulation. In tuberculosis artificially produced in the guinea pig and rabbit by the injection of tubercular matter into the peritoneum, the spleen is, like the liver, always profoundly altered; it is much hypertrophied and a large quantity of bacilli are found in the tubercular nodules and in the cells of the splenic pulp.

Syphilitic tumours.—The spleen is generally hypertrophied in syphilis at the commencement of the disease. This tumefaction is particularly well marked in syphilitic new-born infants (Gée, Parrot, &c.) In tertiary syphilis, the spleen may be also either indurated and cirrhotic, with the capsule much thickened and covered by fibrous growths, or it may be amyloid. Finally, actual gummata may be met with (Rendu, 'Soc. Anat.,' 1870). These are, however, extremely rare, and they must not be confounded with infarctuses, which may also be met with in syphilitic subjects.

Carcinoma of the spleen.—It is doubtful if the spleen may be primarily affected with carcinoma. We would not absolutely deny its possibility, but the cases which have been published as those of primary carcinoma have not been described with sufficient histological detail to induce conviction. It is not, in fact, sufficient to prove a case of carcinoma to describe the naked-eye appearances of large tumours which give on scraping a juice containing large cells. These conditions are present in fact in splenic leucocythæmia. The stroma of carcinoma and the structure of secondary growths in the glands and other organs must be adduced to support and prove the diagnosis of carcinoma. For our own part, we have never observed a case of primary carcinoma of the spleen. Secondary carcinoma is, on the other hand, rather frequent as the sequela of cancer of the stomach, breast, liver, brain, &c. These growths are found in the form of nodules, or as an infiltration which exactly reproduces the characters of the tissue and the cellular elements of the primary tumour.

[1] Cornil and Babès, Communication to the Acad. de Méd., April 1883, and *Journal de Robin*, 1883. . 456.

Cysts.—Mucous cysts of the spleen are extremely rare. A case has been reported by Andral in which many vesicles were present, compared by him to cysts of the neck of the uterus; also a case by Leudet in which there was a large cyst divided into four or five chambers by fibrous septa, lined with pavement epithelium. Cases of Livois and Péan have been reported by Magdelain in which the internal wall of the unilocular cyst was smooth and covered by hard plates, which were formed of carbonate and phosphate of chalk and magnesia. In this latter case the fluid, measuring more than six pints, was of a yellowish brown colour, and contained albumen, lymph cells, red blood corpuscles, and cholesterine. Fœrster describes, in the museum of Würzburg, a serous cyst of the spleen of the size of a nut and with cartilaginous walls. The mode of growth of these tumours is unknown. Andral mentions a case of dermoid cyst of the spleen containing fat and hair.

Parasites.—Cysts containing echinococci may be produced in the spleen. These cysts are extremely rare. They are more frequently developed in the peritoneum, which covers the organ. If they become pedunculated they may project into the peritoneal cavity (Charcot and Davaine). Hydatids of the spleen are generally seen with similar growths in the liver and peritoneum. E. Wagner describes having seen in the human spleen a case of *Pentastoma denticulatum* surrounded by a calcified cyst.

CHAPTER II.

THE THYROID GLAND.

I. Normal Histology.

THE thyroid gland, the functions of which are unknown, is composed of round or oblong vesicles, which communicate with one another. They are united into lobules, but have no excretory ducts. These lobules are separated by septa of connective tissue, which is thicker than that found between the vesicles. These septa are continuous with the fibrous capsule of the gland. The vesicles have a diameter of from 45 μ to 110 μ, and are composed of a hyaline membrane lined with a layer of polygonal epithelial cells, which are finely granular and which measure from 9 μ to 13 μ. The closed cavity is filled with an albuminoid fluid. In the place of this fluid a mass of colloid substance is found so frequently that it may perhaps be considered normal. The blood vessels of the gland are extremely numerous and are derived from the thyroid arteries. These vessels form a rich plexus of capillaries around the follicles.

II. Pathological Histology.

With the exception of goitre or hypertrophy of the thyroid gland, the lesions of this organ are extremely rare. Tumours, strictly speaking, are not found in this gland.

Goitre.—The tumour known under the name of goitre consists in hypertrophy of the follicles and a new formation of glandular substance. The follicles, which contain a larger number of epithelial cells than in the normal condition, increase in size and send out prolongations or lateral buds, which themselves become strangulated and form new follicles (Billroth). This hypertrophy or growth is sometimes regular throughout the gland, sometimes limited to certain lobules. In the latter case the tumour, situated

on one side of the gland, has a tendency to become isolated. The gland is often lobulated by the hypertrophy of some one of its superficial lobules. The vesicles are rather larger than in the normal condition, but their epithelial lining and fluid or colloid contents are almost physiological. If the distension and hypertrophy of the vesicles increase, small cysts are formed, which give the gland a certain feeling of softness (*soft goitre*). These tumours, superficially examined with the naked eye, might be mistaken for cysts, but on examining them under the microscope they are seen to have vesicles slightly enlarged, the septa of which are very distinct. If the formation of cells, fluid, and colloid substance continues, the thyroid gland may be changed into a number of cysts and may increase greatly in size (*cystic goitre*). In some cases the capillaries and small arteries dilate, and the large arteries become cirsoid; the tumour then pulsates, the capillaries project into the follicles, and hæmorrhage occurs. Such is *aneurismal goitre*. The arteries may become encrusted with calcareous salts; at other times the connective tissue of the gland may become so much thickened that a fibrous tissue may be formed, which compresses the follicles and takes their place. This is *fibrous goitre*. In old persons fibrous goitre may become harder in consequence of calcification of the connective tissue, which change may be limited or may invade the entire tumour (*stony goitre*).

Tubercle.—We have already described tubercle of the thyroid gland (vol. i. p. 206) and traced the development of the new growth from the epithelium and connective tissue of the gland. Tubercle of the thyroid gland is rare and does not differ from tubercle of other organs.

Carcinoma.—Secondary carcinoma is extremely rare in the thyroid gland; and primary cancer is still more rare. When present the tumour may attain a large size and show a tendency to invade the trachea and œsophagus; it then causes the same symptoms as primary cancer of these organs. Some years ago[1] one of us observed a tumour of the thyroid gland which had the appearance of carcinoma, but which from its structure and development resembled epithelioma. The cells lining the alveoli of the gland were hypertrophied and proliferating. Most of them were cylindrical and contained large nuclei with large nucleoli. From the walls of the alveoli sprang vascular buds lined with the

[1] Cornil, 'Sur le Développement de l'Epithéliome du Corps Thyroïde,' *Arch. de Phys.*, 2nd series, vol. ii. pl. xxi. 1875.

same cells. Since the publication of this case, Luigi Griffini[1] has published a similar one, and as in this tumour he observed that the number of fleshy granulations projecting into the alveoli was considerable, he gave it the name of *infectious papilloma*.

[1] *Arch. per le Sc. Med.*, vol. iv. No. 7.

CHAPTER III.

THE SUPRA-RENAL CAPSULES.

I. Normal Histology.

The supra-renal capsules are composed of a cortical and a medullary substance, and are surrounded by a capsule from which spring fibrous trabeculæ which penetrate the gland and form its framework. The cortex in adult man is generally of a yellow colour and opaque, which is due to the presence of fatty granules in the cells; it is composed of epithelial cylinders lying from the periphery towards the centre. The cells forming these cylinders are polygonal. These cortical cylinders have no proper glandular membrane and are simply limited by the connective tissue of the substance of the gland. At the internal border of the cortex the cells are generally large and filled with fat granules; when the cylindrical and polygonal cells of the cortex are quite infiltrated with fat, the yellow colour of the capsule sharply distinguishes it from the red colour of the medullary tissue. The stroma of the medullary substance forms round or narrow meshes. In these meshes, pale cells are found which are angular or branched in form; they have one nucleus and nucleolus, and they somewhat resemble nerve cells, from which, however, they may be distinguished. In consequence of post-mortem changes the two substances separate, and between them is a brownish fluid containing blood and large cells filled with fat.

The blood vessels are very numerous and are derived from the phrenic, cœliac, and renal arteries; they form first a plexus on the capsule, then penetrating into the medullary substance, form there capillary networks, as well as in the cortex, where they surround the cortical cylinders. The veins follow the same course. Little is known about the lymphatics. The nerves are very important, both on account of their number and the size of their trunks. They are derived from the semilunar ganglia and the renal plexus. They are so numerous that in a single capsule

Kölliker counted thirty-three small nerves, each from 0·25 mm. to 0·5 mm. in size. The nerves are accompanied by ganglia composed of multipolar cells, and are situated in the medullary substance.

II. Pathological Anatomy and Histology.

The lesions of the supra-renal capsules are not much better known than their physiological function, and it is very difficult to say precisely what is the relation between morbid changes in these organs and the symptoms observed.

Hyperæmia and hæmorrhage.—Congestion of the supra-renal capsules, which is rather frequent in the new-born or in very young children, is scarcely ever observed in the adult except in chronic cardiac disease accompanied with considerable hinderance to the circulation. Hæmorrhage of the supra-renal capsule is not entirely unknown; it only occurs in the medullary substance, which is softer than the cortex. The effusion of blood collected into foci in this part of the gland may be of considerable size. Thus in a case reported by Rayer in an old woman, the capsule, converted into a sac full of a brownish fluid, weighed four pounds. Many other cases have been observed in which the hæmorrhagic cyst had attained a large size; but most frequently the hæmorrhagic foci are not larger than a pea or a nut. When the blood is reabsorbed these foci may give origin to cysts containing a more or less stained serous fluid. This lesion does not cause any special symptoms.

Thrombosis.—Klebs observed infarctus of the cortex of one of the supra-renal capsules in a case of pyæmia in a woman, the result of resection of bone. The cortex showed spots of yellowish-brown colour, in which the capillaries were obstructed by fibrinous clots. The epithelial cells of the cylinder were necrosed and in a state of complete fatty degeneration.

Fatty and amyloid degeneration.—Infiltration of the epithelial cells of the cortex with small drops of fat is normal in man; it is not known if from this, pathological fatty degeneration may spring. Amyloid degeneration is rare in the supra-renal capsules, and it only affects the vessels of the medullary substance, and not the epithelial cells. Similar lesions appear at the same time in the spleen, kidney, and liver.

Inflammation of the supra-renal capsule.—Suppurative inflam-

mation of one of the capsules is very rare, and simultaneous inflammation of both is still rarer. Suppuration may be sometimes diffused throughout the entire organ, and may even extend to the surrounding cellular tissue; sometimes it terminates in abscess. Caseation of the pus has been mistaken for tubercles. An abundant formation of new connective tissue may be observed in the supra-renal capsules and constitutes actual cirrhosis. This will be studied later with tuberculosis when considering Addison's disease, which is caused either by tubercle or by interstitial inflammation of the capsules.

Tumours.—Primary sarcoma has been observed in children. Ogle ('Arch. de Méd.,' vol. i. p. 4), quoted by Klebs, describes a case of sarcoma in the form of a whitish mass in the two supra-renal capsules. Primary melanotic sarcoma has been observed by Küssmaul. The tumour was as large as a man's head; metastatic nuclei followed, and death was caused by embolism of the pulmonary artery. Another case of melanotic sarcoma has been reported by Dœderlein. Carcinoma of the supra-renal capsules may be primary or secondary. The encephaloid form is most frequent, and the tumour then contains a large number of vessels more or less dilated, as in hæmatoid carcinoma. Though carcinoma is very rarely primary in the supra-renal capsules, yet we have seen many cases. When cancer attacks the kidney primarily, secondary cancer may occur in the capsule; it may also follow cancer of the rectum or ovary. Klebs gives the details of a case of epithelioma which simultaneously attacked the thyroid gland and the supra-renal capsule, but which most probably commenced in the thyroid gland. Islets of newly formed cells in the capsule show stratified calcareous concretions in their centre.

A case of syphilitic gummata of the thyroid gland has been reported by Baerensprung. He describes islets of fibrous tissue with embryonic cells, the centre of the islets being in a state of caseous degeneration. These smooth lobulated islets, firm in consistency, were seated in the medullary substance, which was generally slightly altered. The thickened capsule was adherent, not only to the cortex of the organ, but to the neighbouring parts, so that this new formation of connective tissue in the capsule extended to the adjoining parts and to the ganglia and trunk of the sympathetic nerve. On dividing the gland not a vestige of its normal tissue was found. In its place was a hard tissue, in the midst of which caseous masses of various sizes were found. In

similar cases, the cortex of the capsule has been frequently changed into a semi-transparent tissue, greyish and rather firm, while the whole of the centre was yellow and opaque. At other times the caseous parts are irregularly distributed throughout the whole gland. Nearer the commencement of the lesion the gland may be grey and semi-transparent throughout its whole extent, or be sprinkled over with small caseous nuclei. Microscopical examination of the grey and semi-transparent parts simply shows the connective tissue infiltrated with lymph cells. The fibrous stroma also contains connective-tissue cells. In the yellow and caseous parts there are atrophied lymph cells filled with fine proteic and fatty granules. There is not a vestige of the normal elements of the gland. The subsequent metamorphoses of the altered gland are various; sometimes the caseous part softens and forms a pulpy detritus; sometimes the focus is changed into a cyst containing a caseous soft mass or a fluid resembling pus. At other times calcified spots are found. Absorption of the fluid parts or calcification eventually occurs at the same time that dense fibrous tissue surrounds the calcified parts. Besides chronic inflammation ending in caseation, and which greatly resembles tuberculisation, without, however, the correspondence being exact, acute or subacute inflammation may be seen ending in foci of suppuration. These abscesses, which must not be confounded with caseous softening, contain pus with a large number of free lymph cells.

Tuberculosis, chronic inflammation, and caseous degeneration (Addison's disease).—We unite here tubercle of the gland and interstitial chronic inflammation terminating in caseous change, for these lesions, independently of their common character, constitute the anatomical change observed most frequently in Addison's disease. We will first describe these lesions, and then examine, according to our present knowledge of the subject, what is the relation between the pathological condition and the symptoms. Tubercles either in the form of miliary granulations, or in the form of collections of granulations, having the size of a millet seed or small pea and completely caseous, are not rare in the supra-renal capsules. They are consecutive to pulmonary or ganglionic tuberculosis, and are found either in one or both capsules. Miliary granulations, whether in small numbers in the cortex and under the capsule, or whether disseminated throughout the whole gland, do not differ from those of other organs. They generally commence in the cortex and may invade the

medullary substance; their centres become caseous, and they are surrounded with embryonic tissue. But the gland may be so altered as to be changed altogether into a yellow, caseous tissue, often softened and pulpy; or while its centre has become yellow and friable, its periphery may be grey, hard, and fibrous. This change may be so complete that not a vestige of the normal gland remains. Such is the condition in which the supra-renal capsules are often found in subjects who have succumbed to the cachexia described by Addison. Fibro-caseous change of the capsules is the lesion most frequently observed in Addison's disease. Is this a tubercular lesion? In their appearance and degeneration the glands resemble scrofulous lymphatic glands; but we must recollect that many doubts still exist as to the nature of the disease. In this condition the supra-renal capsule is increased in size; its long diameter may measure 12 centimetres, and it is broad and thick in proportion. It is oval in form. The softened part may be changed into a serous cyst. The two capsules are generally affected to a different degree; sometimes one of them may be normal.

We do not attempt to explain how the lesions of the capsules produce the characteristic symptoms of Addison's disease; that is to say, pigmentation of the corpus mucosum of the skin and of the mucous membranes, and the anæmia and digestive disturbances. The physiological explanations given are far from being satisfactory. The lesion of the nervous ganglia of the capsules and of the sympathetic probably plays some part in the phenomena of pigmentation. It is known, however, that very frequently lesions of the capsules, such as cancer, tubercle, and even a very marked caseous and inflammatory condition, may be present, without the skin being pigmented. The frequency of tubercular or caseous lesions of the capsule without Addison's disease is such that, according to Klebs, out of 141 cases of lesion of the capsule, 100 showed discolouration of the skin, and 41 no discolouration. But on the other hand well-marked Addison's disease, care being taken to clinically distinguish between melanæmia produced by intermittent fever and tubercular and cancerous cachexia, almost invariably coincides with lesions of the supra-renal capsules. Tuberculosis or chronic inflammation with caseous degeneration is what is then most frequently observed. The changes in the other organs noted at the same time, such as bronzing of the skin, vary greatly, but pulmonary tuberculosis and scrofula most usually coincide with it.

Section IV.—The Genito-Urinary Organs.

CHAPTER I.

THE KIDNEYS.

I. Normal Histology of the Kidney.

The kidney is the organ which secretes the urine. The excretory channels and reservoirs are the pelvis and ureters of the kidney, the bladder and the urethra. The kidney is placed in the midst of an adipose cellular tissue and is surrounded by a fibrous capsule which is easily detached in the normal state. On removing the capsule the surface of the kidney appears mammillated in the child and smooth in the adult. On dividing it through its long diameter two substances, differing in form and colour, are observed in the kidney; these are the cortical substance and the medullary or tubular substance, composed of the *pyramids of Malpighi*. The first, which occupies the larger space, is grey or pinkish grey in colour, and translucid, and is contained between the pyramids and the *columnæ Bertini*. Throughout the whole of the cortical substance, including the columns of Bertini, the Malpighian glomeruli are seen as small brilliant points. The pyramids of Malpighi in the medulla are redder than the cortex, and terminate in the pelvis by a free extremity or papilla which is lined by the mucous membrane of the calices. On looking at a kidney in which the blood vessels have been injected red, while the uriniferous tubes have been injected blue through the ureter, it can be seen, even with the naked eye, that the cortical substance is that which is most deeply coloured by the injection. The Malpighian glomeruli are then like so many small red points. The uriniferous tubes, filled with a mass of blue, radiate from the extremity of the Malpighian cones into the pyramids, whence they enter the cortical substance in the form of bundles which compose the *medullary rays*. This is the course of one of these tubes. It

takes its origin in the cortical substance, around one of the glomeruli, the capsule of which is directly continuous with the

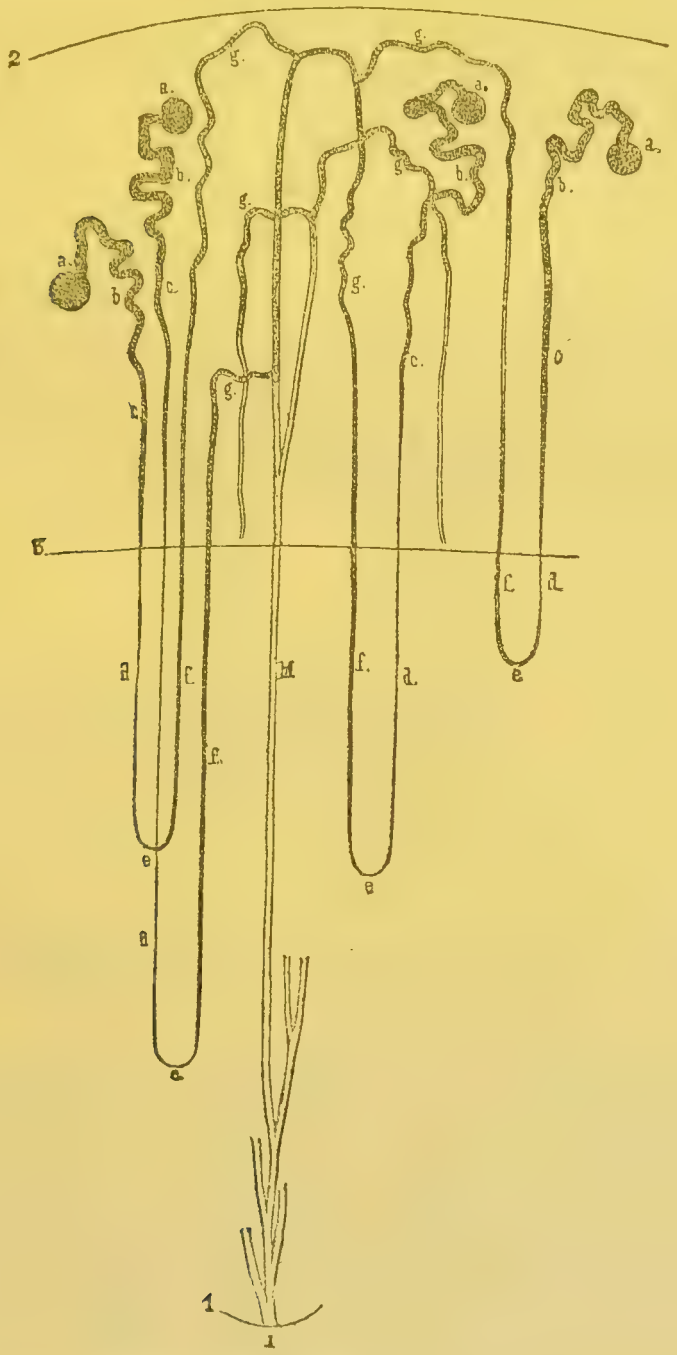

FIG. 167.—DIAGRAM OF THE COURSE OF THE URINIFEROUS TUBES. (Figure borrowed from Gross.)

1. The end of a renal papilla into which is conducted the collecting tube H. 2. Edge of the cortex. 3. Fictitious line of demarcation between the cortex and the medulla; *a*, glomeruli from which spring the uriniferous tubes, *b*, which are continuous to the loops of Henle, *c*, *d*, *e*, *f*, then by the sinuous part *g* to the straight tube H.

proper membrane of the tube. The glomerulus is nothing else, as we shall see later, than a tuft of small vessels emanating directly from the interlobular arteries of the kidney; it is entirely surrounded by a capsular membrane. At the side opposite that where the vessel enters there is a small orifice in the capsule, by means of which it communicates with an uriniferous tube. At its origin, the tube is convoluted and wide, but after making a few turns it contracts, and takes a straight course and reaches the pyramids; here it makes a loop, its convex surface being turned towards the apex of the cone; it then ascends in a parallel direction to the descending portion of the tube, enters the cortical substance, becomes wider and convoluted again, then retracts

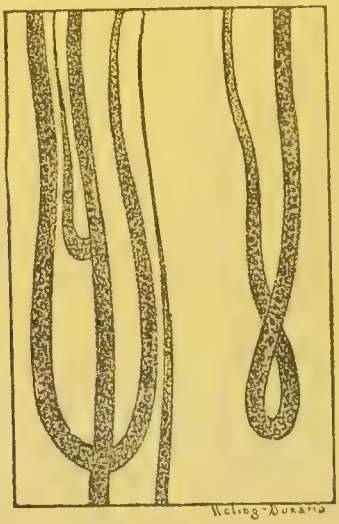

FIG. 168.—LONGITUDINAL SECTION OF THE MEDULLARY SUBSTANCE OF THE HUMAN KIDNEY, SHOWING THE LOOPS OF HENLE. (Figure from Gross.) Magnified 100 diameters.

once more before joining the straight tube. The direction of the straight or collecting tube is rectilinear; it first passes through the cortical substance into the medulla, receiving many single or united tubuli, and it becomes larger as it approaches the extremity of the Malpighian cone, and finally opens into a renal papilla. The urine passes from a collecting tube into the pelvis by an orifice large enough to be seen by the naked eye.

The diameter and structure of a tubule varies according to the different parts of its course from the glomerulus to the papilla. The glomerulus measures from 130 μ to 200 μ; it is spherical; the convoluted tubuli of the cortex measure 40 μ to 50 μ in diameter; in the loops of Henle the tubuli do not measure more

than 15 μ to 20 μ; the largest part of the straight tubes hardly measures from 30 μ to 40 μ, and when united at the terminal extremity of a collecting tube they measure from 180 μ to 200 μ. The capsule of the glomeruli is a delicate hyaline membrane which becomes easily crumpled in every direction. It is united, by its external surface, to the fibrous framework of the kidney. It is lined on its internal surface by a layer of flat polygonal cells furnished with lenticular nuclei.

This cellular lining of the capsule is directly continuous with that of the proximal convoluted tubule. The convoluted tubuli, the loops of Henle, and the straight tubes also have a proper hyaline membrane, which crumples like that of the glomeruli, and

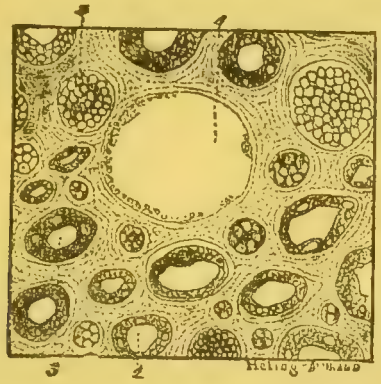

FIG. 169.—SECTION MADE AT RIGHT ANGLES TO A MALPIGHIAN PYRAMID NEAR ITS FREE EXTREMITY. (After Gross.)

It shows the difference in diameter of the collecting tubes and of the loops of Henle. 1. Collecting tube; 2. Henle's tube.

which, according to Ludwig, has some nuclei from place to place. This membrane, which can be isolated, is not present, according to Ludwig, in the large collecting tubes of the pyramids where it becomes blended with the surrounding connective tissue.

The epithelial lining of the tubule changes according to the different parts of its course. In a transverse section of the convoluted tubes the epithelial cells are in the shape of truncated pyramids, with their bases resting on the proper membrane of the tube. The round nuclei of the cells are nearer the base than the extremity. Crowned by a striated free surface, these cells leave a lumen in the centre, through which the urine flows. The protoplasm of the cells is granular, and shows fine striations, which are perpendicular to the hyaline membrane of the tube; these were described by Heidenhain, who looked upon them as small rods. According to this author, their function is to elaborate and

separate from the blood the saline substances which form part of the urine. The striæ make these cells resemble the striated cells of the excretory tubes of the salivary glands. However, on examining sections of the cortex of the kidneys of animals which have been hardened in osmic acid,[1] fine granules placed end to end are seen in the place of the striæ. In these preparations the protoplasm appears clearer at the centre than at the edges of the cells. It is not surrounded by any distinct membrane. The cells are more solidly united to one another than to the lining membrane of the tube; hence it results that in preparations of the kidney made in the fresh state they may be found in tubular masses. The hyaline membrane of the tube is then left creased, though still adherent to the renal tissue. The loops of Henle are lined with small flattened tesselated cells, the nuclei of which project into the lumen of the tube. In the distal convoluted tubes which unite the loops of Henle with the straight tubes, the epithelium again becomes thick, granular, and striated. The straight tubes met with in the medullary rays contain a layer of small, cubical and regular epithelial cells, which become longer as the straight tubes advance into the tubular substance. Here the collecting tubes are lined with a layer of long cylindrical cells springing directly from the walls. The long diameter of these tubuli measures 0·02 m. In the papillæ, the epithelium of the collecting tubes is directly continuous with that of the mucous membrane of the pelvis and the infundibula.

The relations of these tubes to one another, and the composition of the two substances of the kidney must also be considered. The collecting tubes which open into the papillæ pass into the pyramids, and descend, subdividing into the cortex, whence spring the straight tubes which form the medullary rays. The straight tubes are continuous with a distal convoluted or enlarged portion, then with a loop of Henle, and finally with a proximal convoluted and wide tube which ends in a Malpighian glomerulus. The convoluted tubes and the glomeruli which are continuous with the straight tubes of the cortical substance form in the cortex as many secondary pyramids as there are medullary rays; these are the pyramids of Ferrein.

The **blood vessels** have a quite peculiar distribution in the

[1] A fragment of the kidney obtained immediately after the death of the animal is placed in a 1 per cent solution of osmic acid and left there twenty-four hours. It is then washed for an hour in distilled water, and preserved in absolute alcohol.

kidney. The renal artery enters at the hilum and immediately divides; its divisions ramify between the pyramids, and send out branches at the base of the pyramids between these and the cortical substance. The interlobular arteries given off at this point pass directly into the cortical substance perpendicularly to the surface of the kidney, and in their course they give off from place to place arterioles which pass into the glomeruli. The afferent branch of the glomerulus then divides into a certain number of secondary branches, each of which shows loops turned towards the free surface of the glomerulus. The vessels produced by these subdivisions are reunited into a single trunk, the efferent vessel, which passes out of the glomerulus in union with the afferent vessel. In the glomerulus the vessels are as simple in structure as the capillaries. They are lined on their external surface by a delicate layer provided with nuclei, which layer gives the same reactions as connective tissue. The cavity of the glomerulus is lined by the cells of the capsule or Bowman's membrane, and by the connective-tissue lining of the vascular loops of the glomerulus. On issuing from the glomerulus, the efferent vessel again breaks up into capillaries which form a network around the glomerulus and the uriniferous tubes. At the base of the pyramids, where the interlobular arteries of the cortex are given off, other arterioles are also given off, which pursue an opposite course and descend into the pyramids. These are the straight arteries, which form loops with their convex surface turned towards the papillæ of the pyramids. They break up into capillaries which accompany the straight tubes and the collecting tubes.

The blood of the capillaries nearest the surface of the kidney is carried away by the *veins* which are found under the capsule, where they form stellate plexuses. They then unite into larger trunks and descend in the cortical substance parallel to the interlobular arteries. The interlobular vein receives the blood from all the capillaries of the cortex, and conducts it into the large veins situated between the cortical and the medullary substance. The veins derived from the pyramids run in a course parallel to the straight arteries, and also form loops with their convex surface turned towards the papilla. The large venous trunks of the kidney are found between the cortical and the medullary substance. In the medulla, the veins are large and generally full of blood; after death the pyramids are constantly of a deep red colour, while the cortex is colourless.

The most important part of the renal circulation is the *glome-*

rulus; it is here that the passage of the fluid parts of the serum of the blood from the vessels into the uriniferous tubes is at its maximum. In the convoluted tubes of the cortex are elaborated the substances which are carried away by the blood derived from the glomerulus. Thus we see that the physiological functions of the kidney are carried on almost entirely in the cortex, and here also are observed the most frequent marked pathological changes. The medullary substance, at least the straight tubes, for the loops of Henle belong both physiologically and pathologically to the cortex, is simply intended for the passage of the urine; it takes part in the functions and pathology of the excretory ducts, with which it is directly continuous.

The **lymph vessels** of the kidney are easily injected and may be seen in the fibrous capsule and in the hilum. The injection also penetrates into the connective tissue between the uriniferous tubuli. The connective tissue of the kidney is unequally distributed; the fibrous capsule is formed of intersecting connective-tissue bundles, and it sends out fibrous processes which accompany the capillaries into the cortex. The capillaries of the connective tissue give but a feeble resistance to the decortication of the organ. At the extremity of the Malpighian cones, the connective tissue is rather thick and easily demonstrated. Around the glomeruli there is also a very distinct layer of connective tissue. In the rest of the kidney the connective-tissue framework is very delicate and is blended with the vessels. The excretory ducts, the pelvis, calices and ureters, are lined with a non-glandular mucous membrane, the epithelial lining of which is composed of several layers. The pelvis and the ureters also have smooth muscle fibres.

II. General Pathological Histology of the Kidney.

Alterations in the epithelial cells.—The lesions of the epithelial cells of the uriniferous tubes vary according to the region. The cells of the convoluted tubes of the cortex are those that are the most frequently affected. They become larger, swollen, and granular (cloudy swelling) in renal congestion and in the first period of Bright's disease, and also in all forms of temporary albuminous nephritis. Simultaneously with this tumefaction, there will be seen at the free edge of the cells either a hyaline exudation which is agglutinated to them, or a vesicular ball (see *m*, fig. 170), or a clear and granular portion of the protoplasm projecting into the lumen of the tube; at other times, vacuoles filled with a

perfectly transparent fluid. The lumen of the tubes contains either a reticulated colloid exudation or granulation, or clear or colloid balls (*m*, *n*, *o*, fig. 171) secreted by the cells, or fragments of their protoplasm. In consequence of this elimination of the free parts of the cells, they are decreased in height and seem crushed;

FIG. 170.—SEGMENT OF A CONVOLUTED URINIFEROUS TUBE FROM A CASE OF SUBACUTE POISONING BY CANTHARIDIN IN A DOG.

a, proper wall of the tube and connective tissue; *p*, protoplasm of the cells; *n*, their nuclei; *m*, *m*, balls of clear exudation at the summit of the cells. Magnified 300 diameters.

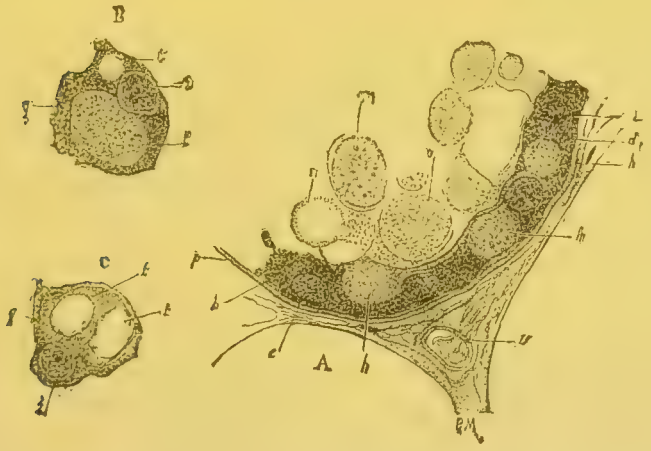

FIG. 171.—A, PART OF THE SECTION OF AN URINIFEROUS TUBE, THE CELLS OF WHICH ARE HOLLOWED BY VACUOLES.

d, protoplasm of the cells hollowed at *h*, *h'*, *h''*, with vacuoles filled with a small granular drop; *e*, *e*, nuclei of the cells; *m*, *n*, *o*, balls of proteic substance which fill the cavity of the tube; *p*, wall of the tube; *v*, capillary vessel.

B, C. TWO CELLS ISOLATED, SHOWING THEIR PROTOPLASM.

q, protoplasm; vacuoles, *l*, *l'*, *l''*, and nuclei, *s*.

a part of their protoplasm and their nuclei are preserved and remain adherent to the proper membrane of the tube.[1] This protoplasm forms a uniform and delicate layer in which the line separating it from the cells is no longer visible. These

[1] Cornil, 'Nouvelles Observations Histologiques sur l'Etat des Cellules du Rein' (*Journ. de l'Anat.* de Robin, 1879).

lesions, which are easily seen after the action of osmic acid, generally coincide with the passing of albumen in the urine.

A certain degree of fatty degeneration is frequently observed in subacute or chronic albuminuria. The fat granules are coloured black by the action of osmic acid; they can also be demonstrated by treating sections of the kidney, cut immediately after death, with acetic acid. Fatty granules are not present normally in the renal cells, neither in the child nor in the adult, though they are found in large numbers in the physiological condition in certain animals, the dog and the cat for example. In old persons fatty granules are met with rather frequently in certain parts of the uriniferous tubes of the cortex without there being any disease of the kidney. In any other case the presence of fat granules is pathological. Fatty degeneration of the epithelial cells is not only found in Bright's disease, it is also found in partial mortification due to infarctus; in certain kinds of poisoning, from phosphorus, sulphuric acid, arsenic, icterus, &c.; and in certain forms of cachexia, pulmonary phthisis, &c., without albumen being present in the urine.

Tumefaction of the cells, their being filled with a granular fluid, partial disintegration of that part of the protoplasm which projects into the tube, do not always lead to mortification of the cells, for they still preserve their nuclei and a portion of their protoplasm adherent to the membrane of the tube. But frequently these lesions, as well as fatty degeneration, cause the complete mortification of the cell, which is then detached from the hyaline membrane and eliminated. Cloudy swelling and fatty degeneration of the cells may be observed in every part of the kidney, but these changes are particularly observed in the large convoluted tubes of the cortex. The loops of Henle are less frequently affected. In the straight tubes of the medullary rays and in the collecting tubes, the epithelial cells rarely contain fat granules; but the lumen of these excretory ducts is often filled with altered, spherical and granular cells derived from the cortex and which are eliminated with the urine. Sometimes several nuclei are observed in the epithelial cells of the convoluted tubes, in cases of recent albuminous nephritis, and particularly in the temporary nephritis of infectious fevers. In consequence of repeated congestion, the colouring matter of the blood may pass into the uriniferous tubes and cause pigmentation of their cells. These cells then contain yellow or brown granules; they become detached and fall into the lumen of the tubuli.

Besides these elementary lesions which belong to inflammation there is another series which results from changes of nutrition in the cells and their infiltration with various substances. Thus in every case of acute icterus, whatever may be its cause, the cells of a certain number of uriniferous tubes contain yellow or greenish yellow granules which give the reactions of the colouring matter of the bile. These altered cells either remain *in situ* or else mortify and fall into the cavity of the tube, either isolated or united into elongated masses. When the bile is present in large quantities in the kidney, crystals of bilirubin are found in the cells and in the connective tissue. In other cases the salts themselves infiltrate the cells, and they become the centres of crystallisation and of calculi which may be microscopic or visible to the naked eye. This is what occurs in new-born children when the renal parenchyma is loaded with urate of soda, or when in gout this salt infiltrates the cells of a certain number of tubuli and is prolonged in the form of crystalline needles into the neighbouring connective tissue. Calcareous salts, alkaline phosphates and carbonates may be deposited in the epithelial cells of the capsule of the glomeruli, which then appear as small, opaque, hard granules on the surface of the kidney, where they are almost visible to the naked eye. Crystals of tribasic phosphate or of oxalate of lime may also be found on the surface of the cells which are free in the lumen of the uriniferous tubuli.

In renal infarctus, when the circulation of the blood has been arrested, as well as in metastatic abscess, the cells become granular, atrophy, and break up into granular molecules, or else mortify entirely. When a part of the kidney is compressed in calculous pyelitis, or in chronic pyelitis, with retention of urine and distension of the calices and pelvis, small cubical or flattened cells (*b*, fig. 172), with a clear and scanty protoplasm or granular cells, are to be found in the atrophied tubuli. The epithelial cells are flattened at the same time that the tubes are dilated, in cases when the urine passes with difficulty, notably in cancer of the uterus, and in intratubular hæmorrhage. Very frequently in the advanced period of Bright's disease cells are seen, either in the uriniferous tubes or in the colloid cysts, in which that part of the protoplasm which is turned to the lumen of the tube becomes colloid, refractive and detached in the form of balls, which accumulate in the cavity of the tube or the cyst. During this process the nucleus and part of the granular protoplasm remain attached to the basement membrane of the tube. Finally these colloid

cysts show a simple layer of flattened cells resting on their membrane (see fig. 172), while they are filled with a hyaline mass.

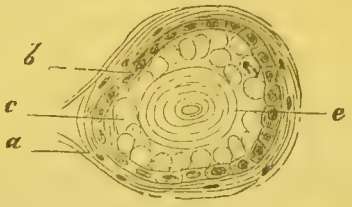

FIG. 172.—COLLOID DEGENERATION OF THE EPITHELIAL CELLS OF A URINIFEROUS TUBE IN A CASE OF INTERSTITIAL NEPHRITIS.

a, connective tissue; *b*, epithelial lining of a uriniferous tube; *c*, colloid balls; *e*, colloid cylinder with concentric layers. Magnified 300 diameters.

The renal cells may sometimes undergo amyloid infiltration, in which case they are changed into translucent bodies, giving the characteristic reactions with iodine and aniline colours.

Hyaline casts and the varieties which are formed in the uriniferous tubuli.—The various changes in the cells just described lead to the secretion of a proteic, hyaline, vitreous substance, which is found in the form of moulds or casts in the interior of the uriniferous tubuli. The cellular elements derived from the uriniferous tubuli are found inside or on the surface of these casts. As they are found on microscopically examining the deposits of the urine during life, it is easily understood how interesting is their study in reference to the diagnosis and prognosis of diseases of the kidney. They give the surest indication of what is taking place in the uriniferous tubes.

The following are the principal varieties:—

a. In the first place the urinary sediment may contain granulo-fatty epithelial cells derived from the epithelium of the uriniferous tubes, atrophied cells or fragments of cells, leucocytes or small hyaline cells. These cells are united by a homogeneous or slightly granular substance. They constitute the **epithelial casts** (1, fig. 173). The cells composing them are the epithelial cells of the tubuli more or less mixed with fat granules and leucocytes.

b. When the kidney is the seat of congestion or slight catarrh accompanied with albuminuria which is hardly perceptible, very pale, narrow, sometimes riband-like sinuous cylinders are formed in the urine, measuring from 1 μ to 2 μ in diameter. They are formed of a soft, finely granular substance and are bordered

by a dark line. On their surface renal cells or lymph corpuscles are often observed. They are recognised with difficulty, owing to their transparency and tenuity. They are generally very long, and are composed of a proteic substance which becomes paler by the action of acetic acid and then still more difficult to detect. These long and delicate filaments, which we have hitherto called **mucoid casts**, have been well described by Rovida[1] under the name of *cylindroids*.

c. **Hyaline casts** are generally observed in large numbers in albuminous nephritis; they are cylindrical, and are formed of a homogeneous, hyaline, colloid, non-granular substance. Their edges are sharp, and bordered by a dark line, and they do not flatten under the cover-glass. They vary in form, both as regards their diameter and their length; most frequently they are not

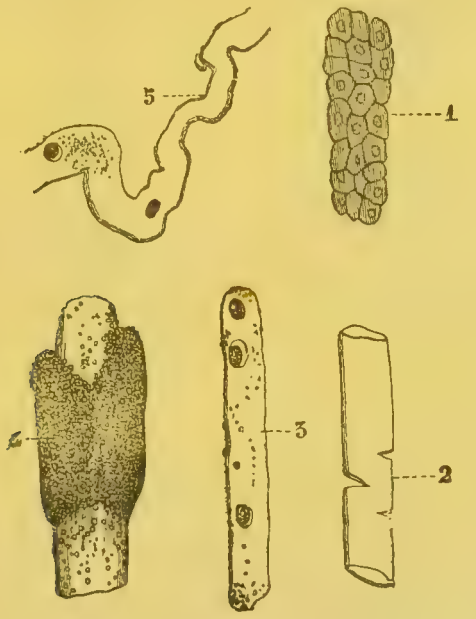

FIG. 173.—HYALINE CASTS IN ALBUMINOUS NEPHRITIS.

1, renal cells; 2, hyaline cast with fissures at its edges; 3, a cast to whic has become attached fragments of cells; 4, hyaline cast covered with fat granules; 5, convoluted cast.

more than 100 μ in length, but they may measure 1 mm.; sometimes they are convoluted, and some of them are very narrow, having been formed in the interior of the loops of Henle. Those formed in the collecting tubes are larger. They may vary in diameter from 5 μ to 40 μ. Transverse slits are sometimes seen in them (2, fig. 173). The older the renal lesion, the harder

[1] *Archivio per la Sc. Med.*, vol. i. 1877.

is the substance of which they are formed. When present in large numbers they always indicate serious Bright's disease ; if they be hard and resistant with shaded edges, they indicate an advanced stage of chronic Bright's disease. Acetic acid does not affect them ; they are easily stained by all staining fluids, carmine in particular. When blood is mixed with the urine in Bright's disease, they are stained a yellowish brown by the hæmoglobin or hæmatin ; they also stain yellowish brown by iodine. By using methyl violet the casts are not stained a red violet, even in the case of amyloid degeneration, which demonstrates that they are not composed of this substance.

The hyaline casts are generally covered either by granular cells (3, fig. 173), by transparent or colloid lymph cells, or by a few colloid epithelial cells. Desquamated cells in a state of granulo-fatty degeneration also adhere to the surface of the casts ; a layer of fine fat granules may even form a complete investment to a hyaline cast (4, fig. 173).

The method of preparing these casts for examination which has given us the best results is as follows: After allowing the sediment of the urine to be deposited in a glass, about a cubic centimetre of it is removed by a pipette, and is thrown into a tube and mixed with an equal quantity of a 1 per cent. solution of osmic acid. Twenty-four hours afterwards the tube is filled with distilled water, shaken, and the deposit again allowed to settle. In this deposit all the casts will be found to have been stained a blackish brown colour, varying in intensity. The most delicate casts, cylindroids if present, are clearly seen, though these are only of a pale grey tint. The hyaline casts are almost or quite black. The form of these various casts is perfectly preserved, for the osmic acid has fixed and coagulated them at the same time that it stained them. By this method may also be seen, better than by any other, the shape of the spiral **corkscrew casts** represented at fig. 174. This form of cast is explained by supposing that the semifluid exudation, which is elaborated in the convoluted tubes, passes into the loops of Henle, where it becomes squeezed out into a long thread ; it is then excreted by the collecting tubes, in which the thread-like cast becomes folded on itself. Thus, in the cast A (fig. 174) we think that the portion *c* passed from a straight tube and became folded on itself, as at *b*, on entering a larger tube, and further on, in consequence of pressure, this gives place to a homogeneous mould, as at *a*. In fact, a spiral cast is often seen to be continuous with a larger cast. Sometimes two casts, either

convoluted or straight, are found united together in a parallel direction. They have probably passed together into a collecting

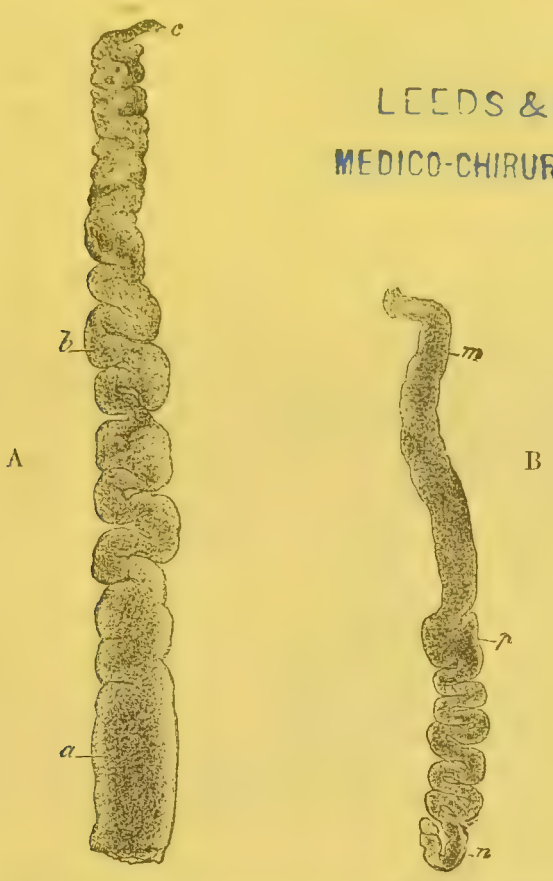

FIG. 174.—SPIRAL CASTS, FIXED AND STAINED WITH OSMIC ACID.

In the cast A a part *c* is convoluted, while the portion *a* is homogeneous. The same in the cast B. Magnified 150 diameters.

tube, where they have become adherent. Sometimes, also, they may be found divided into two branches adherent at one of the ends of the cast, and blended together at the other like a fork, the two prongs of which have been brought together. This probably represents two casts, which have been discharged simultaneously by two straight tubes, and which have become united at their lower extremity on penetrating a large collecting tube. It might be thought that a cast having become convoluted in consequence of pressure, it would easily reassume the regularly cylindrical form by reason of its elasticity. This is the fact in a certain number of cases, but not always. On carefully examining the urinary deposit in acute albuminuria, and staining it with carmine, it will be seen that the spiral casts are deeply stained,

and that they maintain their form owing to a hyaline envelope or bag, which is colourless or stains feebly. The substance of which this envelope is formed is colloid, like that of the cast itself, but it is not so old, nor dense, and consequently stains less readily than the other. Granules of urate of soda, crystals of tribasic phosphate, oxalate of lime, and uric acid may be accidentally seen either in the casts or on their surface. Micro-chemical reagents of hyaline casts show that they are formed of a colloid substance. Their homogeneous and non-fibrillar condition and their resistance to acetic acid distinguish them from fibrin, though they are often wrongly called fibrinous casts. This term is all the more misleading, as true fibrinous casts are sometimes found in the urine. The casts found in amyloid degeneration do not differ from the hyaline casts just described.

How are these hyaline casts formed? Some consider that they consist simply in an exudation derived from the serum of the blood filtered through the membranes of the blood vessels and the tubuli. According to Rindfleisch they are derived from a colloid change of the cells. This opinion is controverted by Klebs. We believe that they are formed both by the fluid parts of the blood and by a secretion of the cells (as already explained, p. 463), and this opinion is based on a minute analysis of the lesions, to be described later when treating of the different kinds of nephritis which may be produced experimentally in animals or observed in man.

d. **In icterus,** whatever may be its cause, hyaline casts are always found in the urine; they are stained yellow and are covered either with yellow granules, or with epithelial cells containing bile pigment or crystals of biliverdine. These *icteric hyaline* casts are found in considerable numbers, though there is very little or no albumen in the urine.

e. **In phosphorus poisoning** the casts found in the urine have the peculiarity of being composed of a granular mass containing fatty molecules; they consequently differ from the hyaline casts most frequently seen in Bright's disease. These are **fat casts.**

f. In **acute congestion with hæmorrhage** into the tubuli, true **fibrinous casts** are produced, characterised by fibrillar fibrin, which swells under the action of acetic acid, and contains red and white blood corpuscles. Instead of being in the form of delicate cylinders, the fibrin is much less exact in outline, and may form small masses with ill-defined edges. Red blood corpuscles are found in these little masses of fibrin. The urine preserves the

red blood corpuscles, but changes their form and they become crumpled or boat-shaped.

Alterations in the walls of the tubuli.—The basement membrane of the convoluted tubes and of the loops of Henle is generally preserved in renal diseases. In Bright's disease, with granulo-fatty degeneration of the cells, proteic and fatty granules will be found on the surface of these membranes on isolating them; but it can be easily demonstrated that these granules are not incorporated with the membrane, which is intact beneath them. In most cases of chronic, parenchymatous, or interstitial nephritis, the hyaline wall of the tubuli is thickened. In suppurative nephritis, and in tumours in the renal parenchyma, this membrane is destroyed and disappears. According to Rindfleisch it should be pierced normally with pores which allow the passage of the lymphatics

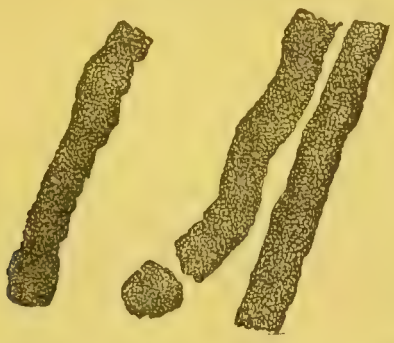

FIG. 175.—ALBUMINO-FATTY CASTS FROM AN ALBUMINOUS URINE IN A CASE OF PHOSPHORUS POISONING.

derived from the blood vessels, with the object of reconstituting the epithelial cells of the tubuli in the normal condition, or forming the cellular elements of pus in renal suppuration. The existence of these pores is far from being clearly demonstrated. In amyloid degeneration, when this lesion, no longer limited to the walls of the arteries and the glomeruli, extends to the uriniferous tubuli, the basement membrane of the latter becomes infiltrated with the amyloid substance and thickened, and gives the characteristic stains of this form of degeneration with the usual reagents.

We have thus far described the pathological changes of the cells and of the basement membrane of the tubuli, and the exudations which may be found within them. We will now consider the changes which the tubuli undergo considered in their entirety, changes in diameter and form.

The tubuli may be uniformly distended. This occurs in retention of urine, and in urinary infiltration of all the elements of the kidney which is the consequence of the first-named condition. Similar distension may also be observed in the first period of Bright's disease, when the epithelial cells are swollen and cloudy, and the lumen of the tubuli contains exudation, desquamated cells, blood, &c. The entire organ is then increased in size. But in the course of Bright's disease a certain number of tubuli may be obstructed by their colloid contents, or by interstitial inflammation, causing obliteration or permanent narrowing of the tube, which then shows above the obstacle irregular headed dilatations or actual cysts. These cysts are generally formed at the expense of the tubuli. The same causes may produce distension of the capsule of the glomeruli.

Narrowing or even complete atrophy of the tubuli may be observed when the kidney is compressed from within by distension of the pelvis and calices; this occurs in pyelo-nephritis. Interstitial nephritis characterised by thickening and induration of the connective tissue is nearly always present in this condition.

Lesions of the connective tissue of the kidney.—The connective tissue of the kidney is slight in quantity, though its presence is incontestable, especially in the capsule, at the extremity of the Malpighian cones and around the glomeruli. The lesions which this tissue undergoes in nephritis vary according to the cause of the disease. In simple congestion the connective-tissue cells absorb a larger amount of nourishing fluid than usually; their nuclei become larger, their protoplasm granular and apparent, and the whole cell enlarges. If the congestion be more acute and persistent, as occurs in cardiac, particularly in mitral disease, extravasation of the colouring matter of the blood takes place, and may be recognised by pigment granules around the cells in the fibrous framework of the kidney. The white cells also almost always proliferate and increase in number. Whence it results that the intertubular septa are thickened, the cellular framework of the kidney becomes firmer than normally, and the whole organ denser, and it resists indentation with the finger-nail. Such is the essential lesion of chronic congestion of the kidney in cardiac disease; it leads to a certain degree of interstitial nephritis, with definite fibrous organisation of newly formed elements. In nephritis with albuminuria, congestion and epithelial changes are accompanied with inflammatory lesions of the connective tissue,

consisting in the presence of a considerable number of round cells (embryonic or lymph cells). These cells are seen in the septa which separate the tubuli and around the capsules of the glomeruli. This lesion is not always present, and it varies according to the parts of the kidney examined. Are these elements derived from the proliferation of the fixed cells of the connective tissue or are they the white corpuscles of the blood and the lymph? Judging by what occurs in induced inflammation in animals, we may infer that diapedesis is the cause. Later, when the kidney atrophies and becomes dense, that is in the final period of parenchymatous nephritis and in interstitial nephritis, the embryonic tissue becomes organised and fibrous. In an advanced stage of Bright's disease, and in renal atrophy caused by chronic pyelo-nephritis, atrophy of the tubes and interstitial induration of the connective tissue become more marked. An actual fibrous tissue then separates the atrophied secreting elements. The capsule adheres closely to the surface of the kidney, which is itself granular and mammillated, like the liver in hepatic cirrhosis.

Tumours of the kidney, fibromata, tubercle, syphilitic gummata, and carcinomata originate and develope chiefly in the midst of the connective tissue of the organ; their earliest stage is thickening of the intertubular septa, which are infiltrated with new cellular elements.

Alterations in the vessels of the kidney.—The renal arteries are rather frequently obstructed either by a migratory clot or by the products of endo-arteritis, due to chronic arteritis with atheroma. The right renal artery is the more often obstructed, or one or more of its principal branches between the cortical and tubular substance, whence result one or more infarctuses. Acute, subacute, or chronic arteritis, whether occurring simultaneously with a similar condition in the whole of the arterial system, due to old age or some other cause, or whether consecutive to embolism or resulting from local irritation of one or more branches of the renal artery, does not differ here from what it is everywhere else. In chronic albuminous nephritis, and particularly in certain kinds of interstitial nephritis, the walls of the arteries are thickened more or less, like the rest of the connective tissue of the organ. Chronic arteritis, marked by thickening, induration, and a tortuous state of most of the vessels of the kidney, and the narrowing of their calibre, shows that the interstitial nephritis is of vascular

origin. In a section of the kidney the arteries will be seen to be gaping, and their course can be traced with the naked eye by white lines. The same lesions may be observed on examining vessels in their longitudinal or transverse section under a low power. The external coat and the most external part of the middle coat are rather opaque. This is sometimes due to the presence of fat granules, but it is most frequently caused by a large number of elastic and connective-tissue fibres which intercept direct light. The internal coat, examined in transverse section, shows all the lesions of chronic endo-arteritis, with more or less considerable narrowing of the calibre of the vessel. This endo-arteritis is always more marked in arteries which have been obliterated in consequence of thrombosis or embolism coinciding with old infarctus of the kidney, and it is never absent even in the parts which have become fibrous in consequence of interstitial nephritis. The renal arteries are the seat of amyloid degeneration of the kidney.

Changes in the Malpighian glomeruli.—Owing to the peculiar structure of the glomeruli, their lesions have a marked and

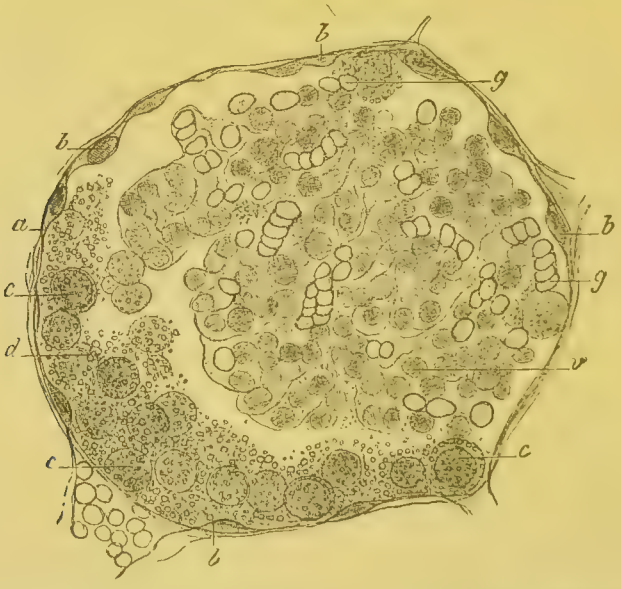

FIG. 176.—GLOMERULITIS IN NEPHRITIS PRODUCED BY CANTHARIDIN, ONE HOUR AFTER THE COMMENCEMENT OF THE POISONOUS EFFECTS.

v', blood vessel of the glomerulus ; *b*, *b*, *b*, cells of Bowman's capsule ; *c*, lymph cells, and *d*, granules free in the cavity of the glomerulus ; *e*, tumefied lymph cells ; *g*, red blood corpuscles in the blood vessels of the glomerulus or free in the cavity of the capsule. Magnified 300 diameters.

peculiar character, and are considered among the most important in the kidney. The glomeruli are almost always affected the first

in kidney disease. This is, however, easily understood on account of their physiological activity and the part they play in the renal circulation. Thus *in congestion*, their vessels being much dilated with blood, a coagulable fluid is exuded into the cavity of the glomerulus between the blood vessels and the capsule. If the congestion be more acute this space may be the seat of an extravasation of red blood corpuscles. In nephritis produced by cantharidin, migratory cells and an effusion of granular fluid may be found in this space almost at the commencement of the poisoning (*vide* fig. 176). *In the acute diffused nephritis of contagious fevers*, which is more marked and typical in scarlatinal nephritis, an effusion of both red and white blood corpuscles, varying in quantity, may be seen in the capsule, or migratory cells along and between the vessels of the glomerulus. *In acute and subacute nephritis*, the glomerulus is the seat of inflammation which affects either the cellular lining of the capsule or the flat cells and cellular membrane lining the vascular loops in the glomerulus. In the first an increase of the epithelial cells of the capsule is the result; in the second, a new formation of cells on the surface of the vascular loops of the glomerulus. These cells vary in form, being hour-glass, battledore shaped, &c. Thickening of the

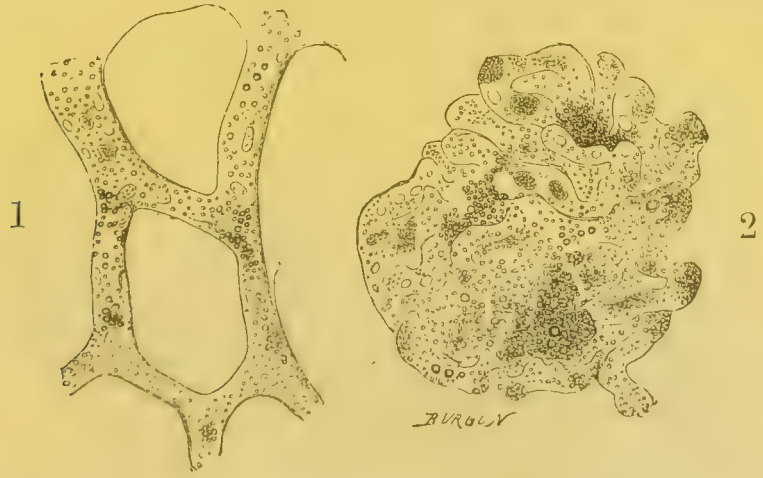

FIG. 177.—FATTY DEGENERATION OF THE VESSELS OF THE KIDNEY IN A CASE OF BRIGHT'S DISEASE.

1, fatty change in the capillaries and stroma of the kidney; 2, vessels of a glomerulus showing a similar lesion. Magnified 250 diameters.

delicate cellular layer lining the surface of the vessels is seen at the same time. In *chronic nephritis*, the cells of the capsule and those on the surface of the tumefied vascular loops may become

charged with fat granules and converted into actual granular bodies. Fatty granules are then seen in the nuclei and small cells belonging to the wall of the vessels and in the wall itself.

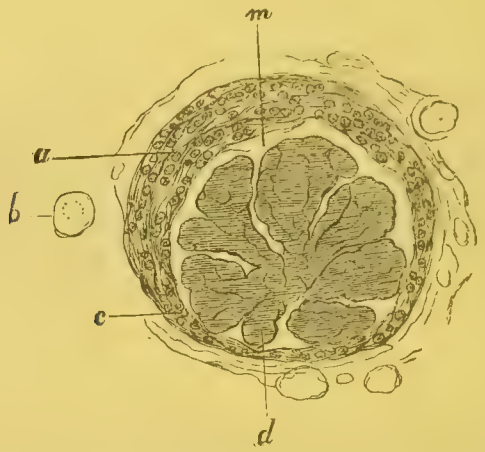

FIG. 178.—SUBACUTE CAPSULAR GLOMERULITIS.

a, thickened capsule; *m*, vascular tuft. Magnified 80 diameters.

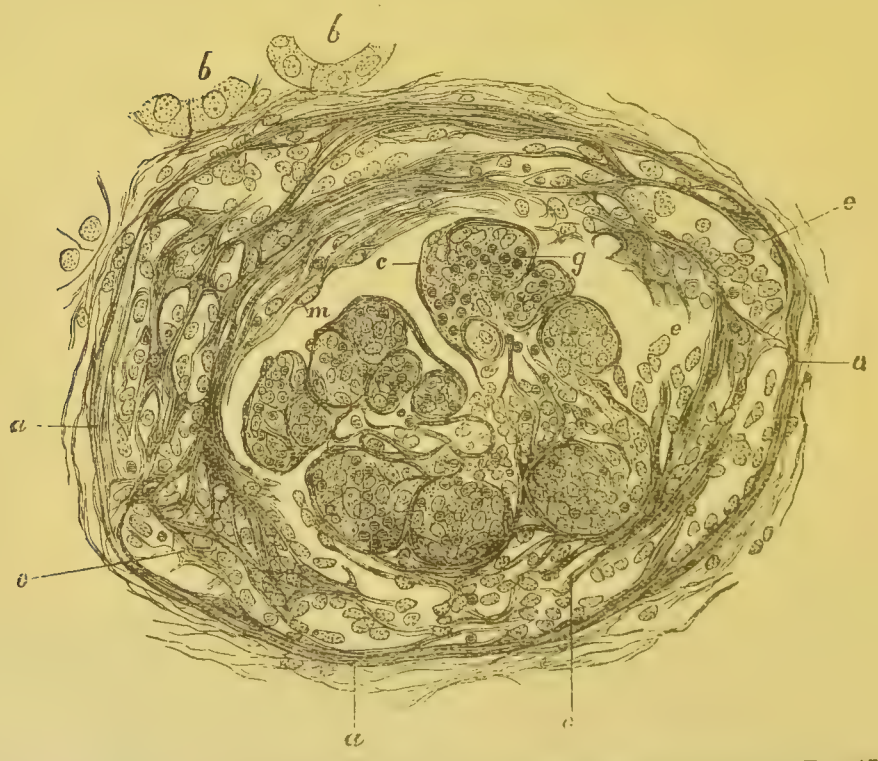

FIG. 179.—SUBACUTE CAPSULAR GLOMERULITIS MORE MARKED THAN AT FIG. 178.

a, *a*, external border of Bowman's capsule; *o*, newly formed fibres of connective tissue, between which there is a large number of cells present; *m*, vascular loops of the glomerulus on the surface of which cells are seen, *c*; *g*, red blood corpuscles in the vessels of the glomerulus; *b*, tubuli. Magnified 200 diameters.

Subacute inflammation of the glomerulus is sometimes shown by the new formation of fibrous tissue, which is produced at the expense of the capsule of the glomerulus of the surrounding tissue, and of the blood vessels within. Thus capsular, circumcapsular, or vascular glomerulitis can be produced (figs. 178 and 179). In *renal atrophy resulting from pressure*, in local arrest of the circulation, in most cases of parenchymatous nephritis, and in all cases of interstitial nephritis, the glomeruli finally atrophy. These vessels show thickening of their walls and narrowing of their calibre. They are united by a tough hyaline connective tissue, between the fasciculi of which a few cells are found; the vascular tuft is changed into a small fibrous mass which is still surrounded by the capsule of the glomerulus, and is impermeable to blood. Sometimes, the capsule being distended by urine or by a colloid substance, the entire glomerulus is changed into a cyst. The glomeruli are the first part of the renal vascular system to be attacked in amyloid degeneration.

After this rapid review of the lesions of glomerulitis, and of degeneration or atrophy of the glomerulus, it is easily understood what an important part the glomerulus plays in renal pathology. If, in consequence of too large an afflux of blood, fluid be exuded into the capsule of the glomeruli, the urine contains albumen and blood. Should the circulation be hindered in the glomerulus, it becomes slower or partially arrested, the entire kidney is insufficiently supplied with blood, and albumen is passed with the urine at the same time that the cells undergo change. If glomerulitis be acute enough to completely stop the passage of blood, there is, simultaneously with albuminuria and decrease in the secretion of urine, a series of symptoms caused by the retention in the blood of excrementitious products, and which is called uræmia.

The lesions of the capillaries of the kidney are not easily distinguished from those of the connective tissue of the septa. To study them, delicate sections must be made of the stroma of the kidney. The capillaries are seen to be entirely obstructed, either by fibrin and blood, or by the products of changes of the fibrin and the colouring matter of the blood in those parts which are the seat of infarctions (*vide* fig. 177, 1). Mortification and fatty degeneration of the cells the capillaries should nourish are the consequences. The carriage by the blood of pathogenic bacteria and their arrest in the capillaries of the kidney lead to various phenomena according to the nature of the bacteria.

While the bacilli of anthrax, in acute experimental poisoning, are found in considerable numbers in the renal capillaries without causing any lesion of the cells, the bacilli of tuberculosis produce tubercle, and those of pyæmia abscesses. In metastatic abscesses, masses of micrococci are found from place to place in the interior of the capillaries and in the vessels of the glomeruli. Around these capillary infarctuses the cells of the renal parenchyma become paler and mortify, at the same time that migratory cells are observed in the renal tissue; the altered tissue undergoes softening and is soon infiltrated with puriform fluid. In albuminous nephritis at the period of fatty degeneration, cells and

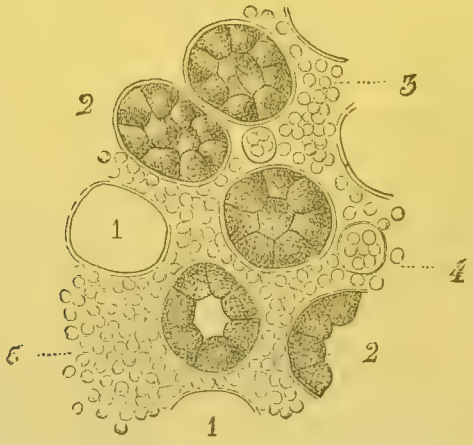

FIG. 180.—SECTION OF THE KIDNEY IN LEUCOCYTHÆMIA.

1, section of a tubule from which the epithelial cells have fallen; 2, tubule the lumen of which is filled with granular epithelial cells; 3, capillary cut across longitudinally; it is filled with white blood cells; 4, transverse section of a capillary; 5, a mass of white blood cells caused by the rupture of a capillary. Magnified 350 diameters.

nuclei infiltrated with fat granules are found in the walls of the capillaries, as well as in the interfibrillar spaces of the connective tissue. In interstitial nephritis the walls of the capillaries thicken by the formation of new elements. In leucocythæmia the capillaries are sometimes gorged with leucocytes, and rupture of their walls, or diapedesis alone, may cause extravasations of these elements into the connective tissue (*vide* fig. 180).

The lesions of the veins of the kidney are thrombosis and acute phlebitis, which cause, as has been shown in several cases, the excretion of albumen in the urine; also chronic phlebitis, which is characterised by thickening of all the coats of the vein, due to the new formation of the elements of connective tissue. Chronic

phlebitis may cause complete obstruction of the vein, and may be observed in advanced interstitial nephritis, in pyelo-nephritis with renal atrophy, and in old infarctuses which have become fibrous.

III. Pathological Anatomy and Histology of Diseases of the Kidney treated separately.

Anæmia.—Anæmia of the kidney is frequent in all chronic cachectic diseases, particularly in cancer and tuberculosis in their last periods. The kidneys are then pale, grey in colour, the cortical substance being paler than the pyramids, which are generally slightly coloured. The kidneys are smooth superficially and generally small. When there is any obstacle to the flow of the urine, as, for example, in cancer of the bladder, uterus, or pelvis compressing the ureters, invading their walls and narrowing their calibre, the ureters dilate above the contracted part. The urine is then driven back into the kidney, which it distends. The capsule of the kidney is smooth, and the parenchyma pale, anæmic, and infiltrated with urine. The tubuli, especially those of the cortex, are abnormally large. Their cells are normal or compressed by the fluid which distends the lumen of the tubes, and thus, instead of being cylindrical, they are flattened against the wall of the tube. In other forms of renal anæmia the cells are not altered.

Congestion.—Acute renal hyperæmia is observed in almost all febrile diseases—intermittent fever, typhoid fever, variola, erysipelas, poisoning by cantharidin, &c. It is thus difficult to distinguish it from acute diffused nephritis, which is most frequently temporary, and which generally accompanies it. Chronic renal congestion is caused by permanent obstruction to the venous circulation, chiefly in cardiac disease. Chronic congestion causes changes in the epithelial and connective tissues, and particularly a certain degree of interstitial nephritis. Congestion is found at the commencement, and often during the course of subacute and chronic nephritis, so that it is difficult to study it apart from these lesions.

Before describing congestion and nephritis observed in man it would be well to give the result of some experiments on animals, undertaken to discover how these changes occur. The first question is to ascertain how the urine passes at the moment that

it is filtered from the blood through the cells and membranes of the vessels and tubuli. To study the method of infiltration of the urine, we injected in the jugular vein of the rabbit from 80 to 150 grammes of a 1 per cent. solution of prussiate of potash. This salt passes immediately into the urine, which fact can be verified by adding a few drops of a solution of perchloride of iron, when a precipitate of Prussian blue is obtained. The animal is then killed, and the renal artery is immediately injected with a 1 per cent. solution of perchloride of iron, and the injection pushed till the capillaries of the kidney are distended. Immediately after this injection fragments of the kidney, which are of a blue colour, are removed with a razor and hardened in osmic acid. This acid gives the parts already stained with Prussian blue a bluish violet colour. The stained parts are easily recognised in sections, and it is seen that the staining is not general. Thus in a transverse section of a convoluted tube, out of the six, seven, or eight epithelial cells which constitute the lining, one, two, three, or four of the cells only are stained; more rarely all the cells are stained. The stain is exactly limited by the cell itself; all the protoplasm and the nucleus are uniformly stained blue; they show no granulation. This staining of the cells is only seen in some of the convoluted tubes. The injected fluid is also found in their lumen. The cells of the straight tubes are not stained, but they sometimes contain bluish-coloured urine. In some glomeruli a coloured fluid is seen between the capsule and the blood vessels. It is thus shown that the fluid part of the blood passes simultaneously through the walls of the blood vessels of the glomeruli and the capillaries of the kidney. It stains the cells of the convoluted tubes before passing into the lumen of the tubes, and from there it is expelled by the excretory ducts.

Effects of ligature of the renal vein.—The liquor sanguinis and the red and white blood corpuscles escape exactly in the same way when the blood tension is increased in the vessels of the kidney. This may be proved by the following experiment: If the renal vein be tied in the living rabbit, the kidney is immediately seen to swell, and to become red and tense. On removing the kidney two or three minutes after the ligature has been placed, and on hardening a portion in osmic acid, all the capillaries in the cortex will be seen to be gorged with blood. In the capsule of the glomerulus, between the membrane and the vessels, a fluid will often be found containing red blood corpuscles, and which coagulates with osmic acid. A certain number of the con-

voluted tubes contain the same fluid and corpuscles. The liquor sanguinis and the red blood corpuscles find their way, mixed with urine, into the uriniferous tubuli, and cylindrical coagulations result. If, instead of killing the animal and removing the kidney after the ligature of the vein, the wound be reopened, and the kidney examined twelve or fifteen days after the ligature, a large number of hyaline casts will then be found in the tubuli. There is also partial mortification of the cells of the tubuli, which contain numerous fatty granules. This condition of the kidney is not without analogy in Bright's disease. In this experiment stasis of the blood with congestion has been first produced, and the circulation has been afterwards more or less completely re-established by the capsular vessels.

Cantharidin albuminuria.—We have just seen how experimental congestion of the kidney of the most violent type is produced; the following experiments clinch the question, and enable us to realise the conditions of congestion and albuminuria caused by temporary nephritis. If an animal be poisoned with cantharidin or with powdered Spanish flies, nephritis with albuminuria varying in intensity and duration is produced, according to the dose of the poison and the continuity of its action. The administration of a single dose of poison we will call acute poisoning, and that which is caused by repeated doses subacute poisoning.

Acute poisoning by cantharidin.—If a solution of cantharidin[1] containing from $\frac{5}{1000}$ to $\frac{1}{100}$ of a gramme of the poison be injected under the skin of a rabbit, albumen will be found in the urine half an hour after the injection. At this time the cortical substance of the kidney has already undergone marked changes. To the naked eye it seems congested and tumefied. On microscopically examining sections, cut after hardening in osmic acid, a certain number of glomeruli will be found, in which there is an effusion of fluid and lymph cells between the membrane and the vascular tuft. The cells of the convoluted tubes, which are in connection with the glomeruli and those of the ascending branches of the loops of Henle, seem to be immersed in a fluid containing fine granules. Forty minutes or an hour after the injection the

[1] We make use of a concentrated solution of cantharidin in acetic acid. The degree of solubility is in relation to the temperature. At the temperature of from 15° to 18° (centigrade) an injection of four cubic centimetres of the solution may cause accidents which sometimes terminate two or three hours afterwards in the death of the animal.

lesions of the cortical substance are much more marked. We propose to describe them in detail, for we shall find them again in the acute nephritis of fever, and sometimes in chronic nephritis. On examining the glomeruli under a power magnifying from 100 to 200 diameters, a granular zone, varying in width, will be seen between the capsule and the blood vessels. This zone is present all round, except at the hilum of the glomerulus, for here there is no space between the capsule and the vessels. In this zone numerous granules and a considerable quantity of round cells are

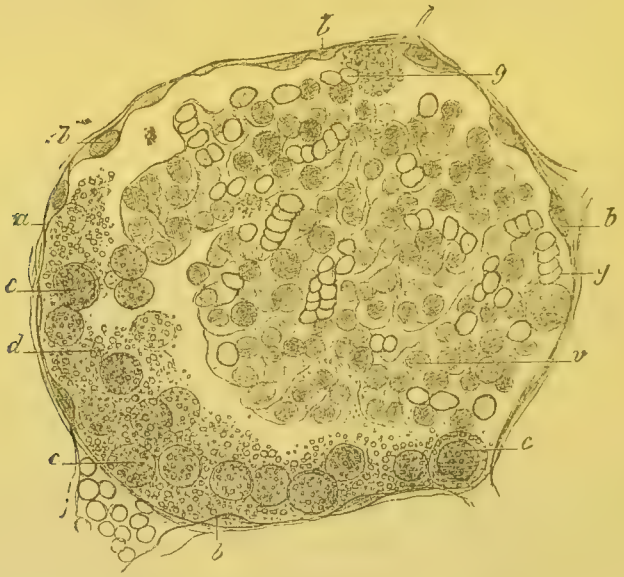

FIG. 181.—A MALPIGHIAN GLOMERULUS AND BOWMAN'S CAPSULE FROM A RABBIT THREE-QUARTERS OF AN HOUR AFTER THE COMMENCEMENT OF ACUTE POISONING FROM CANTHARIDIN.

a, investing membrane of the capsule ; *b*, *b*, flat cells of the capsule forming a more or less complete investment ; *v*, vessels of the plexus containing both red, *g*, and white, *c*, blood corpuscles ; *e*, lymph cells extravasated with a fluid containing many granules, and which is located between the capsule and the blood vessels. Magnified 350 diameters.

seen. These cells are lymph cells, the large and tumefied nucleus of which stains distinctly with carmine. The lymph cells are tumefied, because they are immersed in a fluid, and they have the same appearance as when swollen by the action of water. They are much larger than those which are still within the capillaries of the glomerulus. The flat cells take no part at the commencement of the process in the formation of the round cells, which can be recognised half an hour after the subcutaneous injection of cantharidin. But in other glomeruli, particularly one hour and a half or two hours after the commencement of the

poisoning, the flat cells of the capsule are tumefied, and many of them are detached, become spherical, and fall into the cavity of the glomerulus. The wall is sometimes quite denuded. Sometimes one of these parietal cells may be seen containing two nuclei. Simultaneously the lumen of the convoluted tubes is seen to be distended, and to contain a fluid filled with fine granules. Red blood corpuscles and lymph cells may also be met with here; they are chiefly, if not entirely, derived from the cavity of the glomerulus. For an hour and even for an hour and a half from the commencement of the poisoning the glomeruli and the convoluted tubes are alone altered. The excretory passages, the delicate loops of Henle, the straight and the collecting tubes are intact. Contrary to an opinion widely held, cantharidin nephritis, as well as the temporary nephritis of fever, commence in the labyrinth, and it is here where the most important changes take place. As we have seen, the lesions are not very marked, and their explanation is not easily given at once. It may be summarised thus: acute congestion, affecting principally the glomeruli; increased tension of the blood in the vessels; and passage through their walls of the fluid part of the serum, carrying with it granules and a few red and white blood corpuscles, which accumulate in large numbers in the cavity of the glomerulus. This exudation finally finds its way into the system of tubuli.

An hour or an hour and a half after the commencement of the poisoning, the epithelium of the straight tubes commences to show very remarkable changes, which take place very rapidly. In the rabbit, as in man, the straight tubes have a cubical epithelium, which becomes cylindrical in form as the extremity of the pyramid

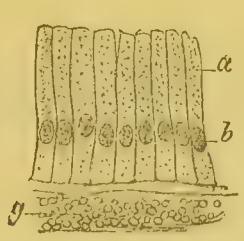

FIG. 182.—NORMAL EPITHELIAL LINING OF THE COLLECTING TUBE OF THE RABBIT SITUATED AT THE EXTREMITY OF A PYRAMID.

a, cylindrical epithelial cells; *b*, nuclei of the cells; *g*, red blood corpuscles contained in a vessel outside the tube. Magnified 200 diameters.

is reached, and the epithelium of the collecting tubes formed by the union of the straight tubes is markedly cylindrical. These cylindrical cells are arranged in single layers, and they leave a

large lumen free in the middle of the tubes. The cylindrical cells of the collecting tubes show, instead of the regular arrangement seen two hours after the commencement of the poisoning, a polyhedral form, and are flattened by reciprocal pressure. They are moreover so increased in number as to fill the entire cavity of the tubes. If a transverse section of the extremity of one of the cones be examined under a power magnifying 100 to 150 diameters, the large collecting tubes will be found distended and filled with polyhedral cells. Under a power magnifying 350 diameters these cells are seen to have numerous facets, which correspond to those of neighbouring cells. Their granular protoplasm sometimes contains a few red blood corpuscles, which are also seen rather frequently between the cells. Their nucleus, more or less regular, is discoid and spherical, while the nucleus of normal cells is ovoid. These cells are everywhere adherent to

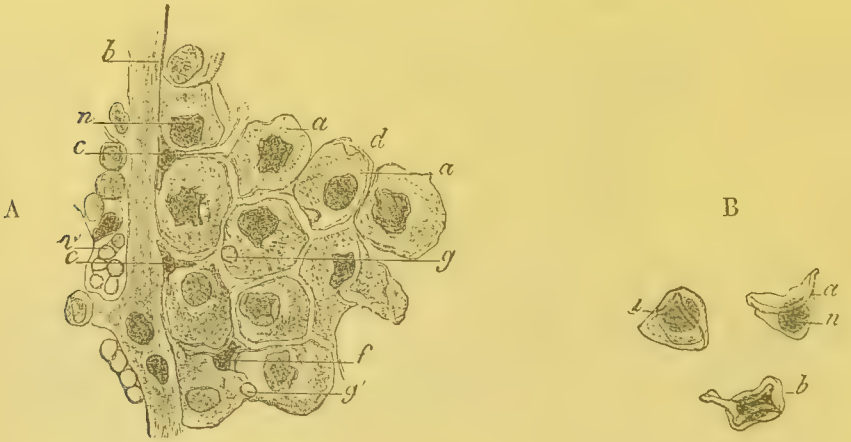

FIG. 183.—A, COLLECTING TUBE OF THE KIDNEY OF A RABBIT IN POISONING BY CANTHARIDIN, TWO HOURS AFTER THE SUBCUTANEOUS INJECTION OF THE POISON.

b, *b*, proper wall of the tube; *a*, *a*, pavement cells; *n*, their nuclei; *c*, small migratory cell; *f*, small cell of the same nature, irregular in form, with its surfaces moulded by neighbouring cells; *g*, *g'*, red blood corpuscles contained in the protoplasm of the cells and between them; *v*, capillary vessel. Magnified 350 diameters.

B, THREE SMALL ISOLATED MIGRATORY CELLS,

a, *a'*, *b*, containing a nucleus, *n*. Their surfaces are moulded by the convex surfaces of the polyhedral cells.

the wall of the tube, except in the centre of the tube, which they fill, and where they are generally free. Some of them have two nuclei. Pressed against the walls of the straight and the collecting tubes, wedge-shaped cells are often seen; they are placed between the pavement cells, with their base flattened

against the wall of the tube and with their extremity insinuated between two pavement cells which are much larger than themselves (*c*, fig. 183). They have a small round nucleus, and they stain deeply with carmine. On isolating these small cells after fixing them with osmic acid, they are seen to have concave or plane facets, and ridges caused by pressure. These facets are moulded on the neighbouring cells, and the ridges demonstrate the flattening of their protoplasm by larger cells which press on them (see cells *a*, *b*, B, fig. 183). These wedge-shaped or stellate cells seem to us to be produced by diapedesis of the white corpuscles of the blood. They are in fact more often adherent to the walls of the tubes, outside of which white blood corpuscles are seen in the connective tissue.

The multiplication of cells and their change in form from the cylindrical to the regularly polyhedral takes place in the usual manner. The protoplasm of the cells swells and becomes granular; the tumefied cell sends out buds, which project into the lumen of the tube; the nuclei divide, remaining spherical or lenticular; the protoplasm divides and the cells mutiply. There is at the same time diapedesis of the lymph cells. To recapitulate: cantharidin first causes in the kidney, almost immediately after its introduction under the skin, the extravasation of white and red blood corpuscles from the vessels of the glomeruli, then acute catarrhal inflammation of the straight and the collecting tubes. We have then acute diffused nephritis.

Slow poisoning by cantharidin.—If, instead of acting on the kidney by a dose of cantharidin which proves rapidly fatal, slight doses are employed on a dog, and repeated every two or three days for a month,[1] renal congestion is produced at every injection of the poison, with the passage of red blood corpuscles, albumen, and hyaline casts in the urine. If, at the end of a month, the animal be killed, there will be found in the kidney all the lesions of subacute diffused nephritis, such as is observed in man. In the glomeruli of the cortex a reticulated exudation, containing a few red blood corpuscles and still fewer white, will be seen between the capsule and the vascular plexus. The endothelial cells of the capsule are tumefied, and the vascular loops of the glomerulus are adherent to one another. In preparations made with osmic acid, the convoluted tubes are seen to be much dilated, and in their enlarged lumen are seen a few white corpuscles, or clear or granular

[1] Cornil, 'Recherches Histologiques sur l'Action Toxique de la Cantharidine,' *Journ. de l'Anat.* (Robin), 1880, p. 564.

globes, varying in size, sometimes smaller, sometimes larger than the white corpuscles. Sometimes the cells of the convoluted tubes show, in that part of the protoplasm which is turned to the lumen of the tube, a vesicle containing a clear or granular fluid which

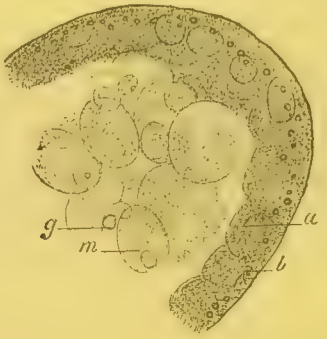

FIG. 184.—FRAGMENT OF A CONVOLUTED TUBE IN SUBACUTE POISONING BY CANTHARIDIN IN A DOG.

a, protoplasm of the cells; *b*, fat granules. The exudation contained in the tube is composed of globes which are clear and have granular contents. *m*, lymph cells and red blood corpuscles, *g*. Magnified 300 diameters.

raises the membrane. This liquefied part of the cell separates and falls into the cavity of the tube. These cells are then reduced to that part of the protoplasm which is adherent to the basement membrane and their nuclei. In other tubes the enlarged

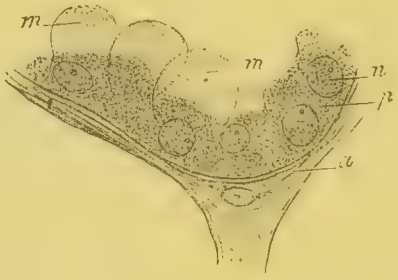

FIG. 185.—SEGMENT OF A CONVOLUTED TUBE IN SUBACUTE POISONING BY CANTHARIDIN IN A DOG.

a, proper wall of the tube and connective tissue; *p*, protoplasm of the cells; *n*, their nuclei; *m*, *m*, globes of clear exudation which cover the tops of the cells. Magnified 300 diameters.

lumen is filled with a reticulated exudation, the more or less delicate trabeculæ of which, often including red blood corpuscles, converge from the free border of the epithelial cells towards the centre of the tube. The epithelial cells are capped by this exudation. Elsewhere the liquid contained in the lumen of the tubes is coagulated by the osmic acid and stained a homogeneous tint, and contains clear or granular globes or red blood corpuscles.

These exudations, which accumulate in the interior of the convoluted tubes, finally find their way into the straight tubes and the loops of Henle, where they are drawn out into threads, or become agglutinated in the form of hyaline casts; thence they penetrate into the convoluted tubes intermediate between the ascending branches of the loops of Henle and the straight tubes, then into these latter, the collecting tubes and the pelvis, and are finally expelled with the urine. These lesions of the cells, which are very well shown in pieces hardened by osmic acid, are not less distinct, though less evident to an untrained eye, when the specimens are hardened in Müller's fluid and bichromate of ammonia. In chronic poisoning by cantharidin the changes in the cells are the same as in subacute or chronic albuminous nephritis in man, and they explain the abundance of the exudation found in the tubuli of the cortex. In the pyramids, the loops of Henle, and the collecting tubes numerous hyaline casts are also found. Besides these changes in the cells, leading to pathological secretion and exudation of proteic substances, the protoplasm of the cells of the convoluted tubes also frequently contains fat granules. Chronic cantharidin intoxication is not limited in its action to the cellular parenchyma, for it also simultaneously causes marked changes in the connective tissue of the kidney. Along the minute arteries of the glomeruli a quantity of small round cells are seen, indicating the commencement of interstitial nephritis. This lesion of the connective tissue was first described by Aufrecht.[1]

Artificial hæmoglobinuria.—In researches in artificial hæmoglobinuria undertaken by Marchand and Lebedeff,[2] they observed changes in the cells of the convoluted tubes similar to those already described in cantharidin albuminuria. To induce the passage of hæmoglobin into the urine, the blood of another animal, or blood dissolved in water, or iodine and glycerine, must be injected into the veins of the animal under experiment. The same result may be obtained by extensive burns of the skin, or by poisoning the animal with poisonous fungi, or by giving increasing doses of chlorate of soda for several days.[3] According

[1] Aufrecht, 'Die Schrumpfniere nach Cantharidin,' *Centralblatt für die med. Wissenschaft*, November 25, 1882.

[2] Lebedeff, Virchow's *Archiv*, 1883, vol. i. p. 267.

[3] Lebedeff gives chlorate of soda in small and increasing doses, so that sixty grammes are ingested in the course of nine days. The polyuria caused by this salt is followed by hæmoglobinuria and death.

to the description and drawings of Lebedeff, the effusion of hæmoglobin into the lumen of the tubuli, the changes the cells undergo in this species of pathological secretion, and the exudation contained in the tubes, correspond identically to the lesions already described in cantharidin poisoning. This may be deduced from the following description:—The striated cells of the convoluted tubes are often hollowed by vacuoles, and show on their free surface homogeneous drops which are secreted by them, and are detached to become free in the lumen of the tube. The tubes contain either small drops or a homogeneous reticulated exudation. In the loops of Henle, and in the straight tubes, hyaline casts are found, which often become granular in the collecting tubes. The number of the tubes is in direct relation with the intensity of the poisoning and the lesion of the cells. The capillary loops of the glomeruli are filled with blood; the lesion of the capsule of the glomeruli is limited to a small quantity of homogeneous or granular deposit, crescentic in shape, between the capsule and the vessels. The endothelium of the capsule is hypertrophied or partly desquamated. In hæmoglobinuria a coagulable secretion is always present, which is derived from the striated epithelium of the convoluted tubes.

Renal congestion in man.—Renal congestion is characterised by redness of the surface of the kidney and distension of the stellate venous plexuses. On dividing the organ, the blood flows freely from the vessels, and red points are observed in the cortex, due to congestion of the vessels of the glomeruli. On examining sections of hardened specimens under the microscope, the red blood corpuscles are seen to be present in varying numbers in the capsule of the glomeruli and in the lumen of the tubuli. The blood keeps its natural conditions, or the hæmoglobin escapes and mixes with the urine and the tubular exudations, staining the hyaline casts yellow; pigment granules are seen in places in the cells of the convoluted and straight tubes. Such are, in a few words, the lesions common to all forms of congestion of the kidney; but they vary greatly according as the congestion is simple or complicated with various forms of nephritis, or if the congestion borrows special characters from certain diseases. Among the latter, it will be necessary to describe hæmaturic congestion of intermittent fever and renal congestion consecutive to cardiac disease.

Renal congestion consecutive to malarial disease.—The hæmaturic or hæmoglobinuric congestion of malarial diseases, due to

the destruction and elimination of red blood corpuscles, exactly reproduces the lesions obtained by Lebedeff in artificial hæmoglobinuria in animals. Kiener and Kelsch[1] profited by their hospital practice in Algeria to draw out an excellent table. When a patient, who has not suffered previously from malaria, succumbs to an attack of pernicious fever, after having passed urine coloured brown from dissolved hæmoglobin and containing hyaline casts, white and red blood corpuscles, and moulds formed of a granular brown substance, or even urine reddened by the presence of a large quantity of red blood corpuscles, the kidney will be found at the autopsy to be highly hyperæmic and increased in size. On examining under the microscope the cells obtained by scraping the cortical substance, they appear to be granular before any reagent is used. Their protoplasm is coloured brown, which is due either to diffused staining or to the presence of very fine pigment granules. In sections, obtained after hardening in alcohol or Müller's fluid, the epithelium is seen in most of the tubes to have an unequal, fringed, and broken contour. From place to place the epithelial cells are swollen, granular, and dark at their base, and they terminate at their free edge by a hemispherical colourless and translucid swelling. These are the vesicular cells, ready to discharge their liquid contents. In the lumen of the tubes are collected translucent spherical or brown granular elements, hyaline or granular globes, red blood corpuscles, and often also the nuclei of epithelial cells. These various exudations constitute, on becoming concrete, the hyaline casts or moulds, which are either homogeneous, pale, resembling a solution of gum arabic, or granular, opaque and brownish, if they contain a certain proportion of hæmoglobin. They carry with them a few red blood corpuscles, leucocytes or epithelial cells, either inside them or on their surface. The epithelium of the convoluted tubes is most changed in this hæmoglobinuric congestion of short duration. It is seen by this example with what rapidity the modified blood acts on the renal epithelium. The straight tubes may, however, be loaded with casts and crowded with red blood corpuscles, without their epithelium being affected. Leucocytes filled with black pigment are often seen in the vascular loops of the glomeruli. We know that in malarial attacks, particularly in pernicious fever, the lymph cells of the blood become filled with black pigment (melanæmia). But these elements are arrested in the vascular plexus of the glomerulus, and do not seem to be able to get out by

[1] *Archives de Phys. Normale et Path.*, February 15, 1882.

diapedesis. Between the plexus and Bowman's capsule a mucous exudation is found in the form of globes. The cells of the capsule are often tumefied and detached. The lesion of the kidney is certainly secondary in pernicious fever, but in the collection of symptoms caused by an alteration in the blood, the kidney no longer performs its part in the economy. The kidney allows dissolved hæmoglobin to pass after destruction of the blood corpuscles, and its ducts become laden with the products which should pass through them, so that the tubuli no longer fulfil their proper functions. We simply mention here the few cases of *paroxysmal hæmoglobinuria* in which the urine is coloured by hæmoglobin, though red blood corpuscles are not found in the urinary deposit. The pathology of the kidney in this form of hæmoglobinuria is not yet sufficiently understood.

Renal congestion due to cardiac disease.—The kidneys are generally hyperæmic in cardiac disease, and particularly in mitral disease accompanied with asystolism. They are at the same time increased in size. The capsule is easily detached. The surface is smooth, very red, and the stellate venous plexuses are easily seen, distended with blood. On cutting across the long diameter of the kidney, the cortex and the pyramids are seen covered with venous blood; on washing the kidney the pyramids appear to be of a much darker red than the cortex. In the latter, however, small red points are perceived, caused by the distended plexuses of the glomeruli. The glomeruli are often seen as small brown ecchymotic spots, when there has been hæmorrhage into the capsules, and if they be distended with blood, the red colour does not disappear on washing. Sometimes red sinuous lines are seen with the naked eye, which might be mistaken, at first sight, for dilated blood vessels, but they are the urinary tubuli filled with blood, as may be demonstrated under the microscope. The cyanotic kidney of cardiac disease is generally indurated, more resistant than usual on attempting to indent it with the finger nail, which resistance corresponds to slight thickening of the connective tissue. On examining sections made in the fresh state under a low power, no lesion can be discovered in most of the convoluted tubes; the capillaries of the glomeruli and those lying between the tubuli are distended with blood. However, from place to place groups of tubuli or isolated tubules may often be found, which are opaque to transmitted light; on examining these under a higher power, fatty degeneration of the cells will be observed. The epithelial cells of some of the tubuli contain, moreover, yellowish or

brown pigment granules, derived from the colouring matter of the blood. Sometimes glomerular apoplexy takes place between the plexus and capsule of the glomerulus, and red blood corpuscles are accumulated in varying quantity, or a hyaline colloid substance, which is stained yellow brown by the blood; some of these glomeruli are changed into small cysts by the compression caused by the exudation, and atrophy of the vascular tuft. When the tubuli are filled with normal blood and numerous red blood corpuscles, as sometimes occurs, the epithelial cells are compressed, flattened and driven against the hyaline wall of the tube by the effusion of blood. On examining delicate sections of the cortical substance, after hardening in osmic acid, exudation and a few red blood corpuscles are generally found in the tubuli, and the free edge of the epithelial cells is often broken, transparent and striated with parallel lines running in a perpendicular direction. These are definite cellular changes, though not far removed from the normal. The lesion of the connective tissue consists in a slight thickening of the tissue separating the tubuli or surrounding the capsules of the glomeruli, and in an increase of the number of cells; sometimes a few round cells are found. To examine these lesions, delicate sections should be stained with picrocarminate or hæmatoxylin. Cüffer attributes this interstitial nephritis of cardiac origin to lymphatic œdema, or to perilymphangitis following venous stasis ('France Médicale,' 1878). This very slight form of general interstitial nephritis is not accompanied with a granular condition of the surface of the kidney, and does not show any tendency to terminate in true interstitial nephritis. In such a case the urine rarely contains a marked quantity of albumen, and when found it may be considered as being chiefly derived from the blood which passes into the urine and discolours it. It is rare for true Bright's disease to be found in patients suffering from an organic affection of the heart, while the congested, slightly hypertrophied and indurated kidney described above is the rule. As these cyanotic kidneys are found at the autopsy of patients who have shown for years all the signs of organic disease of the heart with asystolism, we may conclude, contrary to the opinion held by Klebs, that congestive lesions of the kidney have no tendency to produce interstitial granular nephritis with renal atrophy. If cardiac affections cause a characteristic renal congestion, Bright's disease, and particularly the small granular kidney, is also accompanied with a morbid change in the heart, an interstitial carditis of which we shall speak later. It is therefore sometimes a difficult question to answer

if it be in the heart or the kidney that the primary pathological change is to be found.

Infarctus of the kidney.—Infarctus of the kidney is the result of embolism of a branch of the renal artery. These emboli are derived from the heart, aorta or the renal artery; they are fragments of fibrin with or without débris from the endocardium or intima affected with endocarditis or endo-arteritis. The circulation is arrested in all that part of the kidney which the obstructed artery supplied. The capillaries of this part are often filled with blood, which causes the infarctus to be, from the first, of a reddish brown colour, and to project slightly on the surface of the kidney. But, instead of being red, the affected part may be grey or anæmic from the commencement; the experiments of Vulpian, Prévost and Cotard, and Germont, in which renal embolism followed by infarctus was produced, leave no doubt on this point. The infarctus is generally in the form of a cone with the base turned towards the surface of the kidney, the apex corresponding to the spot where the artery is obliterated. Later the infarctus becomes opaque and of an orange or yellow colour. Then, on examining a section under the microscope, it will be seen that the capillaries are all filled with blood undergoing retrogressive changes, with granules derived from the destruction of the fibrin and red blood corpuscles, and with proteic, fatty, and pigment granules; the latter are brown or red, and are due to the destruction of the red blood corpuscles. The epithelial cells of the tubuli are swollen, granular, and also contain fat granules. The infarctus soon decreases in size, sinks in, and is characterised by a superficial depression, which still preserves its yellow colour and opacity. Such is the lesion which Rayer described under the name of rheumatismal nephritis. The flattening and shrinking of the infarctus, due to partial necrosis of the kidney, coincides with a granulo-fatty degeneration which accompanies desiccation. Reabsorption of the proteic and fatty granules, the result of mortification, has already commenced, which may be proved by examining the tubuli situated at the borders of the infarctus. Here the circulation is more active than normally and the necrosed tissue is surrounded by a hyperæmic zone. On examining the cells of the tubuli, in sections hardened in osmic acid, they are found to be tumefied and vesicular. Their protoplasm, adjacent to the basement membrane of the tube, is granular and opaque, and contains a few fat granules. The nucleus of the cell is normal, but that part of the protoplasm which borders the lumen of the tube

is projecting, clear and vesicular, and contains fat granules in suspension. The enlarged tubes are full of an exudation containing

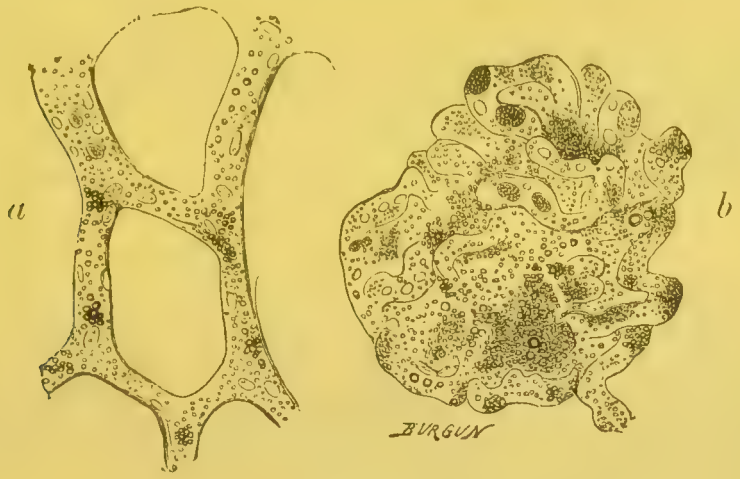

FIG. 186.

a, intertubular capillary vessels of the kidney filled with granular fibrin, from a case of infarctus of the kidney; *b*, the vascular tuft of the glomerulus, in which fat granules are seen on the surface of the vascular loops.

hyaline or colloid globes and fat. According to the data supplied by cases examined a certain time after the commencement of resolution of the infarctus, it seems evident that absorption is effected not only by means of the circulation of the blood and lymph, but that the urinary tubuli also take part in it. The living epithelial cells absorb a part of the molecular detritus resulting from mortification, appropriate it or throw it out, according to their peculiar mode of secretion, into the lumen of the tube, whence it is carried away with the urine. This mode of reabsorption is obviously very slow. Gradually the renal tissue, which was the seat of the infarctus, disintegrates; the granular tissue resulting from the destruction of the cells is eliminated; but the fibrous framework persists and shrinks, the tubuli diminishing in size as their contents are eliminated. Consecutive to this process newly-formed elements appear in the thickened connective tissue which surrounds the depressed infarctus, new blood vessels penetrate it, and slowly, both within the infarctus and around it, connective tissue is formed, which becomes organised and fibrous and constitutes an actual cicatrix. Old infarctuses on the surface of the kidney are thus replaced by a depressed fibrous cicatrix which caps the capsule, itself more or less thickened, and lines its external surface with a cellulo-adipose tissue in the place of the loss of substance of the kidney. In that part of the cortex which was

originally the seat of infarctus, vestiges of the structure of the kidney may be found in sections, that is to say atrophied glomeruli, reduced to a small nodule of fibrous tissue, and very small urinary tubuli lined with a layer of small cubical indifferent cells, which are nucleated and without differentiated protoplasm. Thickened connective tissue, containing small round or ovoid cells, is present around these tubuli and vestiges of glomeruli. Thus we see that arrest of the circulation in a limited region of the kidney causes mortification without putrefaction, and a degeneration of the cells followed by their reabsorption, also chronic inflammation with fibrous contraction of the tissue.

Nephritis.

Inflammation of the kidney may be divided into two distinct groups. In the first is that form of inflammation which is essentially characterised by the passage of albumen in the urine—albuminuria—but in which one variety differs markedly from another by the quantity of albumen excreted and by the pathological character of the morbid changes described under the name of catarrhal nephritis, diffused or parenchymatous nephritis, and interstitial nephritis. Amyloid and fatty degeneration will also be described with these forms of albuminous nephritis. The second group includes all those forms of nephritis which occur in consequence of purulent infection, contusions, traumatism, inflammation of the excretory ducts, such as is caused by calculi in the pelvis and ureters, compression of these ducts and retention of urine; these forms of nephritis, which show a great tendency to suppuration, constitute the surgical kidney.

History of albuminous nephritis.—In 1827 Richard Bright[1] discovered the disease which bears his name, and recognised the relation which exists between albuminuria and certain lesions of the kidney. He described three different anatomical forms, corresponding to varieties of chronic albuminous nephritis—the three final stages of Rayer—without pronouncing on the question if there were three distinct renal affections or three stages of the same disease. Christison,[2] Gregory, Elliotson, Copland, &c., brought

[1] R. Bright, *Report on Medical Cases*, London, 1827; 'Renal Disease accompanied with Secretion of Albuminous Urine' (*Guy's Hosp. Reports*, 1836; ibid. 1840).

[2] 'Observations on a Variety of Dropsy which depends on Diseased Kidney,'

forward cases in support of Bright's discovery. Rayer studied the pathological anatomy of albuminous nephritis more profoundly, and in his work 'Maladies du Rein'[1] he described six forms of nephritis, of which the two first are temporary albuminous nephritis and the four latter permanent albuminous nephritis. There were, according to Rayer, different stages of the same morbid evolution. Martin Solon[2] reduced the number of these forms of the same disease to four. But before the lesions of the kidney and the urinary deposits were begun to be studied under the microscope, A. Becquerel[3] had remarked hypertrophy of the Malpighian bodies; Gluge, Henle, Vogel, Canstatt gave the rudiments of microscopic observation. William Gairdner,[4] George Johnson[5] made use of, in studying the pathology of the kidney, Bowman's discoveries on the delicate structure of the organ. Virchow,[6] Reinhardt,[7] and Frerichs[8] occupied themselves long with these questions. The treatise of Frerichs was for a long time the best on the subject. He considered there were three stages in albuminous nephritis: 1, the stage of hyperæmia and commencing exudation; 2, the stage of exudation and metamorphosis of the exudations; 3, the stage of retrogression and atrophy. According to these observers, the changes in the renal epithelium are of the first importance, and the lesions of the connective tissue correspond to the final stage in the evolution of the disease. The treatise of Rosenstein[9] carried on these earlier researches; but with the researches of Beer, Traube, Samuel Wilks, Handfield, Jones and Todd, and those more recent of Lecorché,[10] Kelsch,[11]

Edinb. Med. and Surg. Journ., vol. xxxii.; ibid. *Granular Degeneration of the Kidney*, Edinburgh, 1839.

[1] *Traité des Maladies du Rein.* J. B. Baillière, Paris, 1839–41, 3 vols. in 8vo., and atlas in folio, 1837.

[2] *De l'Albuminurie ou Hydropsie causée par une Maladie des Reins.* Paris, 1838.

[3] *Séméiotique des Urines, suivie d'un Traité de la Maladie de Bright.* Paris, 1841.

[4] *Contributions on the Pathology of the Kidney.* Edinburgh, 1848.

[5] *Medico-Chir. Transactions*, vol. xxix. p. 1, vol. xxx. p. 165; and Todd's *Cyclopædia*, article 'Kidney,' by Johnson.

[6] *Virchow*, quoted by Nieman, *De Inflammatione Renum Parenchymatosa*, Berlin, 1848; and Virchow's *Archiv*, vol. iv. 1852, pp. 261–325.

[7] Reinhardt, *Deutsche Klinik*, 1849, No. 5; *Annalen der Charité*, Berlin, 1850.

[8] *Die Bright'sche Nierenkrankheit und deren Behandlung.* Brunswick, 1851.

[9] *Die Pathologie und Therapie der Nierenkrankheiten*, 1863.

[10] *Traité des Maladies des Reins et des Altérations Pathologiques de l'Urine*, 1875.

[11] 'Revue Critique' in the *Archives de Phys. Norm. et Path.*, 1874.

Lancereaux,[1] and Charcot,[2] albuminous nephritis enters on a new phase; the lesions of the connective tissue take a larger importance, and two distinct types of nephritis, both from the pathological and clinical point of view, are established, namely, parenchymatous or epithelial nephritis and interstitial nephritis.

From the clinical point of view parenchymatous nephritis is characterised by œdema, anasarca, scanty urine, which is cloudy, deeply coloured, very rich in albumen and contains an abundant deposit of hyaline casts, and by its relatively rapid evolution, terminating often in pneumonia, gangrene or erysipelas of the œdematous parts; by the marked influence of damp cold on its development, and by the youth of the subjects attacked.

Interstitial nephritis is, on the contrary, characterised by the fact that œdema is absent or hardly perceptible; by an abundant urine, which is clear, pale, slightly albuminous, and which contains only a few casts; by its slow evolution, and by its peculiar complications, such as hypertrophy of the left side of the heart, albuminuric retinitis, and different kinds of hæmorrhage, and by uræmia, which is its usual termination; it is also characterised by the influence which gout, lead poisoning, alcoholism and atheroma have on its development, and by the advanced age of its subjects.

From the pathological point of view, typical parenchymatous nephritis is characterised by a large smooth kidney, the cortical substance of which is thickened, grey, or whitish, and by lesions bearing chiefly on the epithelium. This is the large white kidney.

Interstitial nephritis is, on the contrary, characterised by a small kidney, with a capsule closely adherent and a congested and granular surface. In sections, the atrophy is seen to chiefly affect the cortical substance. The lesions are seated chiefly in the connective tissue. This is the small red or granular kidney.

Is there in reality such a complete anatomical and clinical dichotomy in albuminous nephritis? We do not hesitate to reply in the negative. It would be more exact to say that these two varieties of nephritis are almost always associated, though in different degrees, with predominance in certain cases of lesions of the epithelial parenchyma, and in others of the connective tissue. This results distinctly from observations we have carried on for many years; such also is the result of the researches of

[1] 'Maladie de Bright,' *Dict. Encycl.*, 1881; article 'Reins,' *Dict. Encycl.*, 1875.

[2] *Leçons sur les Maladies du Foie et des Reins*, 1877.

Weigert[1] and Ernst Wagner.[2] Many authors who had warmly supported the division of Bright's disease into parenchymatous and interstitial nephritis, Kelsch in particular, have reversed their first opinion. In most cases of parenchymatous nephritis changes in the glomeruli, thickening of the proper membrane of the tubuli and the connective tissue surrounding them, occur. On the other hand, in all cases of interstitial nephritis accompanied with albuminuria there are lesions of the renal epithelium, the cloudy and vesicular condition, fatty degeneration, intratubular exudations, and hyaline casts. Pathology demonstrates this almost constant mixture of lesions affecting simultaneously the epithelium and the connective tissue; it cannot be otherwise clinically. Experimental pathology furnishes us with examples of nephritis which affects at the same time both the epithelial parenchyma and the connective tissue. In acute and subacute cantharidin nephritis there are, besides the epithelial lesions, exudations and hyaline casts, migration of the lymph cells, and changes in the connective tissue. In experimental poisoning by lead, induced in guinea pigs by mixing carbonate of lead with their food, acute interstitial nephritis is produced, preceded by parenchymatous nephritis (Olivier, Charcot and Gombault[3]). The lead first causes actual infarctuses in the loops of Henle, by depositing carbonate of lead in the epithelial cells, which leads to their proliferation and desquamation. Subsequently, all the lesions of granular kidney are observed. We have here interstitial or cirrhotic nephritis of glandular or epithelial origin. In certain exceptional cases changes, localised exclusively in the parenchyma or connective tissue, may be produced experimentally. For example, in phosphorus poisoning, lesions exclusively epithelial—cloudy swelling of the cells, large quantities of fat granules in the protoplasm, exudation into the tubuli, fat and hyaline casts—are observed without any interstitial lesions; while, on the other hand, in the nephritis produced by Charcot and Gombault[4] by ligature of the ureters the lesions are

[1] 'Die Bright'sche Nierenerkrankung vom pathologisch-anatomischen Standpunkte,' *Klinische Vorträge*, pp. 162–63; *Innere Medicin*, No. 55.

[2] *Deutsche Archiv für klinische Medicin*, vol. xxv.

[3] *Arch. de Phys.*, 1881, p. 127.

[4] Straus and Germont ('Des Lésions Histologiques du Rein consécutives à la Ligature de l'Uretère,' *Arch. de Phys.*, 1882, vol. ix. p. 385) have shown that if the precautions of antiseptic surgery be scrupulously observed in ligature of the ureter the results obtained by Charcot and Gombault are modified. But whatever may have been the method employed by these observers, and however much septic bacteria may seem to have played a part, the result of their experiments, that is to say, the production of interstitial nephritis, remains the same.

almost exclusively interstitial. The same conditions are found in man, particularly in old men the subjects of general atheroma, in whom the kidneys are affected with chronic interstitial nephritis without albuminuria. But in a general manner it may be stated that in most cases of nephritis the parenchyma and the connective tissue are simultaneously affected, though in different degrees.

From what precedes it is understood how much acute and chronic nephritis varies. These variations are in relation not only to the numerous causes of the disease, but also with the constitution of the patient, his hygienic condition, pathological antecedents, and concomitant diseases. It is necessary first of all to divide nephritis into its temporary acute, or permanent subacute, or chronic forms. The first group, generally related to febrile or infectious diseases, is not accompanied with dropsy, and constitutes, so to speak, an epi-phenomenon which often passes unobserved, for it is not always of marked gravity. The second group is of extreme gravity and pathological importance. It constitutes Bright's disease, and is marked by a set of symptoms, general or localised œdema, uræmia, &c. In temporary nephritis, as well as in subacute chronic parenchymatous nephritis, all the elements of the kidney are affected, the epithelial parenchyma, and in a less degree the connective tissue also. We call this form *diffuse nephritis*. In contradistinction, we apply the term *systematic nephrites* to those forms which affect especially the connective tissue surrounding the renal lobules (saturnine nephritis), and to those forms also which, consecutive to endo-arteritis and peri-arteritis, cause thickening of the connective tissue, seated chiefly around the blood vessels (interstitial or vascular cirrhosis).

Diffuse Nephrites.

Acute, diffuse or temporary nephritis.—This form of nephritis was originally called catarrhal, in consequence of the opinion that it consisted chiefly in a slight inflammation of the epithelial lining of the straight and collecting tubes, and in catarrh of the excretory urinary ducts. But this view is erroneous, as both Brault and ourselves have proved by research. Inflammation is, on the contrary, localised in the labyrinth, the secreting part of the cortical substance, the glomeruli, and the convoluted tubes. This form of nephritis is seen in the course of variola, measles, cholera, erysipelas, typhoid fever, recurrent fever, malaria, yellow fever, septicæmia, puerperal fever, scarlatina, pneumonia, &c. It

is due to a change in the blood, and probably to elimination of the microbes peculiar to these virulent diseases. But each of these diseases gives origin to a specially characteristic form of nephritis, and to be complete a description must be given of each of these varieties. **In cholera,** the renal symptoms follow each other in the following order: anuria; excretion of a small quantity of albuminous urine which contains numbers of hyaline casts and epithelial moulds; then an abundant excretion of urine without albumen. The whole evolution only takes from twenty-four to forty-eight hours. **In typhoid fever,** the affection lasts longer, and the cells undergo granulo-fatty degeneration. In diphtheria and scarlatina the nephritis is still more acute. **In scarlatina,** the kidney lesion, by its acuteness, its long duration, by the large amount of albumen passed, and by the anasarca which often accompanies it, establishes the transition between temporary and permanent nephritis. In scarlatina, the albuminuria, which is generally temporary, may exceptionally become chronic.

Notwithstanding the differences which the kidney shows in the various diseases just enumerated, we will give a general description of acute temporary nephritis, and will take the nephritis of variola as the type.

In variola, when a patient dies in the first week of the disease, the kidneys are found to be large, and their capsules are easily

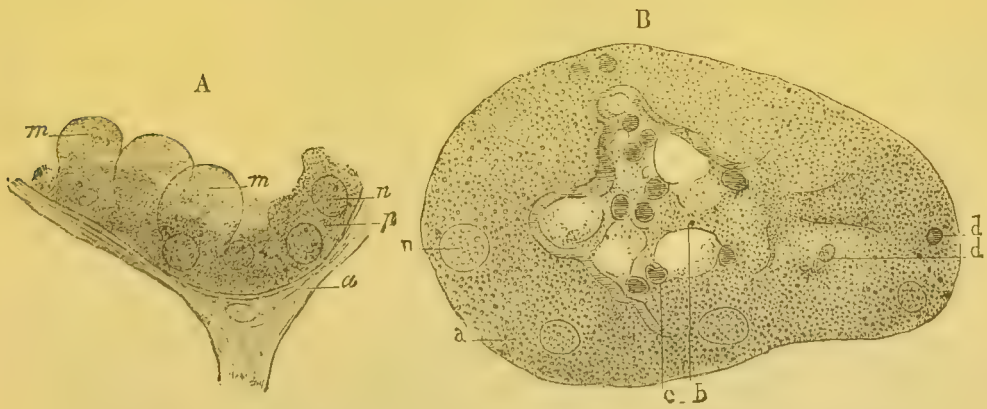

FIG. 187.—LESIONS OF THE EPITHELIAL CELLS IN ACUTE DIFFUSE NEPHRITIS.

A, cantharidin nephritis in a dog; *m*, *m*, clear globes of exudation on the free surface of the cells; *n*, nuclei; *p*, protoplasm of the cells.
B, section of a tubule in diphtheritic nephritis; the protoplasm, *a*, of the cells is fused together; the lumen of the tubule, *b*, is filled by a reticulated exudation with leucocytes, *c*; *d*, red blood corpuscles; *n*, nuclei of the cells. Preparation made after the action of osmic acid.

removed. The surface of the organ, as well as the surface of a section, is found to be congested, and the kidney tense and indu-

rated. The cortical substance is sensibly larger than normally, and is generally highly congested and of a reddish yellow colour; the medullary substance is of a deeper red. In preparations hardened by osmic acid and examined under the microscope the cells of the convoluted tubes are seen to be in a state of cloudy swelling; they sometimes contain several nuclei and proteic granules, and at their free extremity clear globes are often seen projecting into the tubes; these become detached and fall into the tube in the form of mucous or colloid colourless drops; the cells then appear eroded along their free edge and are atrophied and flattened. The globes form masses in the tubes of Henle, and then constitute hyaline casts. In some of the convoluted tubes, the cells no longer show lines of separation, and the epithelial lining is composed of a granular protoplasmic mass, disseminated with nuclei. Lesions are at the same time present in the glomerulus, the vessels of which are filled with blood, and there is sometimes an effusion of blood and an exudation containing white corpuscles into Bowman's capsule. Thus in the nephritis

FIG. 188.—GRANULAR AND TUMEFIED CELLS OF THE CONVOLUTED TUBES, FROM A CASE OF ALBUMINURIA IN TYPHOID FEVER.

b, *d*, cells containing three nuclei; *c*, cell containing two nuclei; *a*, cell with one nucleus; *t*, wall of the tube; *v*, vessel. Magnified 250 diameters. Section made after the action of osmic acid.

of variola, examined during the first days of the eruption, the lesions are found to be of the tubuli and glomeruli, but there is no fatty degeneration; this is only observed if the nephritis last longer. In **typhoid fever**, where the evolution is slower, this condition will be found if the autopsy be made a month or six weeks after the commencement of the disease, whether albuminuria has persisted, which is rare, or has disappeared. In certain groups of convoluted tubes, the epithelial cells will be found to contain fine fat granules. To the naked eye the renal lesion is characterised by appearances related to the long duration

of the enteric disease and the exhaustion of the patient. The capsule peels off easily, and the surface of the kidney is smooth and pale. The organ is large, soft, and flaccid. On dividing it, the cortical substance is seen to be thickened and grey, or whitish with yellowish white and rather opaque striæ. The opacity and grey or yellowish grey discolouration of the cortical substance are related to the fatty degeneration of the cells of a more or less considerable number of tubuli. As regards the other lesions recognised under the microscope, such as the granular and vesicular condition of the cells of the convoluted tubes, the exudation which here and there fills their cavities, the hyaline and epithelial casts, the exudation found in the glomeruli, these are the same as in nephritis caused by variola. Bouchard con-

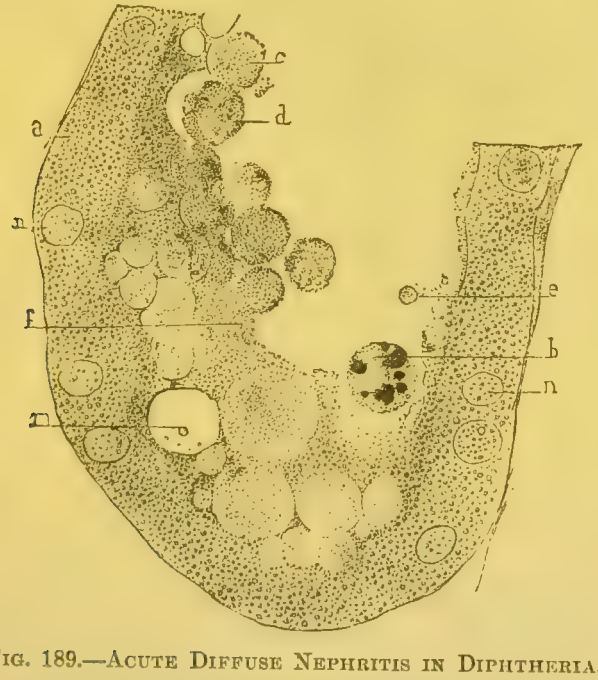

FIG. 189.—ACUTE DIFFUSE NEPHRITIS IN DIPHTHERIA.

The dilated lumen of the tube is filled by numerous granular and dark globes, and by leucocytes. All separation between the cells has disappeared. *a*, protoplasm; *b*, leucocytes containing fat granules; *c*, *d*, *f*, granular globes, varying in size; *e*, red blood corpuscle; *m*, cavity from which the contents have escaped. Section made after the action of osmic acid.

stantly found rod-shaped bacteria in the urine of typhoid patients whilst the albuminuria lasted.[1]

Diphtheritic nephritis.—In diphtheria the renal lesions are more marked and constant than in the preceding diseases, and the albuminuria is generally more acute. The naked-eye appear-

[1] *Transactions of the International Medical Congress at London*, vol. i. p. 316.

ances of the kidney vary. Brault [1] in five autopsies found more or less marked congestion in two; in the others there was nothing remarkable. Fürbringer,[2] as well as E. Wagner, found the kidney either pale or normal in appearance. Sometimes the cortical substance is greyish or opaque. It is really curious to see frequently such a large amount of albumen excreted by kidneys which do not appear at all diseased to the naked eye. But histological examination reveals marked and characteristic lesions. These are principally seated in the glomeruli and the convoluted tubes. Between the vascular plexus and the capsule of the glomerulus a certain number of lymph cells are seen, and an exudation formed of colloid

FIG. 190.—GLOMERULITIS FROM A CASE OF ALBUMINURIA CAUSED BY BRONCHO-PNEUMONIA.

p, Bowman's capsule; *a*, *a*, vascular loops of the glomerulus; *g*, *m*, exudation composed of irregular blocks and of a granular mass occupying the entire space between the vascular plexus and the capsule; *v*, *v*, capillaries outside the capsule. Magnified 300 diameters. Section made after the action of osmic acid.

globes or a reticulum (*m*, fig. 190), and sometimes red blood corpuscles extravasated in considerable numbers. The epithelium of Bowman's capsule becomes tumefied, proliferates, and desquamates. Most of the tubuli are dilated. The cells of the

[1] Note on the 'Lesions of the Kidney in Diphtheritic Albuminuria' in Robin's *Journ. de l'Anat.*, 1881.

[2] 'Zur Klinik und path. Anat. der diphtheritischen Nephritis,' Virchow's *Archiv*, vol. lxxxi. p. 385, 1883.

convoluted tubes are opaque and granular, and they are sometimes so much hypertrophied as to obliterate the lumen. Clear globes are found at their free edges, which become detached and fall into the lumen of the tube. The free edges of the atrophied cells border a passage which is irregularly star-shaped, and which is filled by a grey, homogeneous exudation containing clear globes (fig. 189). In the lumen of some of the convoluted tubes a reticulum is formed of trabeculæ which are homogeneous, varying in thickness, and of colloid consistency, and which separate the colloid drops and the red and white blood corpuscles. The epithelial cells atrophy, flatten against the wall of the tube, but still remain *in situ*; it is only the superficial part of the cell which is eliminated, so that the expression *desquamative nephritis*, used by George Johnson and others after him, is, as a rule, inexact. The cells of the straight tubes generally proliferate. There is also diapedesis of white blood corpuscles, which insinuate themselves between the cells, becoming wedge-shaped, and finally lying free in the lumen of the cell. In the deposit of the urine numerous hyaline casts and refractive colloid casts are found, as well as red blood corpuscles.

Such is the state of the kidney in diphtheria. If the illness be prolonged, and if the patient die at the end of ten, fifteen, or twenty days, partial fatty degeneration of the epithelial cells may occasionally be found, and even a slight lesion of the connective tissue, causing slight interstitial nephritis.

Diphtheritic nephritis has given rise, like the other forms of nephritis in infectious diseases, to a discussion whether the microbes causing these diseases pass through the kidney and manifest their presence in the cells and urine. Ortel states that he has almost always found microbes in the Malpighian corpuscles and in the tubuli. Eberth has met with them in the centre of the cells. Gaucher and Litten have seen them in the blood and urine; Hiller and Fürbringer have, on the contrary, found nothing characteristic. The question evidently requires further study.

Scarlatinal nephritis.—The nephritis which is observed in scarlet fever, at the end of the second or in the third week, or even a month after the commencement of the disease, is the most acute of all forms of temporary albuminous nephritis. It sometimes becomes chronic, and may last months, a year, or even longer. It frequently, however, terminates in recovery. It is distinguished from other forms of nephritis in fever in that it is often accom-

panied by more or less general œdema, uræmia, and by fibrinous or purulent inflammation of the serous membranes, so that patients sometimes succumb to this combination of serious accidents. It varies, however, according to the epidemic. Sometimes scarlatinal nephritis passes into the state of permanent, incurable nephritis. In this form very varied renal conditions will be found, and all the intermediate forms between temporary and permanent nephritis. Thus in studying the kidney in scarlatina we shall have occasion to notice most of the lesions of subacute, diffuse, or parenchymatous nephritis.

The microscopical examination of the kidneys in the acute period of scarlatinal nephritis has given rise to contradictory results. In 1867 E. Wagner described ('Archiv der Heilkunde,' vol. viii. p. 262) the kidney in scarlatina as hypertrophied, whitish, or marked with white patches, and he found an extravasation of round cells into the glomeruli and into the connective tissue around the glomeruli as well as between the tubuli. These round cells resembled white blood corpuscles more or less. He gave the name of *acute lymphomatous nephritis* to this lesion. In three such cases observed by him the patients succumbed rapidly, two among them with uræmic symptoms. Similar cases were reported by J. Coats, Klebs, Kelsch and Charcot. In these cases the connective tissue around the glomeruli and tubuli was in places infiltrated with round cells. The glomeruli seemed to be entirely covered and filled with round cells, so that they were changed into a mass of embryonic tissue. These lesions are always extremely grave; they cause arrest of the excretion of urine, with all its consequences, and lead to accumulation in the blood of the excrementitious substances which normally pass away in the urine; hence the symptoms of uræmia. Kelsch and Charcot look upon the kidney in scarlatina as the type of acute interstitial nephritis. It is necessary to discover the exact seat of the round cells in the glomeruli, to ascertain if they are found in the empty space which is present between the vessels and the capsule, or if they adhere to the surface of the vascular loops, or again if they are derived from proliferation of the epithelial cells of the capsule. On carefully examining the lesions of the glomeruli in scarlatina, migratory cells will be rarely found between the vascular loops in what histologists look upon as the connective tissue of the glomerulus, but they are generally found between the vascular plexus and the capsule. We think that in the cases quoted above there was diapedesis of the white blood corpuscles which

accumulated in the cavity of the glomerulus, between the plexus and the capsule, at the same time that the endothelial cells of the

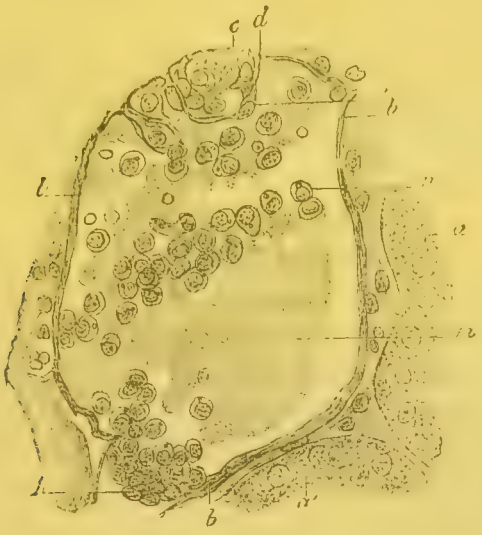

FIG. 191.—SECTION OF THE CAVITY OF A GLOMERULUS FILLED BY AN ABUNDANT CELLULAR EFFUSION (DIAPEDESIS IN ACUTE NEPHRITIS).

c, *d*, fragment of the vascular plexus, the rest of which has been removed in section; *b*, Bowman's capsule; *n*, lymph cells immersed in a granular exudation, *m*; *h*, cells accumulated in the lumen of the tube continuous with the capsule. Section made after hardening in osmic acid. Magnified 250 diameters.

capsule became tumefied and desquamated. The flat cells, which line the free surface of the vascular loops, also probably took part in the inflammatory process. Glomerulitis constitutes, however, only part of the renal changes observed in scarlatinal nephritis. Many cases published in recent years have shown this. Litten has reported a case in which the connective tissue was normal, and the epithelium of the tubuli were alone affected with granulo-fatty degeneration. E. Wagner[1] also connects most of the facts of scarlatinal nephritis with acute diffuse nephritis and the large white kidney, in which the lesions are chiefly epithelial. According to the majority of observers,[2] and according to our own researches, the same lesions of the cells, and the same contents of the tubuli, are seen in the renal parenchyma which we have already studied in temporary nephritis, and which need not be repeated here. Depending on certain published cases, we might be induced to distinguish two varieties in scarlatinal nephritis: one

[1] 'Beiträge zur Kenntniss des acuten Morbus Brightii,' p. 544 (*Deutsche Archiv f. klinische Medicin*, vol. XXV.

[2] This question is ably discussed in the article 'Rein,' by M. Labadie-Lagrave, in the *Dict. Pratique des Sc. Méd.*, edited by Jaccoud.

characterised by glomerulitis and acute interstitial nephritis, and the other by diffuse or parenchymatous nephritis. But we avoid this distinction for the simple reason that scarlatinal nephritis is always characterised by lesions chiefly affecting the epithelium and the contents of the tubuli. When the disease is very acute, there is marked inflammation of the glomerulus, diapedesis of cells into the cavity of the glomerulus and into the connective tissue surrounding it. This does not surprise us, for we observed the same facts in acute and subacute cantharidin poisoning, and in temporary nephritis we have found a certain degree of glomerulitis, less marked, it is true, than in scarlatinal nephritis. This combination of inflammation of the glomeruli with lesions of the epithelium in diffuse nephritis will be seen more clearly in the description of chronic nephritis.

To recapitulate: scarlatinal nephritis is the type of acute diffuse nephritis. The whole kidney is altered, the glomeruli are inflamed, sometimes very acutely, but the epithelial parenchyma is also inflamed. In every case the epithelium of the convoluted tubes is cloudy, granular, and tumefied; the lumen of the tubes contains exudation, casts, &c. The epithelial cells are often in a state of fatty degeneration. This is temporary nephritis, similar to that already described but more acute; it may pass into the chronic condition, and take then all the characters of parenchymatous nephritis (large white kidney).

Permanent albuminous nephritis; diffuse nephritis, subacute and chronic; parenchymatous nephritis.—There are many varieties. We will first describe permanent subacute nephritis, which has lasted several weeks or two or three months; it results from various causes, cold and alcoholism among others. In this subacute form the kidney is congested; the stellate veins under the capsule are congested and plainly seen; the organ is normal in size or slightly hypertrophied; on section it does not show that pale colour characteristic of white kidney; sometimes, however, the surface of the kidney is marked with white, or the cortical substance is of a yellow or reddish yellow colour. But in most cases, the existence of lesions of the kidney cannot be affirmed till it has been examined under the microscope. The following will be the result of this examination. The glomeruli are often altered in one or more of their constituent parts. The flat epithelium lining the internal surface of the capsule generally shows marked proliferation, and a layer of polyhedral or spherical cells, which are larger than normally, projects; the cells become detached or remain adherent to

the capsule by one end, or they are arranged in superimposed layers. They are then irregular or polyhedral from reciprocal pressure (fig. 193). Sometimes these cells form a mass in the

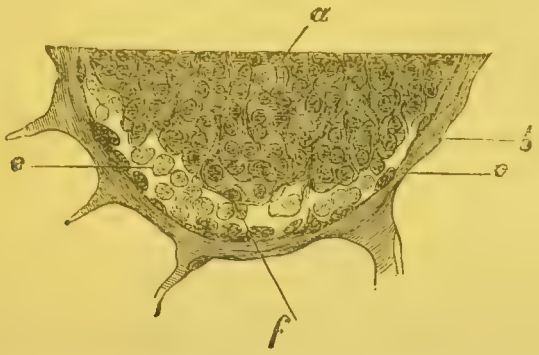

FIG. 192.—SEGMENT OF AN INFLAMED GLOMERULUS.

b, *c*, Bowman's capsule with its parietal cells more or less tumefied; *e*, round cells free in the cavity of the glomerulus; *f*, cells which adhere to the vascular loops of the glomerulus; *a*, vascular plexus. Magnified 200 diameters.

capsule, at the spot where the convoluted tube commences. Very often multiplication of the cells of the very delicate layer of connective tissue, which normally lines the free surface of the vascular

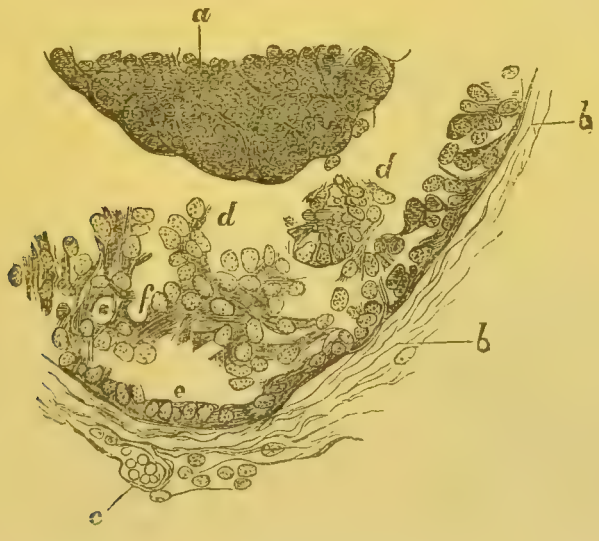

FIG. 193.—PART OF A GLOMERULUS IN CHRONIC INFLAMMATION.

a, segment of the vascular tuft; *b*, *b*, Bowman's capsule, the wall of which has become fibrous; *c*, vessel outside the capsule and filled with red blood corpuscles; *e*, modified epithelial cells of the capsule which have become polyhedral; *d*, *d*, newly formed cells accumulated in the cavity of the glomerulus. Magnified 200 diameters.

loops of the glomerulus, is seen at the same time. The nuclei present in this layer proliferate, project, become surrounded by a granular protoplasm, and give origin to as many new cells. These

form a marked projection in the surface of the loops (fig. 194). Seen in profile, they have the form of a crescent, or of a cap at the end of the vascular loops, and they become detached at a certain moment. They have been well drawn by Langhans. Their variable forms have given them various names, and they are called

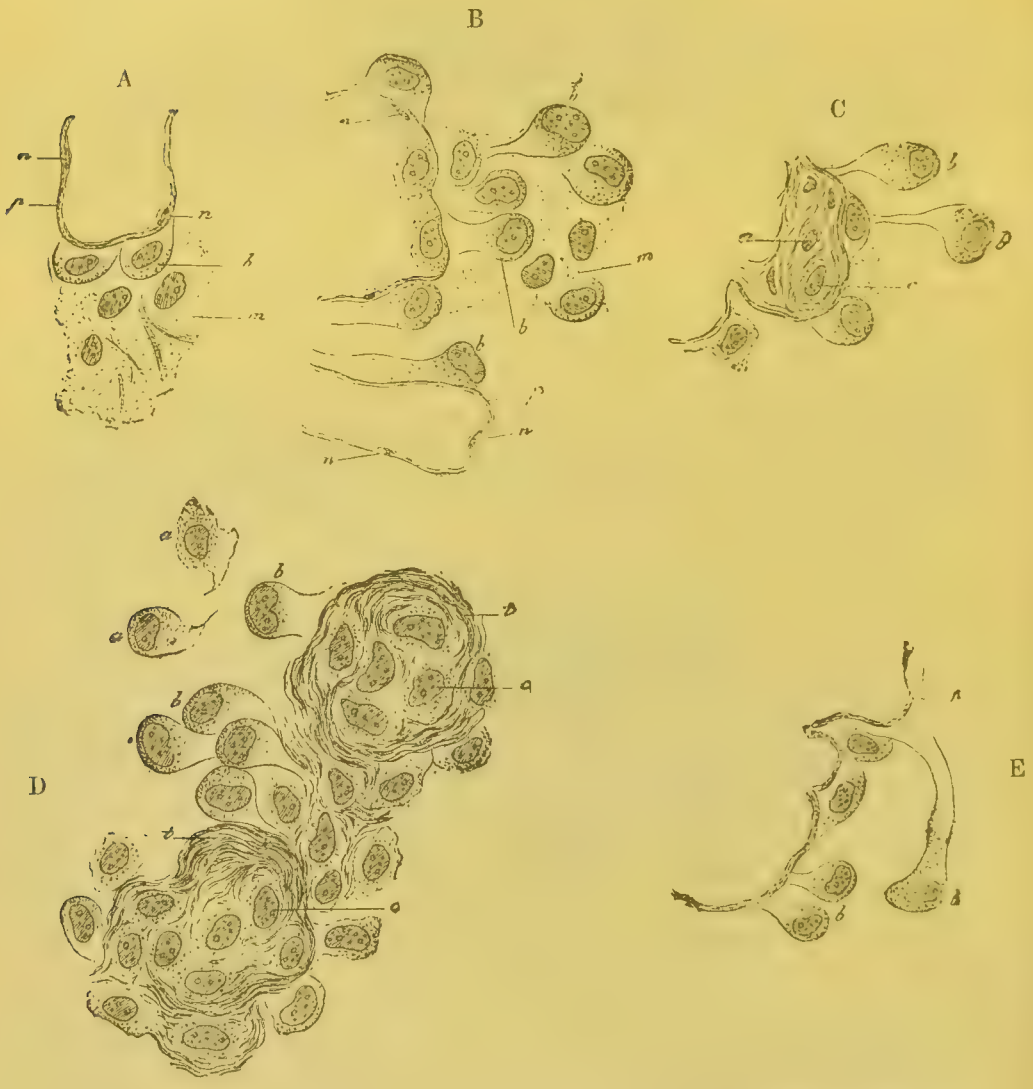

FIG. 194.—VARIOUS FORMS OF INFLAMMATION OF THE CELLULAR LINING OF THE VASCULAR LOOPS OF THE GLOMERULUS.

A. *p*, wall of a capillary of a vascular loop; *n*, *n*, its nuclei; *b*, cells lining the vessel; *m*, protoplasmic plates detached and containing nuclei.
B. *n*, *n*, nuclei of the vascular walls; *b*, *b*, sessile cells in the form of a club, adherent by one of their extremities to the vascular wall.
C. *n*, nucleus of a vascular loop; *b*, *b*, club-shaped cells.
D. *a*, *a*, free cells with pointed extremities. The two irregular zones *t*, *t*, formed by bundles of connective tissue, represent two vascular loops cut across and obliterated by the proliferation of peripheral cells and by the formation of fibres of connective tissue.
E. Cells adherent to the wall *p* of the vascular loops. The cells *b*, *b* are implanted by a very long pedicle in the vascular wall.

club-shaped, frondlike, pendulum cells. After adhering for a certain time to the surface of the capillaries of the glomerulus, they fall into the cavity at the same time that they are replaced by other cells; whence results an accumulation in the cavity of the glomerulus of flat, polyhedral or spherical, irregularly shaped cells, which are often adherent to the vascular plexus. A similar proliferation, though less acute, takes place between the vessels composing the glomerulus, at the same time that the walls of these vessels thicken and their lumen contracts (D, fig. 194). These lesions are very important to know, and their consequences are most serious. If most of the glomeruli are inflamed in this manner, the conditions under which urinary secretion takes place are completely changed. As the infiltration of the water of the liquor sanguinis takes place chiefly in the glomerulus, the quantity of urine excreted diminishes in a marked manner if the vessels be only slightly permeable, whence uræmic complications occur. In consequence of inflammation of Bowman's capsule, bundles of connective tissue are sometimes formed on the internal surface of this membrane. Thus, in an observation of Brault's, there were

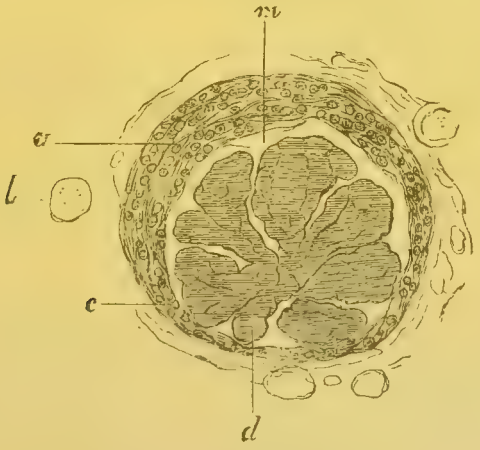

FIG. 195.—VERY ACUTE GLOMERULITIS, CHIEFLY AFFECTING THE CAPSULE.

a, fibrous tissue and cells formed on the internal surface of the capsule; *m*, cavity of the glomerulus; *d*, vascular tuft; *b*, section of a tubule. Magnified 80 diameters.

found adhering to the internal surface of Bowman's capsule a large number of round or irregular cells which had large nuclei, and were separated by plates or fibres of connective tissue; whence a retiform tissue resulted, the connective-tissue trabeculæ of which were united to Bowman's capsule, and the meshes filled with free or agglomerated cells, in contact with one another or

adherent to the fibrous fasciculi (figs. 195, 196). This is the most marked form of inflammation of the capsule of the glomerulus.

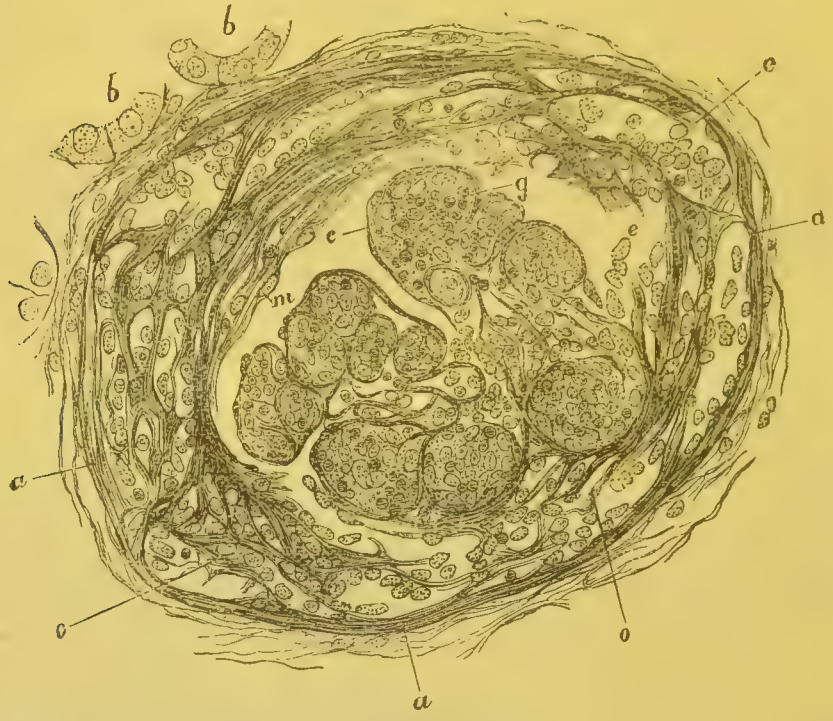

FIG. 196.—THIS FIGURE GIVES THE DETAILS OF THAT REPRESENTED ABOVE, MAGNIFIED UNDER A HIGHER POWER.

a, *a*, Bowman's capsule, inside which is a new tissue showing fibres of connective tissue, *o*, *o*, and forming a network in which round and polyhedral cells, *e*, are found; *m*, cavity of the glomerulus; *g*, vascular loops. Magnified 250 diameters.

The most advanced degree of subacute or chronic inflammation of the vascular tuft is seen in its fibrous atrophy, in which it is changed into a nodule of fibrous tissue, impermeable to blood. These lesions of the glomerulus, even when they are acute, almost always affect the renal connective tissue at the edge of the capsule and around the external coat of the blood vessels, vein and artery, which are found at the hilum of the vascular tuft. The proper wall of the capsule is also frequently thickened in a marked degree. These are the lesions of glomerulitis, an important factor in subacute or chronic diffuse nephritis, but which also in a lesser degree is found in diphtheritic and scarlatinal nephritis.

The tubuli show at the same time the lesions which we have already frequently described, exudation, casts, &c., and which need not be redescribed. One interesting cellular change consists in

the vesicular condition which one of us has described.[1] Vacuoles are seen in the part of the cell turned towards the lumen of the

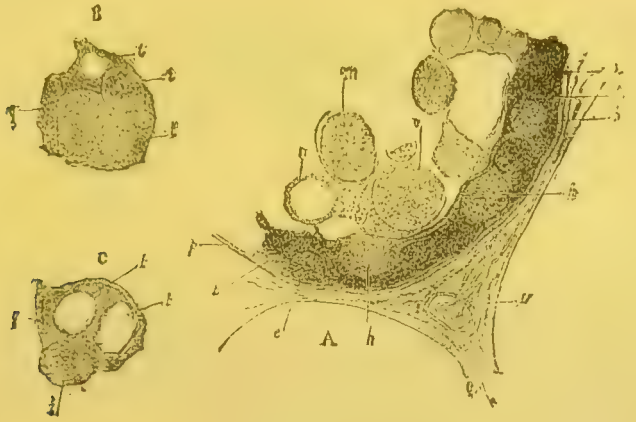

FIG. 197.—SEGMENT OF A CONVOLUTED TUBE IN THE CORTICAL SUBSTANCE IN SUBACUTE DIFFUSE NEPHRITIS.

h, h, vacuoles hollowed in the protoplasm of the cells; *m*, granular colloid globe, and *o*, clear globe contained in the lumen of the tubule; *v*, capillary.
B, C, two isolated vesicular cells; *t, t*, vacuoles hollowed in the protoplasm of the cells; *n*, nucleus. Magnified 400 diameters.

tube. They project outwards (*h*, *h*, fig. 197), and their protoplasm forms a border around the edge of the cell, while their oval nuclei are depressed towards the basement membrane of the tube. The greatly enlarged lumen of the tubes contains clear and granular globes stained by osmic acid. Isolated cells (B, fig. 197) contain one or more transparent vesicles, *t*, *t*, surrounded by a protoplasmic layer containing one nucleus. Fig. 198 represents a transverse section of an entire convoluted tube which has undergone this morbid change. In certain convoluted tubes, the various exudations secreted by the cells, the red blood corpuscles, and probably also substances derived from the blood, form a colloid mass, festooned at its edges and moulded on the epithelial cells and balls of mucus. This colloid substance penetrates into the straight tubes of the loops of Henle, where it is drawn out into a thread and constitutes hyaline casts. The epithelial cells of the straight tubes have hardly changed; within them, however, exudations are found which constitute the hyaline casts of urinary deposits. On examining a urinary deposit after first submitting it to the action of osmic acid, the casts are seen stained brown; they are sometimes of a spiral shape, with an unequal diameter

[1] 'Nouvelles Observations sur l'Etat des Cellules du Rein dans l'Albuminurie' (*Journ. de l'Anat.*, 1879, pl. xxix. et xxx.)

(p. 467), and they sometimes have vitreous fissures, or transverse slits. If the congestion has been acute, and there has been

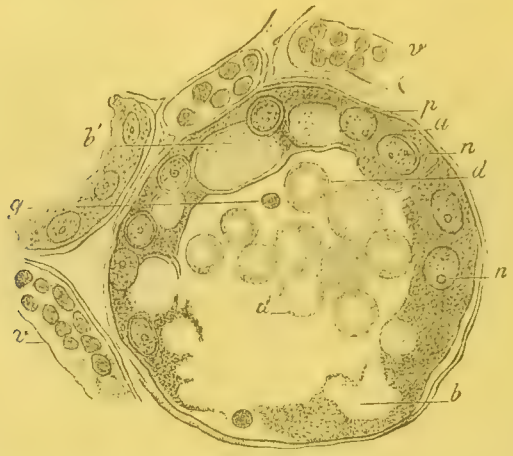

FIG. 198.—SECTION OF A CONVOLUTED TUBE IN THE CORTICAL SUBSTANCE FROM THE SAME CASE AS THE PRECEDING.

a, protoplasm of the cells; *n*, their nuclei; *p*, hyaline wall of the tube. In the protoplasm of a certain number of the cells, near the lumen of the tube, vacuoles, *b*, *b*, are seen in which fluid is secreted; *d*, balls of mucus in the interior of the tube; *g*, red blood corpuscles; *p*, proper wall of the tube; *v*, *v*, blood vessels outside the tube. Section cut after the action of osmic acid. Magnified 400 diameters.

hæmorrhage into the interior of the tubuli, fibrinous casts are found characterised by their fibrillated appearance; they swell on adding acetic acid, and they contain red and white blood corpuscles. Casts are also often found composed of a granular mass containing fat globules.

It may be asked, what is the relation between fatty degeneration of the cells and the changes in the glomeruli just described? It is highly probable that fatty degeneration is consecutive to changes in the circulation, caused by the anæmia resulting from chronic inflammation, and by narrowing of the lumen of the afferent vessels of the loops of the glomeruli. It, however, frequently happens that the epithelial cells of the tubuli show no fatty degeneration, though the glomeruli are acutely inflamed. In the subacute form of diffuse nephritis just described, fatty degeneration of the epithelial cells of the kidney is generally absent; it begins to be seen when the disease has lasted a long time, and then it is slight and generally partial. The best way of deciding the presence of fatty degeneration is to make sections of the kidney in the fresh state, and to treat them with formic or osmic acid. On examining them under a power of 40 diameters, a considerable number of the tubuli will be seen to be of a dark

colour and opaque. Under a higher power, the opacity will be found to be due to a quantity of small fat granules in the epithelial cells of the tubuli.

The various lesions already described in the acute form may become combined in various ways, and thus form a great number of varieties of nephritis, on which we need not insist.

Chronic forms of diffuse nephritis. Parenchymatous nephritis. The large white kidney.—The chronic form of permanent nephritis corresponds generally to what we call the large white kidney. This lesion is observed as the result of syphilis, alcoholism, cold, and sometimes also pulmonary tuberculosis. It is found also in women who have died of eclampsia. The kidney is larger than normally, but this increase in size varies greatly; it may be hardly enlarged, while at other times it may be twice its natural size and weight. In colour it is white, sometimes a dead white, but more frequently a yellow white. It is of a soft and pasty consistency. On section, the yellowish white colour is seen to be limited to the cortical substance, and contrasts with the red colour of the medulla; the increased size of the organ is also due to thickening of the cortical substance. Phlebitis of the renal vein is sometimes found in this form of Bright's disease, an accident which has been noted three times by Rayer and many times by ourselves.

Under the microscope, the convoluted tubes show the cellular lesions already described; vesicular condition of the cells, globes,

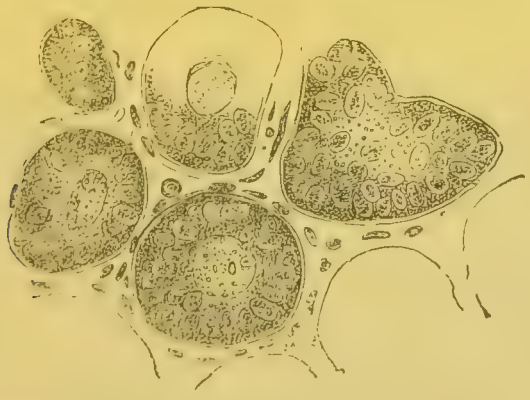

Fig. 199.—Section of a Kidney affected with Bright's Disease.

The cells lining the tubuli are filled with proteic and fatty granules. At the centre of the tubes sections of hyaline casts are seen.

and exudation into the lumen of the tubes; but what is peculiar in this form is the fatty degeneration, which is much more marked

than in the varieties considered hitherto. This degeneration is very irregularly distributed; the cells are sometimes completely degenerated, and often become detached from the wall of the tubes; but they generally remain in situ, and there is no epithelial desquamation, in the sense attributed by Dr. George Johnson to desquamative nephritis. In fact, if a few epithelial cells fall, the wall of the tube is not thereby denuded, for new cells are formed and remain attached, thus replacing those which have been desquamated and carried away by the urine. On examining a section of the cortex after hardening it in osmic acid, the convoluted tubes are found to be dilated, filled with exudation and lined with a row of large cells varying in size. Sometimes these cells are flat and nucleated, sometimes they are normal in size, and sometimes very large. The fat granules, which are stained black by the osmic acid, are almost always regularly arranged in rows, near the insertion of the cells on the basement membrane of the tubes (*o*, fig. 200). When the cells are very large, however, often all the

FIG. 200.—SECTION OF A TUBE THE CELLS OF WHICH ARE IN A STATE OF FATTY DEGENERATION.

m, internal surface of the cells, showing a striated border; *n*, nuclei; *o*, fat granules. Preparation made with osmic acid.

protoplasm is infiltrated. These fatty cells may also contain vacuoles. We have seen extremely well-marked fatty degeneration in the kidneys in gouty albuminuria. In some cases of diabetes, in which during life there was little albumen, which appeared irregularly, and with complete cessation at times, fatty degeneration of the cells of the convoluted tubes has been observed by us. In one of these cases, there was even evident multiplication of the nuclei of the cells. We have seen fat granules in the kidney of a diabetic subject who had never had albuminuria during life as long as he was under our observation. Fatty degeneration also affects the cells of the narrow tubes of the loops of Henle and a certain number of the straight tubes, but it is always less marked here than in the convoluted tubes. In the glomeruli, besides the lesion of glomerulitis, the endothelial cells are sometimes seen

in a state of fatty degeneration, and also the cells on the surface of the vascular loops. Fine fat granules are also found in the

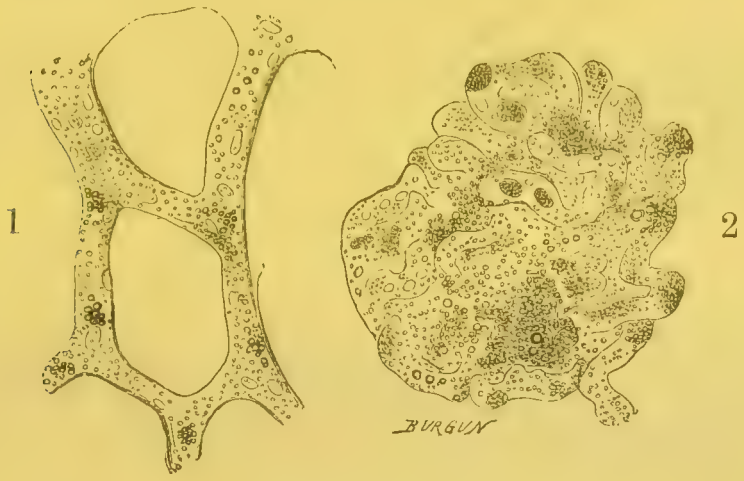

FIG. 201.—FATTY DEGENERATION OF THE VESSELS OF THE KIDNEY IN A CASE OF BRIGHT'S DISEASE.

1. Fatty change in the capillaries and stroma of the kidney. 2. Vessels of a glomerulus showing a similar change. Magnified 250 diameters.

connective-tissue trabeculæ between the tubuli, in the protoplasm of the connective-tissue cells and between the fasciculi around the vessels. Further, in large white kidney, the lesions of interstitial nephritis are almost always found; a new formation of round cells, for example, between the vascular loops of the glomeruli. It is rare, in large white kidney, for some of the glomeruli not to be changed into small masses of connective tissue quite impermeable to blood; they are then atrophied and useless. Very often also Bowman's capsule and the walls of a certain number of tubuli are two or three times thicker than normally, and are transparent and hyaline; but these interstitial lesions are neither very marked nor general in smooth white kidney.

Diffuse nephritis with predominance of the connective-tissue lesions. Granular white kidney.—The large white granular kidney, called by Rayer, **kidney with Bright's granulations**, has yellowish white spots on its surface, and often opaque granulations of the same colour which project in an appreciable manner. The size of these granulations varies greatly; they may be as large as a pin's head, generally smaller, though sometimes larger. They are surrounded by a pink zone indicating congestion of the peripheral renal tissue. The veins of the cortex are generally distended with blood. Sometimes these granulations are not regularly

round, they are prolonged into the cortical substance, and they may be seen in section as small round islets, or as yellowish white striæ. On examining them under the microscope, they are seen to be composed of tubes which are either normal in diameter or dilated, while the tubuli surrounding them are atrophied. The lumen of these tubes, which is larger than normally, is filled with cells in a state of fatty degeneration, or with cellular débris, or true granular bodies. The endothelial cells are hyperplastic and contain fat granules. The granulation, which is formed at the expense of Ferrein's pyramid, projects on the surface of the kidney. The base of the pyramid is generally the seat of this change.

On making a transverse section parallel to the surface of a kidney thus altered, rather large convoluted tubes are found in the middle of the small granulations, and around them tubuli which are only a third or a quarter their normal size; these latter are surrounded by somewhat thick bands of connective tissue; also in the periphery, a considerable number of glomeruli are found which are atrophied like the tubes derived from them. These lesions explain the formation of the granulations on the surface of the kidney, which project as the newly formed connective tissue around them contracts. The granulations are opaque because the cells of the convoluted tubes are in a state of fatty degeneration; but this degeneration varies, and if the cells be slightly altered or simply vesicular, the granulations may be transparent. This sometimes occurs.

In chronic Bright's disease, the kidney may be rather frequently granular, and at the same time smaller than normally, or much atrophied. This is then called **small white granular kidney.** The granulations are pale, often grey and opaque, and are generally irregular and surrounded by a zone of congestion; the cortical substance, seen in section, is spotted with granulations, opaque striations, or greyish white striations; it is generally much atrophied, as well as the pyramids. On examination under the microscope, the tubuli and glomeruli will be found, as in large white granular kidney, to be atrophied in the midst of bands of connective tissue developed around the granulations, and in which the tubuli are seen to be normal in size or dilated, with altered epithelial cells often in a state of fatty degeneration. In this form of diffuse nephritis, with predominance of connective-tissue lesions, the renal sclerosis is irregular; it probably commences around the tubuli; while in interstitial nephritis or cirrhosis of vascular origin, the lesions of the

connective tissue accompany the blood vessels affected with sclerosis. The atrophied tubuli found in the midst of the newly formed connective tissue, always have an epithelium made up of small, irregularly cubical cells, with clear contents, and round or oval nuclei which stain deeply with carmine. This is an embryonic epithelium, with none of the characteristics of the normal cells of the kidney. At the autopsy of gouty subjects with albuminuria, ordinary diffuse nephritis is sometimes found, or white kidney of medium size, or small white granular kidney, or sometimes interstitial nephritis.

We propose to describe here amyloid and fatty degeneration of the kidney, though these lesions may exist without causing inflammation of the parenchyma, and are quite distinct from nephritis when isolated. But as, on the other hand, they frequently complicate diffuse nephritis with albuminuria, their study completes the description of this disease.

Amyloid degeneration.—The large white kidney might be mistaken by its naked-eye appearances for an amyloid kidney, which is often of the same size and appearance. Knowledge of the cause would not enable us to avoid this diagnostic error, for the amyloid kidney is the result of syphilis, scrofula, and tuberculosis, as well as the large white kidney. However, on examining an amyloid kidney the peculiar translucency of the glomeruli often reminds the observer of this lesion; but this appearance cannot be trusted, for in certain white kidneys there is a subacute glomerulitis with increase in size of the glomeruli, which then have a semi-transparent look. The only certain method of confirming the diagnosis is to pour an iodine solution over a section of the kidney, and to see if the glomeruli and arterioles stain brown. In delicate sections, treated either by a weak iodine solution or by methyl-anilin violet, all the parts which are transparent and hyaline, owing to amyloid degeneration, become brown with the iodine and red with the methyl violet. These parts are the walls of some or all of the vascular loops of the glomerulus, the walls of the different arteries, the basement membranes of the tubuli and of the glomeruli, and sometimes even the connective-tissue fasciculi of the kidney. On adding sulphuric acid after the iodine, they often stain green, orange, and blue. The effect of this lesion on the coats of the blood vessels is to thicken them considerably, so that the lumen of the vessels becomes gradually smaller, and finally disappears. The blood does not then enter the diseased glomeruli, and the kidney is anæmic. Fatty degeneration of the epithelial cells

follows, albuminuria, and often the serious symptoms of uræmia, in consequence of retention in the blood of the excrementitious products which are normally eliminated by the kidneys. The concomitant lesions of the epithelium, vesicular condition, fatty degeneration, mucous and colloid secretion, hyaline casts obstructing the loops of Henle and the straight tubes, all these lesions are the same as in albuminous nephritis, described above. Thus amyloid degeneration blends symptomatically with Bright's disease. But it is not so in certain cases of local amyloid degeneration of the kidney, affecting only the vasa recta of the medullary substance, and only partially affecting the glomeruli. The lesions of the cells are then absent. Litten[1] has published a number of these cases, and Strauss,[2] in a similar case, has insisted on the absence of albuminuria. Amyloid degeneration often accompanies interstitial nephritis with atrophy of the kidney, and the formation of small colloid cysts.

Fatty degeneration.—Fatty degeneration, or simple adiposity of the epithelial cells of the kidney, is not generally accompanied with albuminuria; sometimes, however, a small quantity of albumen is passed. Thus, in certain cases of *phosphorus poisoning* albuminuria is observed, still it is absent in others. In old subjects, particularly in tubercular and other cachectic conditions, partial fatty degeneration of the epithelium of the tubuli is observed without the urine being sensibly changed. These cases may be compared to the physiological fatty condition of the epithelial cells of the tubuli in many animals, particularly in the cat and dog. Poisoning by arsenic or by sulphuric acid produces a steatosis similar to that of phosphorus, but less acute. Typical acute fatty degeneration of the kidney resembles that caused by phosphorus poisoning. In the guinea pig, six hours after poisoning, changes are already observed in the epithelial cells; these are very marked twenty-four hours after, on treating specimens with osmic acid. The cells of the convoluted tubes are in situ, but they are cloudy, granular, and contain fine fat granules stained black; the nucleus is large and contains clear proteic granules, and it stains less deeply with picro-carminate than in the normal condition. The centre of the tubule is occupied by a blackish homogeneous coagulum containing a few granular balls. Four days after the poisoning, the epithelium of the convoluted tubes

[1] 'Zur Lehre von den amyloïdes Entartung der Nieren' (*Berliner klin. Wochens.*, 1878, Nos. 22 and 23).

[2] *Société Médicale des Hôpitaux*, June 10, 1881.

is almost entirely destroyed; what remains of the protoplasm is adherent to the basement membrane and is infiltrated with large fat granules, and the nuclei of the cells are no longer recognisable, they are blended together. The endothelium of the intertubular capillaries and glomerular vessels is sometimes granular and fatty; the cells of the external lining of the glomeruli are swollen and contain a few fine fat granules.

In man, in phosphorus poisoning, the kidneys are rather larger than normally, which is due to increase of the cortical substance; the capsule peels off easily, and the surface is smooth and of a yellowish grey colour. The cortex, seen in section, is opaque and uniform in colour, showing at the same time a variable amount of congestion. The medullary substance, redder than normally, is also rather opaque when the blood has been washed away. The mucous membrane of the pelvis is normal. In microscopic specimens, the cells and the lumen of the tubuli of the cortex are seen to be full of fat granules, which are larger than those observed in parenchymatous nephritis. The lesion is uniformly distributed through all the convoluted tubuli and the tubes in loops; the straight tubes of the cortex are also altered, but their epithelium contains less fat than that of the convoluted tubes; they give passage to a large number of free granules, and fatty cells derived from tubes higher up, and to granular casts.

FIG. 202.—LONGITUDINAL SECTION OF THE TUBULAR SUBSTANCE OF THE KIDNEY IN A CASE OF ALBUMINOUS NEPHRITIS DUE TO PHOSPHORUS POISONING.

The tubes in loops are seen to be more altered than the straight tube between them.

The lining of the collecting tubes is almost normal. When albumen is found in the urine in phosphorus poisoning, the

protoplasm of the epithelial cells is found to be infiltrated with proteic and fat granules, which are generally smaller than in steatosis without albuminuria. The connective tissue and blood vessels of the glomeruli are normal in both cases. The casts found in the urine in albuminuric steatosis, due to phosphorus, are characterised by being composed of a granular mass containing fat molecules, while in all other cases of Bright's disease they

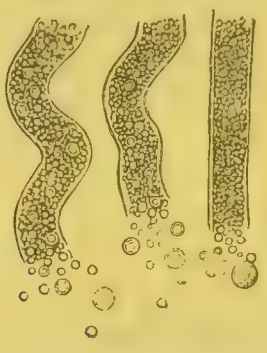

FIG. 203.—TUBULI OF THE CORTICAL SUBSTANCE OF THE KIDNEY IN THE NON-ALBUMINOUS FORM OF PHOSPHORUS POISONING. (SIMPLE STEATOSIS.)

are, with rare exceptions, perfectly hyaline. The fat granules observed then are only on the surface of the cast, which is quite hyaline underneath. In the fatty kidneys observed in phthisical and alcoholic patients and in old subjects, the steatosis is almost always complicated with another lesion; thus, in phthisical and alcoholic patients parenchymatous nephritis is almost always present; and in old persons, atrophy with condensation of the connective tissue, and atheromatous lesions of the arterioles of the kidney.

In all varieties of *icterus*, the colouring matter of the bile passes through the tubuli of the kidney. The same phenomenon takes place in man, and in animals rendered icteric; as, for example, in icterus produced in dogs by poisoning with toluilendiamine.[1] When the elimination of the bile pigment is very active, a peculiar parenchymatous inflammation of the kidney is produced which we will describe here, as the epithelial cells show partial fatty degeneration. The icteric kidney appears slightly larger than normally, smooth with yellow surface, or shaded with greenish lines. The same is seen on section. The tubuli, which contain much bile pigment, are seen both in the cortex and medulla with the naked

[1] Afanassiew, 'Ueber Icterus und Hæmoglobinurie,' &c. (*Zeitschrift für klin. Medicin*, vol. vi. fasc. 4, 1883).

eye as yellow lines. On squeezing the cones of the pyramid, an icteric urine can be pressed out, containing yellow casts covered with epithelial cells infiltrated with bile pigment. In sections, fatty degeneration of the cells of some of the tubes of the cortex, though not of all, will be seen. The fat granules may be large, as in phosphorus poisoning. The same cells contain bile pigment, sometimes actual crystals of bilirubin. The connective tissue around the tubuli also contains bile pigment and even biliary crystals. The tubuli often contain desquamated cells and hyaline casts. That the renal cells contain bile pigment during life is proved by the urine of icteric patients containing pigmented cells and casts. This condition of the kidney is rarely accompanied by marked albuminuria. The most marked degeneration of the renal cells is seen in acute icterus.

Systematic Nephritis. Interstitial Nephritis. Renal Cirrhosis.

In contradistinction to diffuse nephritis, in which the lesions affect simultaneously and irregularly all the tissues of the kidney, there are forms of nephritis in which the change is limited, at the commencement, to one of the elements of this organ.

To these lesions, which may be limited, at first, either to the blood vessels or the connective tissue surrounding them, or to certain of the tubuli, succeed changes which are always systematically and regularly distributed, whence the name systematic nephritis.[1] Such is the interstitial nephritis consecutive to chronic arteritis and to lead poisoning, also the nephritis observed in gouty subjects. Before describing the pathology of these forms of inflammation of the kidney, it will be necessary first to describe similar conditions artificially induced in animals. There are none more characteristic than the saturnine nephritis produced experimentally by Charcot and Gombault.

A. **Artificial lead poisoning.**—Charcot and Gombault gave guinea pigs white lead mixed with their food, in small doses at first; but they were afterwards obliged to suspend the administration of the poison from time to time. There was no albumen in the urine, except when blood was present. The urine contained

[1] For the discussion and critical classification of nephritis see *Les Études sur la Pathologie du Rein.* Cornil and Brault, 1884.

pure lead or lead salts. The animals generally died in the last stage of emaciation, sometimes in convulsions and sometimes with general anasarca. When the poisoning has lasted a long time, many months or a year, the lesions of the kidney are more marked. The kidney is increased in size and smooth at the commencement of the poisoning; granular and red on its surface, normal in size or increased, or slightly atrophied in intoxication of long standing. Cysts are sometimes present in the cortical substance. Under the microscope, even in the least advanced cases, small calcareous blocks are found in the tubes of Henle. Treated by acids, these deposits become clear and leave a substance which stains red by carmine, and which contains a few nuclei. The large branches of the loops of Henle are dilated, as well as the convoluted tubes, and their epithelium is embryonic. The amorphous wall of the tubes thickens and the peripheral connective tissue proliferates. The commencement and topography of this interstitial inflammation is well seen in transverse sections of the middle of the cortex, examined under a low power after staining with carmine. At each transverse section of a pyramid of Ferrein, the newly formed connective tissue may be divided into three distinct parts: 1, a central fibrous spot corresponding to the middle part of Ferrein's process; 2, a peripheral zone composed of fibrous fasciculi interposed between the glomeruli; 3, tracts radiating from the central point to the peripheral zone. In an advanced stage of the disease, cirrhosis is more marked, and the central spot, intermediate trabeculæ, and peripheral zone are more accentuated; the tubuli in the sclerosed part atrophy, though at the same time certain tubuli or systems of tubes remain isolated or almost healthy. It is these which form the prominent granulations on the surface of the kidney, and which rise above the sclerosed parts surrounding them. Bowman's capsules are often dilated at the commencement; they are surrounded by connective tissue rich in small cells; they become thickened, and when the connective tissue contracts they adhere to the glomeruli. The latter often remain intact throughout the whole of the cirrhotic evolution, and only accidentally show lesions. It is the same with the blood vessels; the large vessels are normal, only the arteries which cross the sclerosed parts are affected with periarteritis, their lumen remaining permeable. At a more advanced stage of the lesion the kidneys resemble the small red granular kidney. On removing the adherent fibrous capsule, part of the superficial renal tissue is torn away, and cysts are seen due to

distension of certain tubuli, and typical granulations surrounded with depressed fibrous cicatricial tissue. It is probable that this chain of pathological phenomena is subordinate to the initial production of calcareous blocks arrested in the loops of Henle, whence result irritation of the tubuli situated above, dilatation, and the formation of cysts. But it must be remembered that the kidneys of guinea pigs show a tendency to form those calcareous blocks as the result of other forms of poisoning, without interstitial nephritis being produced. The lead poisoning induced by Charcot and Gombault in guinea pigs and rabbits results in producing quite a special form of nephritis. The tubuli are gradually changed piece by piece from their origin to their end. Their atrophy, followed by interstitial nephritis, is regularly distributed and systematic, while other tubuli preserve their integrity almost completely, and form the projecting part of the granulations.

B. **Lead poisoning observed in man.**—The kidneys are generally altered in chronic lead poisoning. Ollivier,[1] Lancereaux,[2] and Charcot have reported a great number of cases. Interstitial nephritis is always present, characterised by atrophy of the organ, adherence of the capsule, granulations on the surface and in the cortex, and cysts ; and under the microscope by atrophy of a certain number of the tubuli with thickening of the connective tissue. Lead poisoning, such as is observed in subjects who have died with cerebral symptoms, identically resembles the artificially induced nephritis described by Charcot and Gombault. In a case reported by Brault the kidneys were smooth superficially and diminished in size from atrophy of their cortex; they were pale and slightly indurated, and showed atrophy of the tubuli and formation of connective tissue at the centre of the medullary rays, also a zone of atrophy and sclerosis around the glomeruli and sclerotic radii binding the centre to the peripheral zone. The convoluted tubes were atrophied in places, and at others perfectly intact. In the atrophied tubes, the small cubical non-granular epithelial cells were stained red by picrocarminate, and the nuclei a deeper tint, while in the tubes which were less altered or healthy, the epithelium was formed of large, granular, and yellow-brown cells. Around the altered tubes the connective tissue formed bands of fibrils and cells, which were round or flat according to the advanced state of the sclerosis. Bowman's capsules, surrounded by thick-

[1] *Thèse de Doctorat*, 1863.

[2] *Union Médicale*, Dec. 15, 1863; art. 'Rein' in the *Dict. Encyclop. des Sc. Méd.*

ened connective tissue, were adherent to the more or less atrophied glomeruli. Within the tubuli, neither cellular secretions nor casts were found. The lesions of lead poisoning consist, therefore, at the commencement in a slow atrophy, progressing from certain tubuli to the glomeruli, and accompanied with the formation of connective tissue around themselves. Here, as in experimental lead poisoning, is the type of *glandular or epithelial cirrhosis* of Charcot, that is to say, interstitial nephritis consecutive to changes in the epithelium.

Kidneys, long affected by lead poisoning, show more marked and varied lesions, regular or unequal superficial granulations, more induration, more pronounced atrophy, and various changes in the epithelial parenchyma. Thus, in certain tubes, which may be dilated or normal, abraded granular cells may be seen often containing fat granules, while at the same time the tube is filled with clear or granular globes. Elsewhere cysts are developed from dilated tubes, and hyaline casts are found in some of the tubuli. The blood vessels which traverse the sclerosed parts show a sclerotic thickening of their external coats, but the larger arteries and the renal artery itself are generally intact. Lead poisoning may nevertheless affect the intima of the arteries of the kidney and of the general circulation. In chronic saturnine nephritis, a varying amount of albumen is always found in the urine. As a pathological coincidence hypertrophy of the left side of the heart has often been noted, as well as deposits of urates of sodium in the articular cartilages, particularly in the metatarso-phalangeal articulation of the big toe. These deposits are identical with those of articular gout. Sometimes deposits of urate of sodium are seen in the kidney itself, in the form of white opaque striæ, as in gout.

C. **Gouty nephritis.**—It is quite natural to consider gouty nephritis after saturnine nephritis. In gouty subjects, albuminuria is most frequently seen during the cachectic period of gout, whether the disease be then complicated or not with cardiac disease or with diabetes. Outside of this terminal period, and during the evolution of the gout, there may be remissions of albuminuria, which may last a variable time. In all cases of gouty albuminuria the kidney is changed in a very variable manner. Sometimes it is small and granular, and affected with interstitial nephritis, sometimes it is large with Bright's granulations, and finally it may be small, white, and smooth. These characteristics are not in the least constant; only one alteration

is peculiar to gout, that is the presence of striated concretions of urate of sodium at the lower part of the pyramids. Long, extremely delicate, acicular crystals may be found in these striæ; they are highly refractive and are pressed close together. It is the accumulation of these small crystals which gives the extremity of the cones its characteristic appearance. If these little masses be acted upon by acetic or hydrochloric acid, they are changed into uric acid, and it can be shown that the crystalline deposit is in the cells and fibres of the intertubular connective tissue as well as in the cells and interior of the straight tubes. The deposit formed in the interior of the tubuli is generally amorphous. Rayer has described deposits of uric acid crystals adherent to the substance of the kidney, and formed spontaneously in the parenchyma. These are small red or yellow bodies, hard and varying in size.

D. **Interstitial nephritis, or cirrhosis of vascular origin. (Primary atrophy, granular atrophy of the kidney, interstitial nephritis,** *properly so called*).—We based our classification and description of chronic nephritis on its cause, mode of development, and evolution of the lesions. We saw that interstitial nephritis may be the outcome of old diffuse and parenchymatous nephritis, and also of the nephritis observed in lead poisoning and in gout. In these different cases, the interstitial nephritis is certainly consecutive to lesions of the epithelium, which atrophies after having undergone fatty degeneration, and which ends by becoming small and tessellated. But it is not thus in renal cirrhosis of vascular origin, consecutive to arteritis, particularly to chronic endarteritis, and in which the renal arteries are primarily atheromatous. The lesions of the epithelial cells, instead of being primary, follow those of the vessels. In cirrhosis of vascular origin, the kidney has a finely speckled surface, with rather larger and round granulations in places. The large granulations may be absent; they border grooves in the bottom of which much smaller granulations are seen. Occasionally they are surrounded by dilated capillaries or veins filled with blood; sometimes at the necropsy, pale granulations are seen on a red base spotted with small ecchymoses. In sections, these ecchymotic spots are found to be continuous in the renal parenchyma with small foci of interstitial hæmorrhage. When the nephritis is but slightly advanced, or when the capsule is very thick, the granular aspect of the surface is less apparent. The capsule adheres very closely to the renal substance; it

requires some effort to detach it, and on peeling it off a small irregular layer of renal tissue is always torn off with it. The kidney is generally reddish, but it may be grey or yellowish grey. These varieties in colour depend upon the vascular condition of the organ and the changes in the cells. In a section of the long diameter, the cortex seems more atrophied than the medulla; the pyramids are nevertheless affected and their total volume diminished. The tissue of the kidney is fibroid and resists indentation with the finger nail much more than in the normal condition. The arteries are often found rigid and gaping in the intermediate substance. Cysts are also seen rather frequently on the surface of the kidney; few in number and about the size of a pea or lentil generally, they may become larger and give the organ the appearance of a bunch of grapes. Sometimes also small tumours are seen on the surface of the kidney. They have been described by Sabourin as adenomata.

At the necropsies of subjects who have succumbed to general atheroma, to cardiac disease, or to cerebral lesions at the commencement of the renal lesion, the kidneys are generally found indurated, and the cortical substance diminished. The arteries and a few glomeruli seem alone affected. The labyrinth is respected almost throughout its whole extent, with the exception of the convoluted tubes dependent on the diseased glomeruli. Some of the convoluted tubes can still be recognised, though altered; others are already surrounded by a band of connective tissue, which becomes thinner as it approaches Ferrein's pyramid, the other extremity being in contact with Bowman's capsule. After staining with carmine the rest of the parenchyma is seen to be perfectly healthy. The large arteries of the intermediate substance are affected with endarteritis, and in advanced cases with fatty and calcareous degeneration of the middle and deep layers of the internal coat. The other coats are also altered; the middle coat, which is slightly sclerosed, is seen on section to be so refractive that it might be thought at first sight that it was affected with amyloid degeneration. Sometimes in transverse sections, the external part of the middle coat is seen to take a deep stain, which is due to the abundance of elastic fibres it contains. Periarteritis is irregularly distributed. If the arteriole be distributed to a part of the parenchyma which is but slightly altered, its external coat is almost normal; if, on the contrary, it is near to or traverses a patch of sclerosis, the fasciculi of connective tissue attach themselves to it. Finally, the artery is

entirely obliterated in consequence of acute endarteritis; its external coat is thickened, and the fibrous tissue which lines it may, by contracting, cause either the dilatation or contraction of the neighbouring tubuli. Chronic phlebitis is sometimes so marked as to cause the complete obliteration of the veins, and the zone occupied by the thickening of their membranes is very extensive. The atrophied tubes are situated in the midst of a connective tissue which contains either round or oval cells (*d*, fig.

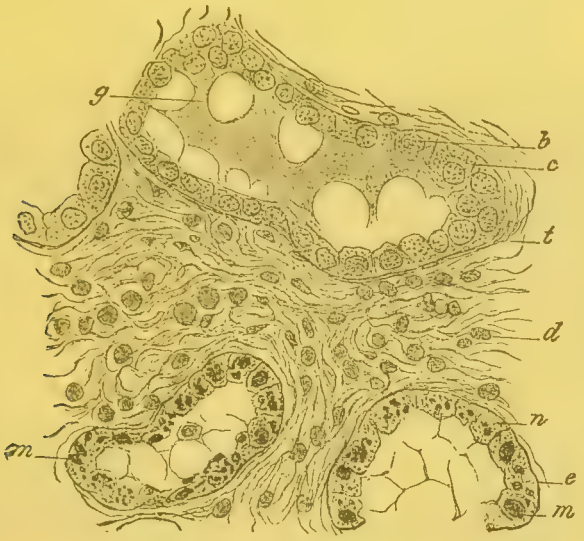

FIG. 204.—SECTION OF TUBULI IN A CASE OF INTERSTITIAL NEPHRITIS.

t, connective tissue containing round or oval cells, *d*; *c*, cells, and *n*, nuclei of the tubuli; *e*, *n*, *m*, epithelial cells in a state of fatty degeneration; *g*, intratubular exudation. Magnified 350 diameters.

204), or flat cells. It forms thick trabeculæ around the blood vessels. The trabeculæ around the atrophied tubuli are at first formed of delicate refractive fasciculi, but later of extremely dense bands. The internal lining of these atrophied tubuli, whether they be convoluted or straight tubes, is always composed of small cubical indifferent cells. Colloid or hyaline casts are often found in these tubuli. They often fill the entire tube, and pressing against the epithelial cells they atrophy them. These cells contain a nucleus which stains deeply. Sometimes Rindfleisch has found two layers of epithelial cells, the external, cubical and flat, with a granular protoplasm and nuclei, and the internal which is mucous and vesicular and secretes a mucous or colloid substance which fills the lumen of the tube and forms a cast. Sometimes these casts are formed of concentric layers (*e*, fig. 205), the most internal of which appear the most dense and stain the deepest,

being coloured brown by osmic acid and dark violet by methyl-aniline violet. The most external layers stain pale violet; neutral

FIG. 205.—SECTION OF A TUBE CONTAINING A COLLOID CAST WITH CONCENTRIC LAYERS.

a, hyaline membrane of the tube; *b*, layer of small pavement cells secreting colloid globes; *e*, cast with concentric layers. Magnified 250 diameters.

carmine also stains them equally well. Granular detritus is also found in these tubuli. The basement membrane of the straight and convoluted tubes of a sclerosed patch are almost as thick as the diameter of the lumen of the tube itself, and they remain for an indefinite period in this state, encrusted in a tissue the vitality of which is necessarily diminished. In other parts of the parenchyma, the tubuli are somewhat dilated, and these are the still active tubuli by means of which, towards the end of life, the secretion of urine is accomplished. The epithelial cells of these least altered tubuli are almost normal, sometimes hypertrophied and at times vesicular. Sometimes they contain no fat granules,

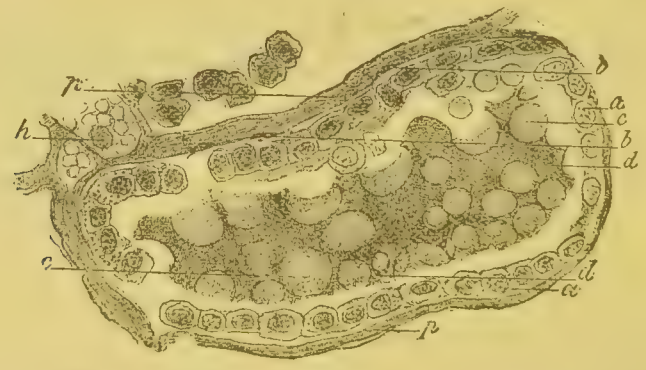

FIG. 206.—CONVOLUTED TUBE IN INTERSTITIAL NEPHRITIS.

p, hyaline wall, much thickened at *p'*; *a*, *a*, atrophied, pavement, or flattened epithelial cells; *c*, *d*, exudation in the tube. Section made after the action of osmic acid. Magnified 400 diameters.

but these granules may be found in the base of the cell as high as the nucleus. Nevertheless fat is generally absent, or present in very small quantities. Thus if the disease lasts long, a distinction is seen between this and the chronic forms of diffuse nephritis. The tubes are empty or contain clear or colloid balls,

different casts, or sometimes a number of red blood corpuscles (*vide g*, fig. 204, and *c*, *d*, fig. 206). These preserved tubuli are grouped two or more together, and are surrounded by bands of fibrous tissue. It is they which form the projecting granulations on the surface, or the opaque spots seen in sections of the kidney.

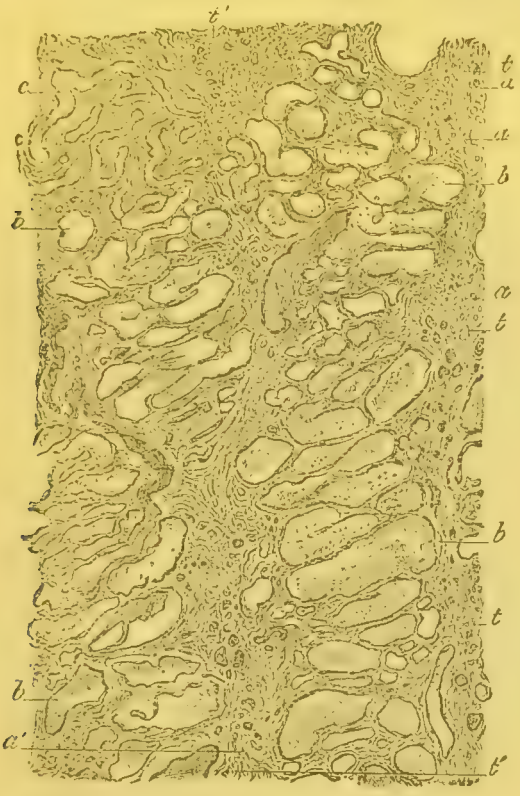

FIG. 207.—LONGITUDINAL SECTION OF THE CORTEX IN INTERSTITIAL NEPHRITIS.

a, *a*, atrophied tubuli in the connective tissue, *t t'*; *b*, tubuli normal in size. Magnified 40 diameters.

The granulations are often injected, or even the seat of actual interstitial hæmorrhage; in these cases, the arteries near are frequently seen to be partly obstructed by thickening of their intima and by adherent fibrinous thrombi. Thrombosis probably takes an important part in capillary hæmorrhage, particularly when cardiac disease is added to the renal affection, and venous tension is increased. Sometimes masses of embryonic cells are found around the glomeruli; this seems to show that there has been an acute stage during the evolution of the interstitial nephritis.

In consequence of atrophy of the tubuli the glomeruli are brought nearer to one another; they then show marked

changes. Their vascular loops become thickened and their membrane hyaline (Thoma), and their nuclei atrophy. The entire glomerulus is changed into a small, hyaline, fibrous mass, in which a few stellate or fusiform cells are seen in the interstices of the vessels, which have themselves become fibrous and imper-

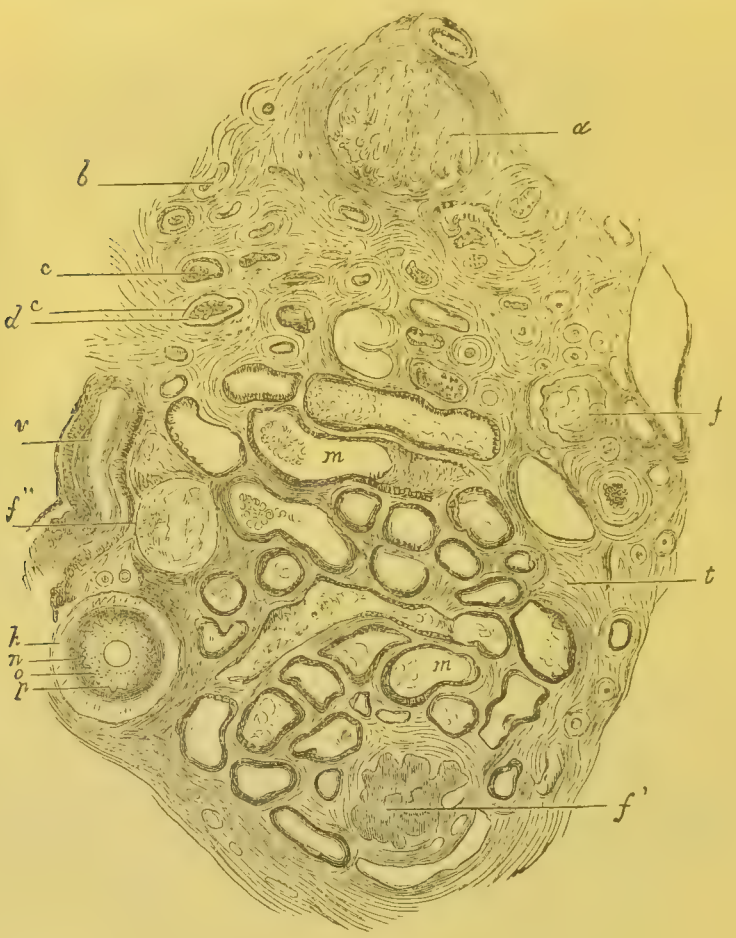

FIG. 208.—TRANSVERSE SECTION OF THE CORTEX OF A KIDNEY AFFECTED WITH INTERSTITIAL NEPHRITIS. SECTION MADE ACROSS A GRANULATION.

The convoluted tubes, *m*, *m*, which constitute the granulation, have preserved their normal size and epithelial lining. The septa of the connective tissue surrounding them are not thickened. The tubuli, *b*, *c*, which surround the granulation are, on the contrary, extremely atrophied, at the same time that the connective tissue, *t*, is thickened and fibrous. In some of the atrophied tubuli, *d*, *c*, hyaline casts are seen. The glomeruli *a*, *a*, *f*, *f'*, are more or less atrophied and fibrous. Around the glomerulus, *a*, the connective tissue is thickened and dense, and the tubuli are in the most advanced state of atrophy. The glomeruli, *f*, *f'*, are extremely atrophied, and one of them, *f*, is hardly recognisable. To the left of the figure arterioles affected with chronic arteritis are observed, both in transverse and longitudinal section: *h*, external coat; *n*, middle coat; *o*, internal coat, comprised between the elastic layer, *p*, and the contracted lumen of the artery, and seen to be much thickened and affected with endarteritis. Magnified 60 diameters.

meable to blood. The thickened, shrunken capsule is lined by concentric layers of connective tissue, and closely covers the

altered vascular tuft. Thus glomeruli, when completely atrophied, do not contain any cellular elements; the connective tissue, which takes their place, is homogeneous, extremely dense, and sometimes shows elastic fibres mixed with the fibrous fasciculi. When the lesion is very advanced, the glomerulus, notwithstanding the increased thickness of the capsule, does not measure more than a third or half its normal size. This vestige of a glomerulus and capsule may be completely isolated, or may be surrounded entirely or for three-quarters of its circumference by normal or dilated tubuli; the last quarter is continuous with a zone of connective tissue which unites it to the medullary rays; this zone contains one or more atrophied convoluted tubes. On carefully examining the glomeruli which are the least altered, multiplication of the cells of the capsule, or of the connective tissue separating the vascular loops, is never seen, contrary to what is present in diffuse nephritis. In this particular kind of renal cirrhosis, atrophy of the glomeruli takes place very slowly and without inflammation. Sometimes hard, grey, opaque spots are seen with the naked eye on the surface of the decapsulated kidney; these are glomeruli in which the vascular loops have undergone calcareous degeneration, and the cells of the capsule are filled with fat and calcareous granules. The diminution in size of the cortex in the final period of renal cirrhosis is shown histologically to be in a great measure due to destruction of the tubuli; the parts destroyed are represented by zones of connective tissue in which tubuli are found in all the different phases they pass through before becoming completely atrophied.

These facts point to the conclusion that there is actually a variety of renal cirrhosis of vascular origin. The relation of nephritis with lesions of the arteries was pointed out long ago by Dr. George Johnson, and later by Gull and Sutton, who were, however, wrong in including all forms of nephritis under the name of *arterio-capillary fibrosis*. More recently Bartels, Debove, and Letulle have shown the exact relations existing between chronic arteritis and renal cirrhosis.

Complications of renal cirrhosis. Cysts.—A. Cysts, the size of a millet seed or of a nut or more, and filled with a transparent citron-coloured fluid, are very frequent in renal cirrhosis of vascular or glandular origin, while they are rare in diffuse chronic nephritis. In the first-named case, ten or more may often be found in each kidney. They are generally caused by dilatation

of the tubuli, and occasionally of Bowman's capsule. All the intermediate changes may be found between dilated tubuli and cysts. Dilated tubuli may be found the epithelium of which is flattened and reduced to a thin floating membrane, while they contain a fluid which holds round granular cells, and hyaline or colloid globes in suspension. The epithelium is sometimes vesicular and contains globes similar to those free in the cavity. It is often, however, so delicate that it becomes detached during preparation, and is found floating in the cavity crumpled and folded on itself. The same appearance of the epithelium and contents is seen in some of the cysts which are visible to the naked eye. The cystic fluid is more or less thick, and stains with osmic acid according to its degree of concentration. The fluid in the large cyst is serous, sometimes blood-stained. This moniliform dilatation of the tubuli is probably caused by the pressure exercised on them by patches of sclerosis, and by their own atrophy in places. When, on the other hand, the cyst developes in the capsule of a glomerulus, which is very rare, a projecting nodule will, on making successive sections, be observed at the circumference of the cyst. This nodule is the vestige of the vascular tuft of the glomerulus in a more or less advanced state of atrophy. The hæmatic origin of these cysts is easily recognised, for blood corpuscles are found in the capsule, and a yellow colloid fluid which also often contains red blood corpuscles and which coagulates with alcohol or the bichromates. The tissue surrounding the cysts always shows the characteristic lesions of interstitial nephritis. The wall of the cyst is generally thin, but we have sometimes seen it composed of a hard fibrous tissue, forming a shell which is almost cartilaginous in consistency and composed of lamellar fibrous or horny tissue.

B. In certain cases of well-marked interstitial nephritis with albuminuria which terminates suddenly by uræmic coma, the kidneys are found after death to be greatly enlarged, and changed almost entirely into cysts of every size, with thin walls and limpid, serous, cloudy, or blood-stained contents. The kidneys have the appearance of a bunch of grapes. This **cystic degeneration of the kidneys** has been well described by Rayer and Cruveilhier. An albuminous fluid and crystals of leucin, tyrosin, cholesterin, oxalate of lime, and blood pigment are sometimes found in these cysts. In sections of the limited part of the kidney which is not invaded by the large cysts, a quantity of fibrous or embryonic tissue is found, and dilated tubes about to become cystic. The

cells of the epithelium of these tubes are often vesicular or flattened and seen in the form of a floating membrane; the tubes also often contain clear vesicular or colloid globes. The same is observed in the small cysts. The walls of the large cysts have an independent capillary circulation, and a thickened membrane with a flat epithelium.

C. In the final stages of atrophy in interstitial nephritis, we have often observed the surface of the cortex to be finely granular, and to have a refractive and semitransparent appearance, which is due to the presence of an infinite number of **microscopic cysts with colloid contents.** Each projection is formed of a small cyst, almost invisible to the naked eye. They are sometimes so near together that in a horizontal section of the surface of the kidney they may be seen like racemose granules. The colloid contents of these cysts are deposited in regular concentric layers.

FIG. 209.—SECTION CUT IN THE FRESH STATE AT RIGHT ANGLES TO THE SURFACE OF THE KIDNEY.

The surface of the kidney, *m*, *m'*, from which the capsule has been removed, is crowded with cysts; some of them, *o*, are empty, others contain colloid contents and granular casts, *c*. At *n* many of these cysts are seen, with concentric colloid contents. *b*, wall of a multilocular cyst of which the granular cast, *c*, is continuous at *d* with a tubule; *a'*, wall of a cyst which is lined with epithelial cells, *b'*, and contains a colloid substance deposited in concentric layers, in the centre of which a granular cast is found; *v*, arteriole the coats of which are thickened. Magnified 60 diameters.

They are developed in the tubules in which bead-like strangulations are present. The membrane of the tube which forms their wall is lined with a single layer of flat cells, which are sometimes slightly granular, thus showing the last trace of their normal condition. They have an ovoid or flattened discoid nucleus. Near these cysts sections of extremely atrophied tubules are seen, which are nevertheless filled with colloid casts. The colloid con-

tents of the cysts may sometimes be seen to be continuous with a cast in a tubule on a lower plane (*d*, fig. 209). The colloid cysts

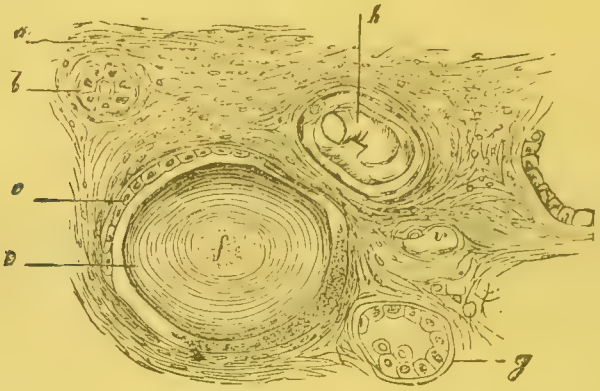

FIG. 210.—SECTION OF A KIDNEY FROM AN ADVANCED CASE OF INTERSTITIAL NEPHRITIS.

a, connective tissue formed of fibres and flat cells; section of an atrophied tubule containing a colloid cast; *h*, tubule also containing a colloid cast; its epithelial cells are flat; *g*, tubule; *c*, flat cells lining a cyst which is formed from a tubule; it contains a colloid substance, *e*, in concentric layers, and a central granular mass, *f*, of broken-down blood corpuscles; *v*, blood vessel. Magnified 200 diameters.

have the same structure as the detached tubules; a hyaline membrane without cells closely attached to surrounding connective tissue, in which cells and fibres are arranged in concentric circles around the capsule of the cyst. Within this membrane

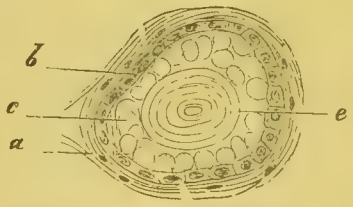

FIG. 211.—SECTION OF A TUBULE CHANGED INTO A SMALL COLLOID CYST.

The connective tissue, *a*, is fibrous and composed of fibres parallel to the wall of the cyst. The epithelial cells, *b*, are more or less flattened, and contain nuclei. Outside this layer colloid cells, *c*, are seen, in the middle of which is a colloid mass, *e*, formed of a concentric layer. Magnified 250 diameters.

there is a complete lining of nucleated cells, which are cubical in the small cysts and slightly flattened in the larger cysts. Within, are the colloid globes already described (*c*, fig. 212), which, when blended together, form the colloid mould which fills the cyst. This mould is sometimes homogeneous, sometimes granular (*e*, fig. 212), and sometimes formed of transparent, refractive, concentric layers slightly tinted yellow, especially at the centre (*f*, *e*, figs. 210 and 211). This mass swells and the concentric circles disappear on adding acetic acid. In the middle,

a true colloid cast is seen, which is older, more refractive, and yellower than the peripheral layer, or a mass of yellow granules,

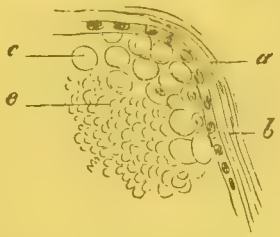

FIG. 212.—SECTION OF A CYST WITH COLLOID CONTENTS LARGER THAN THE PRECEDING.

a, fibrous connective tissue; *b*, epithelial lining composed of flat cells. Within these cells there are many layers of colloid cells, *c*, which break down and become blended into a granular colloid mass, *e*. Magnified 250 diameters.

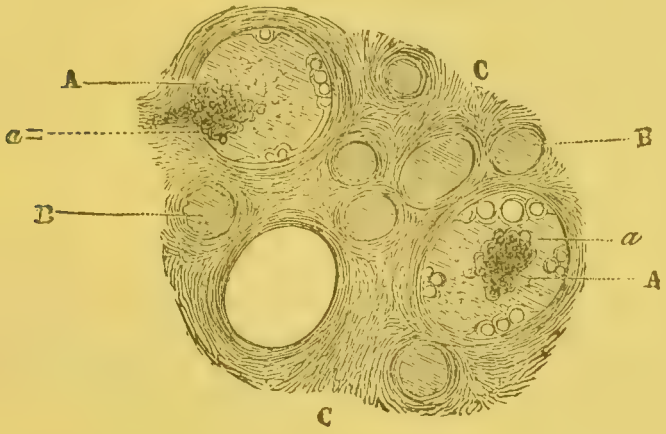

FIG. 213.—INTERSTITIAL NEPHRITIS AND COLLOID CYSTS OF THE KIDNEY.

A, small cysts caused by distension of the glomeruli; *a*, vestiges of partly atrophied vessels of glomeruli which have become cystic; B, nebuli; C, thickened stroma of the kidney. Magnified 40 diameters.

probably derived from altered red blood corpuscles. Everything points to the conclusion that, after the destruction by inflammation of the normal cells of the convoluted tubes, cells are formed which have not the characteristics of the secretory cells, but are cubical or flattened and undergo colloid change, and which finally fuse into a colloid mass, which increases by the deposit of successive layers, at the same time that new cells become colloid at the periphery; the central layers are thus the oldest. Many cysts may blend together to form one, and be surrounded by a common fibrous envelope. In these cystic kidneys, the glomeruli are fibrous or are undergoing fibrous change; some are dilated. The vascular tuft is atrophied and pushed towards the periphery of Bowman's capsule, while the rest of the cavity is filled with a transparent colloid mass holding degenerate and lymph cells in

suspension. In whatever direction sections may be cut, it is often impossible to find any normal renal tissue, neither Henle's nor

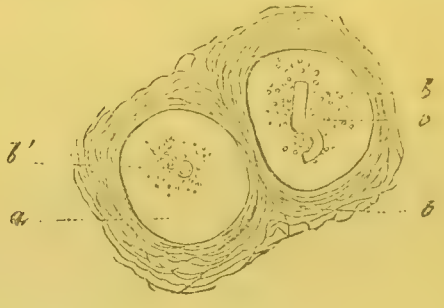

FIG. 214.—SECTION OF TWO CYSTIC TUBULI

filled with colloid matter, *a*, in the midst of which are seen hyaline casts of the same substance, *b*, *b'*.

convoluted tubes. The appearance is always the same, and, whether the kidney be divided vertically or longitudinally, the tubuli show a regularly circular or slightly elliptical section, and at no point are they seen lengthwise. This shows that the tubuli have either been decomposed into a series of small and nearly regularly spherical trunks, or that each tubule has been greatly diminished in size by atrophy. The first hypothesis is the most likely.

D. **Adenoma.**—Adenomata have been accidentally noticed in interstitial nephritis. They have been described by Sturm and Sabourin ('Contribution à l'Étude de la Cirrhose Rénale,' *Arch. de Phys.*, Jan. 1882). According to Sabourin there are two kinds of tumours: 1st, tumours of cylindrical epithelium of the renal type, and which are directly derived from the tubuli in Bright's granulations; 2nd, tumours of cubical epithelium, which are derived from tubular epithelium which is atrophied or indifferent. From the histological point of view adenomata of the kidney are metatypical epitheliomata; from the clinical point of view they are benignant tumours. Owing to the fact that they are almost always subcapsular, Grawitz and Israel have, in a recent memoir (Virchow's 'Archiv,' 1883), enunciated the opinion that these tumours may be due to the development of portions of the suprarenal capsule which has remained adherent to the surface of the kidney during intra-uterine life.

E. Interstitial nephritis may be complicated with **amyloid degeneration** of the blood vessels and tubuli. We have observed it in an extremely atrophied kidney, in which the entire cortex was changed into microscopical colloid cysts. In this case, the

arteries were especially degenerated, and the vascular loops of the glomeruli partially so.

Senile kidney.—Either partial or general interstitial nephritis may be present without albuminuria, which shows that inflammation of the connective tissue is not itself sufficient to cause the passage of albumen in the urine. In old age, interstitial nephritis is sometimes observed with chronic arteritis, affecting many of the larger arteries, the renal artery and its branches in particular. The changes in the parenchyma, the atrophy and partial degeneration of the cells of the tubuli, seem to depend on vascular lesions (Sadler, 'Thèse de Nancy,' 1879). M. Ballet, in a memoir on senile kidney ('Rev. de Méd.,' 1881), concludes that in old persons atrophy takes place tube by tube, as in gout and lead poisoning. We do not consider this has been proved to be the case, and we think that the collapse and shrinking of certain of the tubuli is often secondary to arterial lesions, or may be simply due to the granular condition and atrophy of the epithelium. These lesions do not always go on to actual interstitial nephritis, and may be limited to small areas in the kidney. Whatever may be the cause, albuminuria is scarcely ever present in senile nephritis.

Nephritis due to the presence of Bacteria in the Kidney.

Pathogenic bacteria penetrate into the kidney, and actually cause the acute diffuse nephritis of infectious diseases. We have already described these forms of nephritis, and we need only add in a general way that the bacteria special to these diseases enter with the blood and pass into the tubuli, and thence into the urine (Bouchard, Kannenberg). But bacteria may enter the reverse way, and penetrate by the ureter and pelvis, being derived from the bladder affected with purulent cystitis, induced by calculus for example (Klebs). Pyelonephritis due to compression of the ureters by tumours, the metastatic abscesses of purulent infection, and diffuse suppuration of the kidney, constitute another series of lesions, in which the microbes of pyæmia, circulating in the blood, determine coagulation, thromboses and capillary emboli, with obliteration of the vessels. The pathology of these various renal affections in man is still veiled in obscurity, particularly as the microscopical examination is not made for twenty-four or thirty-six hours after death, when the bacteria of putrefaction have had time to develop. To elucidate the patho-

geny of bacterial poisoning it would be well to describe a few experiments on which it is based. It must be borne in mind that the urine of animals and man, when in good health, does not contain any bacteria (Pasteur).

1. **Certain kinds of bacteria circulate in the blood of the kidney, without producing fibrinous coagulations nor any obvious lesions of the renal parenchyma.** In acute anthrax, such as may be produced by injecting subcutaneously into the guinea-pig a drop of virulent anthrax culture fluid, the animal dies in about twenty-four hours. The blood of all the organs, notably the kidney, is filled with bacilli anthracis without there being any obstruction of the vessels. The renal cells are, however, quite normal. On examining the urine under the microscope, only a few bacilli are found if the fluid contains blood. This urine, notwithstanding even when it contains such a small number of bacteria that they are found with difficulty, gives positive results when used as a culture fluid (Straus and Chamberland, 'Arch. de Phys.,' 1883). Koch [1] has caused septicæmia in mice by the injection of extremely small bacilli, and septicæmia in rabbits by oval and larger bacilli. In both these septic diseases, the blood vessels of the kidney, the vascular loops of the glomeruli in particular, contained large quantities of bacteria without there being arrest of the circulation, nor thrombosis, abscess, nor any lesions of the cellular parenchyma. One of us together with Berlioz [2] studied the conditions under which the bacilli of jequirity infusion entered the kidney. Two or three drops of this fluid, injected under the skin of a frog, gives origin to a general development of bacilli in the blood, which ends in death in about a week. Sections of the kidney show an enormous quantity of bacilli in all the blood vessels, and some in the glomeruli and the tubuli. The urine collected in the bladder also contains bacteria. However, though these organisms have been present in the blood and have been eliminated by the urine for some days, the cells of the tubuli seem normal; the tubuli are not dilated and do not contain the products of pathological secretion. On injecting a large quantity—two or three cubic centimetres—of jequirity infusion into a vein in the ear of a rabbit, bacteria are passed with the urine exactly an hour and a half after the injection.

2. **Certain forms of bacteria cause inflammatory areas, infarc-**

[1] *Untersuchungen über die Aetiologie der Wundinfectionskrankheiten.* Leipzig, 1878.

[2] Cornil and Berlioz, *Arch. de Phys.*, 3rd series, vol. ii. p. 414.

tuses, metastatic abscesses, or diffuse suppuration related to coagulation of the blood and partial obstruction of the vessels. This proposition is deduced from the experiments of Coze and Feltz, who produced metastatic abscesses in rabbits by the subcutaneous injection of putrefied meat infusion, and from those of Koch, who has given a very good description of these lesions. Pasteur, by injecting into the veins of animals his pyogenic microbe taken from the water of Paris, has produced metastatic abscesses in all the organs, the kidneys in particular. All these researches concur in demonstrating that the microbes of pyæmia are, like micrococci and diplococci, arranged in chains. In metastatic abscesses in the kidney, the intertubular blood vessels and the loops of the glomeruli are found at the commencement to be filled with micrococci placed two and two together or in zoogloœa. The circulation is impeded or arrested over a certain area, the fibrin of the blood coagulates, and the peripheral connective tissue and the tubuli

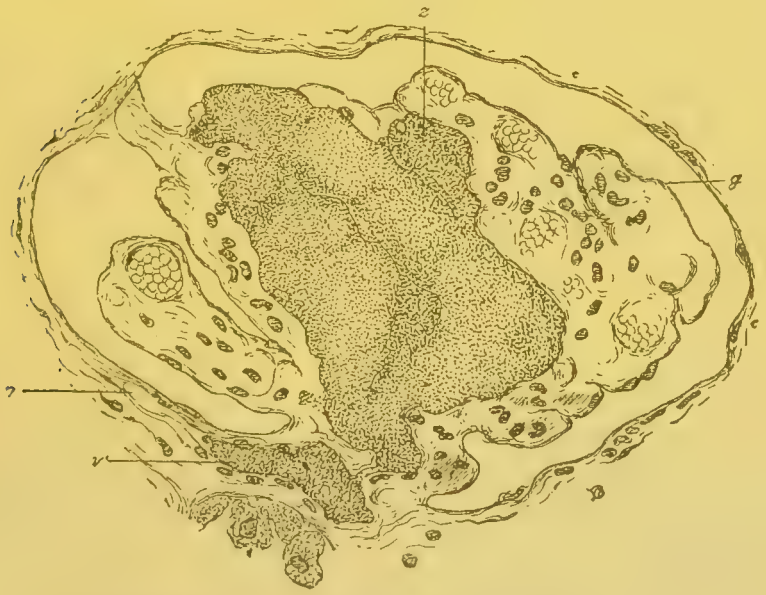

FIG. 215.—SECTION OF A GLOMERULUS MANY VASCULAR LOOPS OF WHICH ARE FILLED WITH MICROCOCCI. (After Babès.)

g, free vascular loops; *z*, loops filled with zoogloœa of micrococci; *v*, afferent arteriole filled with similar microbes. Magnified 400 diameters.

become filled with lymph cells and microbes. Mortification of the previous elements of the tissue, and small foci of pus are the consequences. In puerperal purulent peritonitis, chains of microbes may be present in the tubuli and connective tissue of the kidney without miliary abscesses.

Suppurative nephritis.—Suppurative inflammation of the kidney is seen in man in the form of small metastatic abscesses, or as a diffused infiltration. It may be related to pyæmia, the consequence of a wound or operation, or to puerperal fever, ulcerative endocarditis, typhoid fever, spinal affections accompanied with bed sores, &c. In another series of cases, the suppuration starts from an affection of the bladder or ureter, calculi, catarrhal or purulent inflammation, new growths in the bladder or uterus, or in the parts near to the excretory urinary ducts.

1. **Metastatic abscesses** can, if recent, be studied in their different stages of development in the same kidney. On removing the capsule, isolated spots or circular groups of miliary projections are found on the surface, some of which are dark red, others yellow at the centre or throughout; these are surrounded by a zone of congestion. On making a longitudinal section of one of these groups of miliary foci, they are seen to be continuous with the cortex or medulla and to follow the renal arteries, often showing the form of a cone with the base turned towards the periphery of the kidney. On dividing them a sero-purulent fluid flows out at first; later, the pus collects in the centre of the islet, and the abscess may become as large as a pea or lentil. Small cysts containing a purulent fluid may sometimes be found which existed previous to the pyæmia. A large abscess may be formed by the blending together of many smaller ones. On examining a section of a recent abscess in which the bacteria have been stained with B. methyl violet, the capillaries, vascular loops and afferent vessels of the glomerulus will be found to be filled in places by micrococci which are often united into zoogloœa, partially obstructing the vessels (fig. 215). Often one or more of the vascular loops of the glomerulus are distended with these organisms. The vessels contain at the same time a network of coagulated fibrin, enclosing a few lymph cells and micrococci in its meshes. Migratory cells are found around the intertubular capillaries and in the cavity of the glomeruli and tubuli; the epithelial cells of the latter are granular and necrosed. Congestion and suppurative inflammation are soon developed around the spot where the circulation is arrested.

Instead of miliary abscesses, non-suppurative infarctuses may be met with in the diseases cited. They are caused by the same lesions of the vessels and by thromboses due to the presence of bacteria. In osteomyelitis, abscesses are sometimes found surrounded by hæmorrhagic and necrosed tissue; the vessels, and

particularly the loops of the glomeruli, contain zoogloœa of micrococci.

2. **Purulent foci,** resulting from the break up of small miliary abscesses, contain a smooth, yellow, thick pus, and their walls are formed of congested renal tissue. When older, the pus becomes either thicker by being mixed with calcareous salts, or serous, grey and fœtid. The sac is then formed of connective tissue. After absorption of the pus, serous cysts or a cicatrix with atrophic condensation of the surrounding tissue may be found in the place of the purulent foci. Abscesses sometimes open into the calices or pelvis of the kidney, and give origin to an irregular suppurative ulceration of the mucous membrane of these parts.

Large abscesses may open: *a*, into the pelvis of the kidney; this is a favourable sequela, as the pus is then evacuated with the urine; *b*, into the colon or duodenum, or some part of the intestine (Rayer, 'Atlas,' pl. 19; Gintrac, 'Journ. de Bordeaux,' April 1867); *c*, externally through the abdominal walls, principally in the lumbar region; *d*, into the peritoneum, when peritonitis, proving rapidly fatal, is caused; *e*, through the diaphragm, into the lung or bronchi (Rayer, 'Atlas,' pl. 51); *f*, into the liver (Rayer, 'Atlas,' pl. 20, fig. 2), a case of which has been reported by Rayer, in which the liver ulcerated and formed the wall of an abscess communicating with the kidney. A splenic abscess has also been seen communicating with a purulent sac in the kidney (Rosenstein).

In many cases, suppurative nephritis may terminate by actual gangrene of the kidney; but care must be taken not to mistake cadaveric decomposition, which takes place rapidly in suppurative inflammation, with gangrene.

3. **Diffuse suppuration** may occur as the result of contusions and wounds, or of inflammation spread by means of the excretory canals, or it may be caused by calculi in the pelvis or ureters, or be the result of retention of urine in uterine carcinoma, or in the course of spinal disease. The lesion may be strictly limited to a spot in one kidney, or it may more or less affect both organs at once. It commences by congestion and tumefaction of the kidney. On dividing the organ, blood flows freely, and, on washing this away, red or slate-coloured ecchymoses are observed, which are caused by extravasation of blood into the connective tissue, the capsules of the glomeruli, and the tubuli. At corresponding spots, the capsule of the kidney is deeply injected, and even ecchymotic. When congestion is so marked, it is rare for pus not to be found at some spot, either in one or more abscesses, or

in the cavity of a pre-existing cyst; very often, in fact, suppuration is an acute condition supervening as a chronic lesion, particularly calculus or retention. The kidney, the general shape of which is preserved, is increased in size, and both the cortex and the pyramids may be completely infiltrated with pus; on removing the capsule, the surface is yellow and opaque; its section the same; and thick smooth pus may be squeezed out. On washing the divided surface, it is seen to be infiltrated with pus and friable. Under the microscope, pus cells are seen to be in the tubuli as well as in the cellular tissue. It is generally the cortex which is infiltrated, but the suppuration may be limited to the Malpighian cones and pyramids. In diffuse suppuration as well as in metastatic abscesses, and whether the renal inflammation be primary or secondary to suppuration of the bladder and ureters, micrococci, which are the essential agents of the lesion, are found in the vessels and parenchyma.

IV. Lesions of the Kidney consecutive to Obstruction of the Ureter.

When obstruction to the passage of the urine occurs at some distance from the kidney, the pathological phenomena are simple and are due to increased pressure in the tubuli above the obstacle. This is what occurs in pressure on the ureter by cancer of the uterus. This condition may be produced experimentally by ligature of the ureter, care being taken to perform the operation antiseptically. If, however, the retained urine is changed in its composition and contains irritating substances, such as ferments or microbes, the conditions are changed, and diffuse nephritis with suppuration is the inevitable termination of such a complication. The same result may be obtained in experimental ligature of the ureter without antiseptic precautions.

Experimental ligature of the ureter.—Straus and Germont, who performed this operation with the strictest precautions, observed that, from six to eight days after ligature, the kidney was much larger and paler than the healthy kidney; the following days the pallor increased at the same time that the ureter and pelvis dilated; the surface of the kidney was smooth and the organ seemed larger; but, on evacuating the pale and limpid urine contained in the distended calices, the kidney collapsed and showed an actual atrophy of its substance. From twenty to thirty days after the ligature, the projecting cones of the pyramids

became depressed. On examining sections, the tubuli were found to be dilated, particularly the convoluted tubes and those near the glomeruli; later on, the same tubes became atrophied, and only the glomeruli remained dilated. Bowman's capsule might even undergo considerable cystic dilatation, the vessels being pushed aside to one of its poles; there was fibrous thickening around the capsules and arterioles. These are all the lesions produced by antiseptic ligature; but if the operation be performed without the minute precautions of the antiseptic method, acute inflammation of the kidney is caused, which affects the connective tissue and ends in interstitial nephritis.

Pressure on and obstruction of the ureters in man.—The lesions of the kidney due to obstruction to the flow of the urine, which condition may be caused by calculi in the pelvis or ureters, or by surrounding tumours which narrow these ducts, or by retention of urine in the bladder, or by tumours of the prostate, ureter, pelvis, &c., vary greatly. They may be divided into two groups, according as inflammation of the kidney is present or not. The first case is comparable to antiseptic ligature of the ureter; the second to a septic operation.

A. **Obstruction of the ureter without inflammation.**—We take as the type of this lesion compression of the ureter by cancer of the uterus. The wall of the ureter is thickened and narrowed at a certain spot, and sometimes obstructed by cancerous buds springing from the mucous membrane. The pelvis of the kidney is filled with urine, and most of the tubuli, and even the Malpighian capsules, are distended. At the beginning, the kidney is increased in size, the capsule is easily removed and leaves a smooth surface; it is remarkably pale, of an uniform milky white, the pyramids being scarcely streaked with red lines. On examining hardened sections under a low power, only a certain number of the tubuli are found to be dilated from the papilla to the glomerulus. These tubuli contain no figurate elements, and their epithelium is flattened against their walls, so that they resemble empty veins. Under a higher power, it will be seen that the epithelial cells of all the tubuli, whether dilated or not, are atrophied in a marked degree; their protoplasm contains no granules. The connective tissue of the kidney is slightly thickened, owing to the presence of fluid in its meshes, which fluid is transparent and slightly granular, and contains a few migratory and connective-tissue cells; if the obstruction be old, the connective tissue thickens and

the migratory cells are more numerous. Cystic distension and vascular atrophy of the glomeruli may be present.[1] This condition ends in the collapse of the tubuli and atrophy of the kidney.

B. **Obstruction of the ureter with inflammation.**—The consequences of inflammation are, 1st, marked atrophy of the tubuli with decrease in the size of the kidney and interstitial nephritis; 2nd, in some cases, when purulent catarrh of the bladder, ureter or pelvis is present, suppurative nephritis is observed, and is due to the presence of bacteria. It is seen either in the form of small abscesses or a diffuse infiltration. In the first, atrophic interstitial nephritis, accompanied by dilatation of the ureter, pelvis or calices, is characterised by thickening of the connective tissue around the glomeruli and the arteries of the cortex. The glomeruli are often affected with chronic inflammation, and their capsules frequently dilated and cystic. The atrophy of the cells of the tubuli is very marked; they are flattened and cubical, but their nuclei generally stain less well than in other forms of interstitial nephritis, which shows that their vitality is more deeply compromised. The cortical substance is thin, and the pyramids no longer project; the whole of the renal substance does not measure more than a centimetre or less in diameter, and forms a thin shell around the pelvis and calices, which are extremely dilated. Thus a kidney affected with *hydronephrosis* forms the thin wall of a sac filled with urine, which may contain calculi or not. Before opening the pelvis, the kidneys sometimes seem enormous, at other times almost normal in size; their surface is uneven and cystic. Sometimes, again, they are small, if the lesion be of long standing, and occasionally they may be found much atrophied, about the size of a nut, and surrounded by a thick layer of adipose tissue.

When retention is accompanied with suppuration of the bladder or prostate, calculous pyelitis, cancer with gangrenous ulcerations, &c., either large or miliary abscesses, or diffuse suppuration, are observed in the kidney. Klebs has shown[2] that these conditions are due to pyæmic bacteria passing from the bladder or ureter into the tubuli, and there causing irritation of the epithelial cells, inflammation with diapedesis, and suppuration.

Pyelitis.—The forms of pyelitis vary from temporary superficial catarrhal pyelo-nephritis, such as may be observed as the

[1] Artaud, *Rev. de Méd.*, Nov. 1883.

[2] *Handbuch der path. Anat.*, vol. i. p. 655. Berlin, 1868.

result of the application of a blister, to suppurative pyelitis and to chronic pyelitis due to the presence of calculi.

Catarrhal pyelitis is characterised by redness of the mucous membrane of the excretory channels of the urine, and by desquamation, proliferation, and thickening of the mucous membrane of the pelvis and calices, in which inflammation the straight and collecting tubes are implicated; the urine here is found to hold desquamated epithelial cells and lymph cells in suspension. In a more acute form, the exudation contains fibrin, which forms a membranous or flocculent deposit on the surface of the pelvis and calices (*pseudo-membranous pyelitis*). These cavities are then more or less dilated.

Acute purulent pyelitis is specially observed in the course of chronic disease of the bladder and ureter, of which it precipitates a fatal termination. It also occurs in cancer of the uterus, when the morbid growth has invaded the ureter and bladder, and in purulent infection. The amount of pus accumulated in the pelvis, when there is some obstruction to the flow of the urine, may be considerable; the connective tissue of the mucous membrane is infiltrated with lymph cells. If the disease has lasted some time, vascular fleshy granulations, formed of embryonic tissue, are found on the mucous membrane of the pelvis, and villi which float when examined under water. The cones of the pyramids also suppurate and ulcerate. This condition is generally complicated with abscess or diffuse suppuration of the kidney. There is sometimes, in chronic purulent pyelitis, a large effusion into the cavity of the pelvis. Rayer has described tumours due to distension of the pelvis of the kidney, which contained from 35 to 45 pints of purulent fluid. They have always been caused by temporary or permanent obstruction of the ureter. These large sacs contain, besides pus, ammoniacal products, caseous pus, a white calcareous soft mass, or calculi. The fibrous tissue of the mucous membrane is thickened, and the tumour contracts adhesions with neighbouring organs; the kidney is atrophied and flattened, so as to form part of the wall of the cyst, and the pyramids no longer form projections. Though thickened, the wall of the cyst may ulcerate, and the abscess open into the intestine, or into the lung through the diaphragm, or into the sub-peritoneal connective tissue, in which case the pus finds its way under the crural arch. If in the right side, abscesses may be developed in the liver. Peritonitis and pleurisy are sometimes the final termination.

Calculous pyelitis, which is essentially chronic, is caused by the presence of calculi in the pelvis or calices of the kidney, or in the ureters. Multiple calculi are generally small; but when there is a single calculus, it is either simple or formed by the union of many smaller ones. The calculi are of the same shape as the cavities in which they are lodged. Thus a single large calculus may be found, of which the central part is moulded into the pelvis with lateral expansions into each of the calices, each of which expansion is cup-shaped, so as to receive the cone-like extremity of a pyramid. Calculi are generally composed of only one substance, such as uric acid, urates, oxalate of lime, ammonio-phosphate of magnesium, or phosphate of lime, cystin, &c. Sometimes they are composed of different substances. The kidneys are always affected with interstitial nephritis in calculous pyelitis, with cysts and marked atrophy. The mucous membrane of the pelvis and calices is greatly altered, being thickened, and its surface infiltrated with calcareous salts, which form a sort of crust. At other times it is ulcerated. Hydronephrosis (p. 541) may be caused by the obstruction presented to the flow of the urine by calculi.

V. Tumours of the Kidney.

Tuberculosis of the kidney.—Tuberculosis of the kidney may be primary or secondary. The first-named, which is not so very rare, affects either one or both kidneys, though one is generally less affected than the other. The lesion, whether primary or secondary, can be best studied in the kidney which is least diseased. The tubercles generally begin in the cortex, near the small arteries which lie between the pyramids of Ferrein, or on the surface of the kidney. Along these arteries lines or groups of tubercular masses are seen. Each of these granulations is composed of renal tissue in which the cellulo-vascular septa are thickened and infiltrated with numerous small round cells which compress the tubuli; the epithelial cells are fatty. The glomeruli are sometimes distended and filled with small round cells in a condition of caseous degeneration, while the vascular tuft is more or less atrophied and impermeable to blood. The centre of the small granulation becomes caseous; neighbouring granulations melt into larger masses, and they are found chiefly at the line of union of the cortex and medulla. Koch's bacilli are generally seen in the small opaque tubercles of no great age. In sections,

the bacilli are found in their usual positions, often in the hyaline wall of the vessels and near their edge, in the tissue which has

FIG. 216.—SECTION OF TUBERCLE OF THE KIDNEY.

V, vessel in the centre of the granulation; A, A, tubuli at the periphery of the granulation and near to one another, while the tubuli, E, are separated by the cells of the granulation. Magnified 200 diameters.

become caseous, and in its clefts and losses of substance. They are rather numerous also at the edge of the caseous parts, in the giant cells, and also sometimes in the lumen of the altered tubuli. They are rarer in the old caseous nodules of tubercular infiltration; in fact, they may be even entirely absent.

In subjects who die from primary tuberculosis of the kidneys, there is always a complex morbid condition of the genito-urinary organs. Large tubercular masses are found in the cortical and medullary substance of the kidney, and even the whole kidney may be infiltrated with tubercle; the pelvis and calices are dilated and filled with a caseous pus or a semi-fluid mass containing grumous particles, the products of ulceration. On washing out the distended pelvis and calices, tubercular granulations, either isolated or forming a continuous layer, will be recognised on their surfaces. On section, the submucous connective tissue is found to be thickened and to measure from 1 to 2 mm. It is embryonic, and contains one or more superimposed layers of tubercular granulations, as may be also observed in the pleura and peritoneum. This morbid mucous membrane then ulcerates, and pus and shreds are thrown into the pelvis. The renal tissue is then exposed and attacked, and the caseous parts of the kidney are

softened and eliminated. When the ureter is patent, the urine carries away the products of suppuration, in which case it contains

FIG. 217.—BACILLI IN A CASE OF RENAL AND VESICAL TUBERCULOSIS.

Most of them are in the epithelial cells.

caseous pus and flocculent and opaque débris; this is deposited as a thick muddy layer at the bottom of the vessel. Examined under the microscope, this deposit is found to contain large lymph cells filled with fat granules, a small number of red blood corpuscles, and the débris of connective tissue infiltrated with small fatty cells. This urine contains albumen, like other purulent urine; it is not, however, easily mistaken for the urine of albuminuria, which is generally clear and contains a large number of hyaline casts, while in tuberculosis casts are nearly always absent, and if present are few in number. But the essential diagnostic characteristic of renal or vesical tuberculosis, to be deduced from the examination of the urine, is the presence of bacilli. To discover them, a small drop of the urinary deposit is placed on a slide and left to dry either in the open air or in a stove. The dried layer is then stained with Ehrlich's fluid, decolourised by a 33 per cent. solution of nitric acid, dehydrated by absolute alcohol, and mounted in Canada balsam. The *bacilli tuberculosis* will then be seen if examined under an immersion lens. They are either isolated, in groups, or irregular bundles, in which the rods are seen to be long and lying in various directions. They are sometimes found within a lymph or epithelial cell, but generally they have no connection with the cells. Their well-ascertained presence

in the urine permits of the diagnosis of renal or vesical tuberculosis being made.[1] The ureter is generally affected with the same tubercular lesions as the mucous membrane of the pelvis, but instead of being dilated it is often so contracted as to allow of the urine only passing with difficulty. It may even be quite obliterated. In the final stage of renal tuberculosis, most of the lesions of chronic purulent nephritis may be observed ; namely, calcareous deposits on the mucous membrane of the pelvis, abscesses in the kidney, which show a tendency to become caseous, more or less marked swelling due to distension of the pelvis, and perforations resulting from tubercular ulceration of the mucous membrane, and which establish communications with the peritoneum and intestine. In males, renal tuberculosis frequently implicates all the excretory ducts of the urine, the ureter, bladder, and the urethral mucous membrane. The granulations are seated in the connective tissue of the mucous membrane, under the epithelium, and penetrate more or less deeply into the submucous connective tissue. They set up puriform catarrh. The prostate, seminal ducts, vasa deferentia and testicles, are also sometimes rapidly invaded by tuberculosis, whence results a peculiar form of the disease, limited to the genito-urinary organs. In the female, renal tuberculosis, which is much rarer, may also be complicated with tubercles in the bladder and in the uterus and its appendages. Patients generally succumb to a new development of tubercles in the lungs or intestines.

Gummata.—Gummata of the kidney are very rare. In syphilis, the kidney may be affected with albuminous nephritis or amyloid degeneration. One of us published, in a thesis on the lesions of the kidney in albuminuria (1864), a striking case of gummata of the kidney, coinciding with amyloid change in this organ, and gummata in the liver. The gummata of the kidney, about twenty in number, showed characteristic naked-eye appearances. They were isolated or pressed together, the size of a small pea, hard, fibrous in consistency, and had undergone caseous degeneration. They were all seated in the cortical substance. Examined under a low power, these nodules showed a peripheral transparent part, and an opaque caseous centre. The new growth consisted of embryonic connective tissue, developed at the expense of the pre-existing fibrous septa of the kidney, so that a few Malpighian

[1] The bacilli tuberculosis in the urine have been described by Babès (*Soc. Anat.*, Jan. 26, 1883) and by Rosenstein (*Centralblatt f. die med. Wissensch.*, Feb. 3, 1883).

glomeruli were easily recognised from place to place, either in the fibrous zone or in the caseous centre. In the peripheral zone,

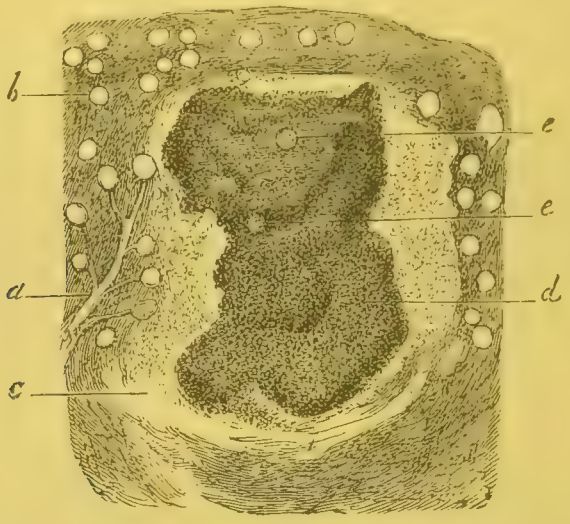

FIG. 218.—OLD GUMMA OF THE KIDNEY.

a, artery, and *b*, glomeruli of the kidney; *e*, *e*, centre of the gumma, in which the glomeruli are still recognisable; *d*, opaque zone in which are fat granules; *c*, peripheral fibrous tissue. Magnified 20 diameters.

the embryonic connective tissue surrounded tubuli which were still visible, though atrophied. The tissue of the gumma did not differ from that of the liver, found in the same case. It is the only case of characteristic gummatous tumour of the kidney that we know of, observed in the adult. Klebs has reported a similar case observed in a child of six months old.

Lymphadenoma.—The kidneys may be the seat of secondary growths, composed of adenoid tissue. These small tumours do not differ from those found in other organs, particularly in the liver. They are developed in the connective tissue. Apart from these tumours, there are also lesions of the kidney related to leukæmia, and characterised by the accumulation of leucocytes in the blood vessels of the glomeruli, within Bowman's capsule, in the capillaries of the intertubular connective tissue, and between its fibres. The epithelial cells of the tubuli simultaneously undergo fatty degeneration. The lumen of the tubuli is sometimes blocked by a mass of lymph cells, and sometimes by hyaline casts.

Sarcoma.—We only know of two cases of sarcoma of the kidney, in both of which the nature of the tumour was made out by one of us. They both occurred in young children. The tumours were enormous and spherical; the centre of each was

composed of a single degenerated, softened kidney; in one case, much blood was infiltrated into the lacunæ of the sarcomatous

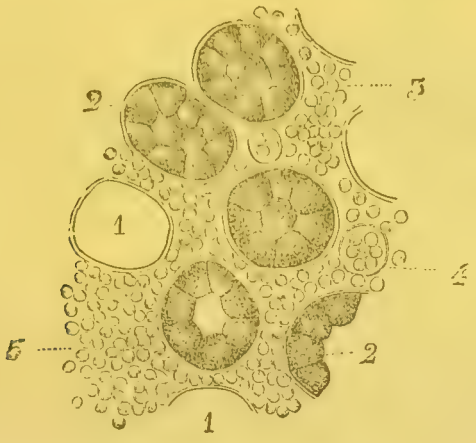

FIG. 219.—SECTION OF THE KIDNEY IN LEUCOCYTHÆMIA.

1, lumen of a tubule from which the epithelial cells have dropped; 2, tubule, the lumen of which is filled by granular epithelial cells; 3, capillary divided longitudinally and filled with white cells; 4, transverse section of a capillary; 5, mass of white cells derived from the rupture of a capillary. Magnified 250 diameters.

tissue. The capsule of the kidney, which completely surrounded the tumour, was thickened; in the kidney, which was flattened under the capsule, the appearance and structure of the cortex could be rather easily recognised at parts, either under the microscope or with the naked eye. The sarcoma was certainly developed in the pyramids, or at the union of the pyramids with the cortex. The centre, which was soft and friable in one of the cases, showed all the characteristics of encephaloid sarcoma with embryonic-walled blood vessels, and those of fasciculated sarcoma in the other. In both cases, the development of the sarcoma, from the centre to the periphery, could be well made out. In one case, the fasciculated sarcoma penetrated the cortical substance by following the course of the arteries. At the edge of these vessels, and in the connective tissue surrounding the tubuli, there was a new formation of round or fusiform nucleated cells, between the fibrils. In one of the tumours, the part played by the cells in the tubuli in the formation of sarcomatous tissue could be easily followed. The tumour developed, in fact, simultaneously in the connective tissue and in the tubuli. In delicate sections of the periphery of the tumour, where the kidney tissue had been well preserved, the tubuli were seen in different stages of morbid change. Some were normal in size, had their proper hyaline membrane and lining of epithelial cells, with an empty lumen in the centre.

Beside these normal tubuli, others were seen, two, three or four times the normal size; in those least dilated, the hyaline basement

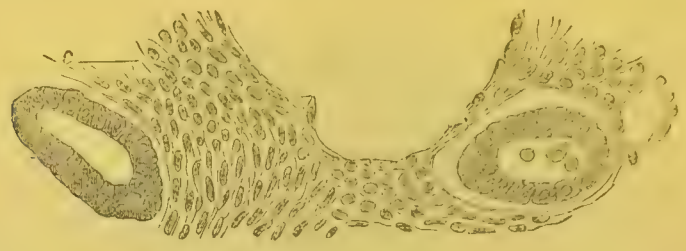

FIG. 220.—SECTION OF THREE TUBULI PASSING THROUGH SARCOMATOUS TISSUE, *c*.

One of these tubes, which is at the centre of the figure, is large; only a part of its circumference is seen, and it is empty. The two others, *o*, are nearly normal in size, and only contain an epithelial layer. Magnified 250 diameters.

membrane was still recognisable, but it was wanting in the tubuli, which were much enlarged. In the former, the epithelial cells formed two or three superimposed layers. These newly-formed layers were composed of cells, which were smaller than they are

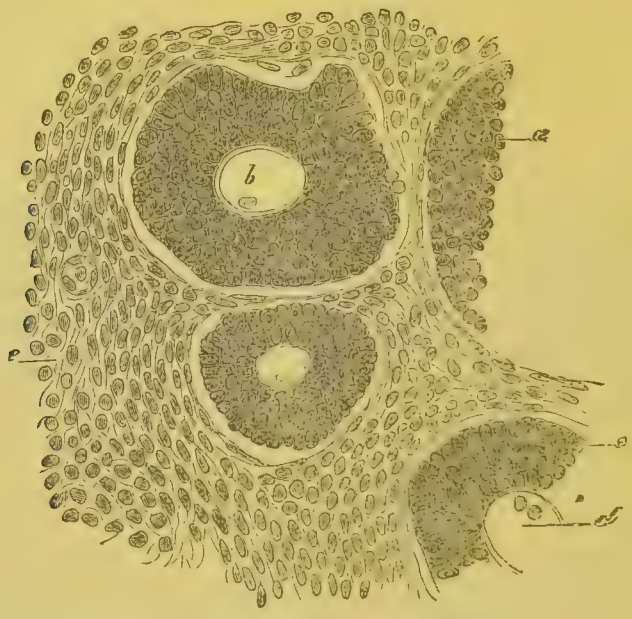

FIG. 221.—TRANSVERSE SECTION OF FOUR ALTERED TUBULI PASSING THROUGH SARCOMATOUS TISSUE.

The tubule, *a*, is only partly seen. The three others have an empty lumen, *b*, *d*, and many layers of epithelial cells. Magnified 250 diameters.

normally, and which had lost the peculiar structure of the secretory cells of the kidney, being only composed of an ovoid nucleus surrounded by a small amount of protoplasm. It was necessary to use acetic acid to distinguish the nucleus from the protoplasm.

These small epithelial cells, arranged in thick layers, were oval or fusiform, and were placed at right angles to the wall of the tube. The centre of the tubuli still retained its empty space. At other parts, the tubuli were only represented by large irregular spaces, without a vestige of the basement membrane, and were filled with round nucleated cells, which in every way resembled embryonic cells. The tubuli, whether normal in size or enlarged, were separated by thick bands of a tissue which was everywhere composed of cells, generally oval, and which were arranged in concentric lines, parallel to the walls of the tubuli, and were supported by a fibrillar tissue; the whole constituted a characteristic sarcomatous tissue. The tissue around the small tubuli was relatively dense and close, but when the tubes were enlarged and filled with round cells, it became friable. Its cells were then round, and its fibrils formed a loose kind of felting. These two cases clearly establish the existence of primary sarcoma of the kidney in children. It is also probable that many cases of tumour of the kidney in children, which are published under the name of cancer, are nothing else than sarcomata.

Carcinoma of the kidney.—Renal carcinoma may be primary or secondary. In the latter case, it is developed in the form of nodules, seated most frequently in the cortex, under the capsule, and which exactly reproduce the structure of the primary tumour. Primary carcinoma is not common. It is generally found only in one kidney. The tumour may be of the scirrhous, encephaloid, hæmatoid, colloid, or melanotic variety of carcinoma; most frequently, however, it is encephaloid, particularly the hæmatoid form. Colloid is rarer than scirrhous carcinoma. The affected kidney varies in size, and may attain the weight of four, five, or even twenty-five pounds. Generally its shape is preserved, for the new growths have invaded the whole organ at once, so that the cortex and medulla are still recognisable; if, however, the whole organ be not affected, it is the cortex which is attacked in the greatest number of spots. The tumour is sometimes diffused and uniform; and sometimes it is developed in the form of more or less irregular nodules, separated by modified though still recognisable renal tissue. The pelvis and calices are affected. The renal tissue, which is preserved near to the cancerous islets, is often the seat of fibrous thickening and atrophic interstitial nephritis, in which case it is compressed by the tumours, and the glomeruli undergo the same atrophic fibrous changes as in interstitial nephritis. At other times, the epithelial cells of the tubuli are

in a state of fatty degeneration, and the vessels filled with blood. Hæmaturia, the usual symptom of these tumours, is caused by the extreme congestion of the renal tissue, as well as by carcinomatous new growths on the surface of the pelvis and calices. At the spots where the tumour is extending into the renal tissue, Waldeyer has isolated casts of epithelial cells derived from the tubuli and which have increased in size by budding. Long ago Robin pointed out that epithelioma developed by a new formation of renal epithelium; but at that time, he confounded under the name of epithelioma of the kidney, not only carcinoma, but other lesions of the kidney, particularly Bright's disease. The memoir of Waldeyer, and other cases published by Neumann, have proved that the tumour developes by budding of the epithelial cells in the tubuli. What we know of the development of tumours in the glands, and the facts already described regarding renal sarcoma, lead us to think that the epithelial cells, as well as the connective tissue, take part in the development and extension of carcinoma. In structure, the tumour does not differ from carcinoma in other organs. In encephaloid growths in the kidney, a large number of enormously dilated capillary vessels are found, which ally them with hæmatoid carcinoma. Small cavities may be found from 2 to 5 mm., or even 1 cm. in diameter, from the walls of which spring loops of extasic vessels. The renal vein is sometimes the seat of cancerous infarctus, which extends for a variable distance and may even reach the inferior vena cava.

Cysts.—The cysts of the kidney are numerous. They have been already described (*vide* p. 527). In advanced interstitial nephritis, there may be numerous small colloid cysts in the cortex; or the glomeruli may be distended with the same substance, which is much less frequently observed (p. 530). In acute congestion, the glomeruli may be changed into cysts containing coagulated and lamellar fibrin (p. 473). In Bright's disease, cysts may be formed by dilatation of the tubuli or glomeruli (p. 533). Cysts may be, however, congenital, and they may then be so numerous, as the kidney to be riddled with them, and their size and that of the organ may be such as to present an obstacle to delivery. They contain a clear fluid, which is nothing else than urine, the flow of which has been prevented during fœtal life by some obstruction in the excretory ducts. These cysts have their starting point in the glomeruli, the capsule of which is much dilated, while the vascular tuft is atrophied and pushed aside. Serous cysts, which are very common in interstitial

nephritis, particularly in kidneys atrophied from senility, contain a clear fluid. They are either numerous and small, about the

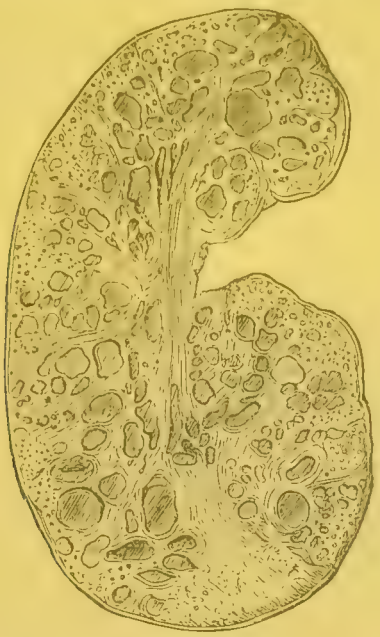

FIG. 222.—CONGENITAL CYSTS OF THE KIDNEY
Figure borrowed from Virchow's 'Treatise on Tumours.'

size of a lentil, or less numerous and larger and the size of a bean or nut. Their mode of origin and development are more difficult to make out. They may, in fact, be surrounded by renal tissue which is absolutely normal, and in which not a vestige of atrophied glomeruli may be found. This is the case in congenital cysts. They are lined by a flat epithelium. Care must be taken not to mistake dilated calices, which penetrate between the pyramids for renal cysts.

Angioma.—Small tumours, composed of an erectile tissue with cavities full of blood, which are, in fact, dilated capillaries, may be found in the kidney. These angiomata are analogous to those found in the liver, but they do not attain such a large size. They are, moreover, unimportant from a pathological point of view.

Parasites.—In Europe, the most important parasites found in the kidney are echinococci; they are, however, rarer here than in the liver and lungs. The hydatid cysts of the kidney exactly resemble those already described in the liver (p. 405). They sometimes open into the pelvis. In Africa, there is a variety of renal parasite which is very common. This is the *distoma* which

exists in the egg state in the excretory channels of the urine, and also in the renal vein and its affluent branches. Griesinger found it in one-third of the autopsies made in Egypt. It causes a pyelo-nephritis, followed in all probability by hæmaturia, which is endemic in that country. The *filaria sanguinis hominis* has been found in the urine of patients affected with hæmatochyluria.

CHAPTER II.

THE URETER, BLADDER AND URETHRA.

Normal histology.—The **ureter** is composed of an external fibrous membrane; a muscular coat in which the external fibres are transverse, and the internal longitudinal in direction, and a mucous membrane. The latter is thin, and contains no glands such as are present in the pelvis; its epithelium is stratified with the deep cells small and cylindrical, the middle layer polygonal, and the superficial flattened. In the **bladder,** under the peritoneal covering which is lined by a fibrous coat, there are muscular fasciculi, the superficial and longitudinal fibres of which intersect those of the internal layer, these being transverse or annular. The first layer is partly continuous with the urachus; the second does not form a continuous layer, its fibres intersect, raise the mucous membrane and are continuous at the neck of the bladder with the internal sphincter. At the lower part of the bladder is the trigone, which is bounded by the urethra in front, and by the orifices of the ureters behind. The connective tissue lining the mucous membrane is here thick, elastic and fibrous, and contains a number of muscle fibres. The mucous membrane of the bladder is white; the epithelium is stratified, the layers being thicker than in the ureters, the upper layers are flattened, while the deeper are cylindrical and polygonal. In the neck of the bladder and at its base, small utricular depressions are found, which may be simple or aggregate. According to Kölliker, they have a diameter of from 90 μ to 140 μ, and an orifice of from 45 μ to 110 μ, and are lined with a cylindrical epithelium. The vesical mucous membrane contains no papillæ.

The **urethra** has a pink, vascular mucous membrane with a stratified epithelium, on the surface of which open, in both sexes, a large number of large acinous glands, called Littré's glands. These glands are nearly 1 mm. in diameter, and their oblique ducts measure from 2 to 5 mm. Their epithelium is caliciform

and secretes mucus. The submucous connective tissue, which forms a membrane rich in elastic fibres, is united to the prostatic tissue in the prostatic part of the urethra, and to the cavernous body in the spongy region.

Pathological anatomy and histology of the excretory ducts of the urine. Inflammation.—*Hyperæmia* of the vesical mucous membrane is seen in some cases of poisoning, by cantharides, for example. It is also present in all acute and chronic forms of inflammation, of whatever cause. In old persons, in spinal diseases, and when tumours are present in the vicinity of the bladder, ecchymoses are often seen in the submucous connective tissue, at the base of the bladder, or around the orifice of its neck. This part of the bladder is also the seat, in certain persons, of varicose veins, which may lead to severe and repeated hæmorrhage. Vesical hæmaturia is, however, more often caused by fungoid or papillary tumours. *Catarrhal inflammation of the bladder*, whether caused by cantharides, urethral catarrh, atony of the bladder, urethral stricture, enlarged prostate, spinal affections or calculi, and whether it be acute or chronic, shows the same pathological lesions which we have already frequently described when considering catarrh of the mucous membranes. In superficial inflammation, induced in the rabbit by the subcutaneous injection of cantharidin, the nuclei of the superficial tesselated epithelial cells proliferate, so that there may be from 2 to 6 present in certain cells. The cells are thrown off and form, with the migratory cells, a white layer on the surface of the mucous membrane. In man, the presence of desquamated epithelial cells and numerous lymph cells in the urine give it a milky appearance, and a mucopurulent sediment is deposited in the vase. Bacteria, due to the presence of the muco-pus, are found in the urine at the moment it is voided, and often signs may be discovered of ammoniacal fermentation. Cystitis is frequently caused by bacteria being introduced in catheterisation. In certain cases of acute inflammation limited to the base of the bladder, small prominent pearl-like vesicles are seen with the naked eye at this spot. They contain a transparent or slightly cloudy mucus, and they resemble small glands or utricles distended by secretion. These glands, hypertrophied so as to be nearly round, measure from 1 to 2 mm. in diameter, and are found at the lower part of the trigone, immediately behind the urethral orifice, where they form a circle around the neck of the bladder. The mucous membrane around them is

deeply congested. At other times, inflammation of the bladder brings about the formation of prominent papillæ on its surface. When catarrh has lasted some time, the irritated submucous connective tissue becomes denser and thicker, at the same time that the muscle fibres of the wall of the bladder undergo hypertrophy. The mucous membrane dips down between the enlarged transverse folds, and pockets are formed. The bladder empties itself incompletely and with difficulty, and the urine, mixed with pus and bacteria, becomes decomposed and alkaline, and urinary calculi are deposited. Acute inflammation of the bladder may occasionally terminate by suppuration of the submucous connective tissue, and by ulceration leading to the formation of a submucous abscess. Perforation of the bladder, inflammation of the surrounding peritoneum, and a fistulous communication between the bladder and the vagina or intestine, may be the consequences. In other cases, the acuteness of the inflammation, paralysis of the bladder and the retained urine, lead to gangrene of the mucous membrane. It becomes softened, brown in places or almost black, and its surface may become irregular with villous débris encrusted with the salts of the urine, particularly phosphate of lime. The bladder contains a brownish fluid containing mucus, pus, and fragments derived from the destruction of the mucous membrane and red blood corpuscles. The consequences are, destruction of the mucous membrane at a certain spot, infiltration of the urine into the neighbouring connective tissue, urinary abscess, and local or general peritonitis. Pyelo-nephritis is also frequently related to acute cystitis. Chronic cystitis is often due to the presence of vesical calculi. These calculi, which are either derived from the kidney or pelvis, or formed in the bladder itself, vary in size, and are either free, or are lodged or impacted in one of the pockets already described. They are formed of uric acid, urate, oxalate, carbonate or phosphate of lime, and ammonio-phosphate of magnesium. Very rarely, they are formed of xanthin. They are accompanied with chronic catarrh of the bladder, and rather frequently with chronic inflammation, which may simultaneously affect both the pelvis and the kidney.

Ulcerative cystitis is seen in pyæmia, typhoid fever, eruptive fevers, &c. A limited and superficial portion of the mucous membrane becomes infiltrated with an exudation composed of lymph cells, fibrin and bacteria; it softens and breaks down, and an ulcer with a grey base is formed (the diphtheritic ulcer of the Germans). Variolous pustules have been observed in the vesical

mucous membrane as well as in that of the urethra. Catarrhal inflammation of the urethra resulting from herpes, catheterisation, or infective coïtus, is generally acute.

Infectious blennorrhagia or gonorrhœa is caused by the presence of micrococci (gonococci), which are found in considerable numbers

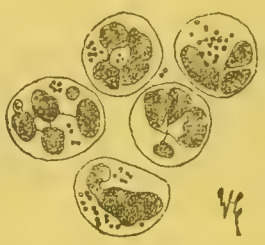

FIG. 223.—CELLS OF BLENNORRHAGIC PUS, TWENTY-FOUR HOURS AFTER THE COMMENCEMENT OF THE EXUDATION.

In these cells the nuclei will be seen to be undergoing division in various ways, and in their protoplasm microbes are seen. Magnified 600 diameters.

in many of the epithelial cells, and in the round migratory cells which are contained in the purulent exudation or free in the peritoneal fluid. These micro-organisms, which have been described by Neisser,[1] Haab[2] and Martin,[3] are easily stained with aniline dyes. Gonorrhœa lasts one or two months, and may be complicated with inflammatory metastases in the serous membranes of the joints and tendons. Gonorrhœa is localised, either in the anterior part of the urethra, as, for example, in the navicular fossa, or in the bulbous portion, such as the prostatic region, or it may be general. The formation of lymph cells, desquamation of the epithelial cells, the extravasation of red blood corpuscles, and vascular congestion occur in the urethral as in every other inflamed mucous membrane. When the inflammation is very acute, the submucous connective tissue is affected to a variable extent, and even the erectile tissue of the corpus spongiosum, whence results inflammation of the lymph vessels of the dorsum of the penis characterised by cord-like tracks. When the inflamed submucous connective tissue is infiltrated with lymph cells, and the corpus spongiosum is also affected, its erectile tissue becomes incapable of erection; this condition, which is so frequent and painful in acute gonorrhœa, causes swelling of the corpus

[1] Neisser, *Centralblatt f. med. Wiss.*, 1879.

[2] Haab, *Corresp.-Bl. für schweizer Aertze*, 1881.

[3] Martin, *Recherches sur les Inflammations Métastatiques suppurées à la suite de la Gonorrhée.* Geneva, 1883.

spongiosum and glans. This condition is commonly known by the name of chordee; the chord is formed by the urethra, and the arc by the cavernous bodies and the swollen glans. Gonorrhœal inflammation of the urethral mucous membrane sometimes becomes localised in an acute form in and around the glands, and in the surrounding connective tissue, so that abscesses may commence either in the navicular fossa or near to Cowper's glands. If these abscesses open outwards it is less serious than when they open into the urethra. In the latter case, the urine may infiltrate into the perineal connective tissue, to prevent which a counter opening is made in the skin without delay. Stricture of the urethra is generally caused by fibroid organisation of part of the inflamed submucous connective tissue. The sequelæ of chronic gonorrhœa are growths resembling fleshy granulations, and winding and irregular false passages in the urethra caused by these growths. Hard fibrous nodules are sometimes found round the urethra, at the base of the glans, or near the navicular fossa; they constrict the passage to such an extent as to cause strictures, which can only be cured by either internal or external urethrotomy.

Tumours.—Tubercles of the vesical and urethral mucous membrane are sometimes observed in man, particularly in the form already described as tuberculosis of the genito-urinary organs. They are exactly the same as in other mucous membranes (see Tubercle of the Kidney and Pelvis). The tubercles, which are developed on the surface of the mucous membrane and in the connective tissue, cause catarrh with purulent or caseous secretion. The tubercles are in patches, and are united by an embryonic tissue. Molecular necrosis of the caseous parts leads to the formation of ulcers which may be large and deep.

Chondroma has been observed in the walls of the bladder by Ordônez ('Gaz. Méd. de Paris,' 1856), and another similar case was reported to the *Société Anatomique* by Landetta. In the latter case, the chondroma was propagated from the pelvic bones to the vesical walls ('Soc. Anat.,' 1861, p. 191).

Papillomata (**vesical fungus**) are frequently seen in the bladder, where they may attain a considerable size. Though the vesical mucous membrane normally contains no papillæ, it gives origin to vascular papillæ in all the irritative processes of which it is the seat, in simple inflammation as well as in cancerous tumours. The neck or the base of the bladder is generally the seat of these newly-formed papillæ. They form either a single mass, or several

tumours disseminated on the surface of the mucous membrane, and they are very vascular. On examining them under water, filaments varying in length, and sinuous papillæ, anastomosed together or free, are seen floating in the fluid. They are composed of a small amount of connective tissue forming an envelope around the vessels, which have thin embryonic walls and terminate with a loop at the end of the papilla. They are covered with one or more layers of irregularly cylindrical epithelial cells, which are pressed together. In the centre of the tumour, these cells, which are produced in large numbers, fill up the spaces between the various papillæ. They give a certain opacity to the fluid which infiltrates the tumour. When papilloma of the bladder is simple, the submucous connective tissue, on which it is based, may be almost normal, being only slightly thickened, while it is quite degenerated in carcinoma and sarcoma. The examination of the base of the tumour and the connective tissue from which it springs is necessary in order to establish the diagnosis between simple papilloma and carcinoma, which latter often shows a great tendency to become villous on the surface of the bladder. Vesical papillomata cause vesical catarrh and more or less severe and persistent hæmorrhage, in consequence of rupture of some of the capillaries, which accident may be brought about by very slight mechanical causes, such as the efforts of micturition, for example. Instead of taking the papillary form with large filaments described above, papillomata may be more compact and dense, and be seen in the form of fleshy granulations composed of embryonic connective tissue, forming a homogeneous mass on the surface of the mucous membrane. More or less acute vesical catarrh may complicate papilloma, particularly when the patient has been catheterised by sounds which were not rigorously antiseptic. Fragments of the tumour mortify and are evacuated with the urine. On staining these with safranin or methyl violet, masses of zoogloea are found which cover the filaments corresponding to the necrosed vessels of old papillæ. Sometimes, rather large, grey, pultaceous masses are passed by the urethra, and on examination they are found to be gangrenous papillæ covered and separated by zoogloea of micrococci.

Carcinoma of the bladder may be primary or secondary; the latter is caused by the connective tissue and muscles of the bladder being directly invaded by an adjacent carcinoma developed primarily in the uterus, rectum or prostate. The mucous membrane is then attacked, and either sessile cancerous granulations

with large base and round projections are developed, or papillary, dendritic growths resting on a carcinomatous base. The latter resemble papillomata, and contain vascular papillæ, covered with epithelial cells. When carcinoma is propagated from the uterus to the bladder, which is very common, the vesical mucous membrane is everywhere inflamed where it is not already the seat of cancerous growths. Its surface is of a deep red, and highly vascular, and projecting vesicles may often be found, which are formed by the utricular glands, filled with transparent mucus or muco-pus. Primary carcinoma of the bladder is most frequently encephaloid; it is rarely fibroid. Its form varies. It often consists in an infiltration of all or part of the mucous membrane of the bladder, particularly at its base or neck. The mucous membrane may then measure from $\frac{1}{2}$ to 1 cm. in thickness. The muscular fibres are hypertrophied and the connective tissue is equally thickened. The white or pink surface of the bladder is ulcerated in places, where slight villous granulations are seen. Section of the degenerated part shows a grey tissue rich in milky juice. At other times, the mucous membrane is only affected at a certain point, in the trigone. Vesical carcinoma is generally villous, and resembles fungoid or papillary growths; but the base of the tumour on which these villi are implanted is composed of carcinomatous tissue, which extends some distance, so that the vesical wall is thickened and degenerated at this spot; this anatomically differentiates carcinoma from papilloma.

CHAPTER III.

THE TESTICLES.

I. Normal Histology.

The testicles are surrounded by the *tunica vaginalis* which constitutes their serous membrane, and they are composed of a fibrous coat or *tunica albuginea*, the *spermatic cords*, the *tubuli seminiferi* which open into the epididymis, and finally the vessels and nerves.

The **tunica vaginalis** has two layers; one parietal in relation with the scrotum; the other visceral which lines the tunica albuginea of the testis and epididymis. Both layers are composed of connective tissue, and are lined with a layer of endothelial cells. The **tunica albuginea** is a dense thick fibrous membrane, which sends out fibrous processes into the testicle, and is directly continuous with the fibrous framework of this organ. The most important of these processes is the *corpus Highmori* or the *mediastinum testis*, which is a septum of firm connective tissue, situated at the posterior part of the testis, and through which pass the seminal ducts on their way to the epididymis.

The **parenchyma** or **glandular substance** of the testicle is composed of ducts, the *tubuli seminiferi*, which divide and subdivide, and sometimes anastomose together; they form conical lobules, the apex of which is bounded by the corpus Highmori, and the base turned towards the periphery of the gland, where they terminate by a free extremity or loop. At the apex of the lobule they become rectilineal, and unite together to form the network of the corpus Highmorianum, called the *rete testis*. From this network spring from seven to fifteen *vasa efferentia*, which perforate the tunica albuginea before reaching the epididymis. These vessels become narrow and convoluted, and form a series of cones, the *coni vasculosi*, which constitute the caput epididymis. They are united into one duct, the canal of the epididymis, which passes along the posterior border of the testicle, describes numerous flexuosities,

and is continuous, after being reflected from below upwards, with the *vas deferens*. The **tubuli seminiferi**, which are easily separated and unrolled for a considerable length, are 0·13 to 0·28 mm. in diameter (Kölliker). They are composed of a dense and thick fibrous membrane, formed of fibrous laminæ separated by flat connective-tissue cells. On the internal surface of this membrane are found a layer of polygonal cells, which may be looked upon as an epithelium, and within the tube there are round seminal cells, which contain one or more nuclei, the peculiar contents of which give origin to the *spermatozoa*. These organisms rarely become free in the testicle itself; for it is in the vas deferens that the sperm is fully developed. The **spermatozoa** have an enlarged part or head, which is flat and pyriform when seen in profile, with a point projecting forwards measuring 1·8 μ in length; the tail of the spermatozoa measures at least 45 μ in length; it is extremely thin, and is united to the head by a central portion. The movements of the spermatozoa are very active; they may continue for some days in the genital organs, or in the uterus of female animals, where this phenomenon has been observed. Water arrests these movements, but they are re-established by alkaline solutions, concentrated solutions of sugar, albumen and urea. Acids, on the contrary, impede the movements. Cold also paralyses these organisms, but after keeping them for three or four days at freezing point, they may be revived by heat. The epithelial lining of the efferent vessels of the epididymis is formed of ciliated cylindrical cells. These cells become extremely long and narrow at the head and extremity, or globus major and minor of the epididymis, and at the beginning of the vas deferens. Thick layers of muscle fibres are found in the efferent tubules, the epididymis and the vas deferens. At a spot in the epididymis, generally at its lower part, a small, elongated, cylindrical body is often seen, it terminates in a free extremity and is called the *vas aberrans* of Haller. Giraldès has described a small organ situated at the upper border of the testis, between the epididymis and the vas deferens (*the organ of Giraldès*). It consists of a varying number of white corpuscles, each formed of a tube measuring 0·7 mm. in diameter convoluted like a glomerulus. They are lined with pavement epithelium, and they represent vestiges of the Wolffian body. The **arterioles** of the testicle are derived from the spermatic artery of the cord, which passing from the caput epididymis, one of its branches is directed into the corpus Highmorianum, while the other branches pass to the anterior

part of the testicle and its surface, and penetrate the testicle with the fibrous septa of the tunica albuginea. The veins take the same course as the arteries. The nerves, which are not numerous, are derived from the spermatic plexus, and reach the testicle with the arteries. Their termination is unknown. The lymphatics, after forming a dense plexus under the tunica vaginalis, penetrate the testicle, according to Ludwig and Thomsa, and form a network of large tubes which surround the tubuli seminiferi. These vessels are lined with an endothelium. The **vas deferens** is a straight cylindrical tube with thick walls, and is continuous with the convoluted canal of the epididymis. It is composed of an external or fibrous membrane, smooth muscle fibres, and a mucous membrane. The muscular fasciculi form many layers, a middle layer of circular fibres contained between two layers of longitudinal fibres. The mucous membrane exhibits prominent longitudinal rugæ, between which are deep saccules. The external part of its connective tissue contains a network of elastic fibres. The epithelium consists of a single layer of tesselated cells, which contain pigment granules giving a yellow colour to the surface of the mucous membrane.

The **seminal vesicles** are nothing else than the terminal cœcal appendices of the vasa deferentia. They are composed similarly of a fibrous membrane, and smooth muscle fibres which penetrate between them and unite the various convolutions. This membrane is more delicate than that surrounding the vasa deferentia. The saccules and depressions in the mucous membrane of the seminal vesicles contain a viscous transparent fluid, in which spermatozoa are found. The mucous membrane secretes a peculiar fluid which enters into the composition of the sperm. In old men, colloid concretions are found, formed of a proteic substance.

The **ejaculatory ducts** have also muscular walls, which are thinner near the prostate. Their mucous membrane is folded into rugæ like that of the vasa deferentia. In old age or in cachectic conditions, such as advanced tuberculosis, spinal disease, &c., the spermatic ducts contain cells in an advanced stage of fatty degeneration, and they subsequently atrophy. On section, the testicle is then seen to be of a yellowish grey colour and opaque, instead of the usual pinkish grey colour. Duplay has, however, seen living spermatozoa in the spermatic fluid of men of eighty years of age and more. Atrophy of the spermatic tubes, and fatty degeneration with atrophy of their cells, are constant facts in most of the lesions of the testicles in which the tubuli are

compressed. This is observed in chronic orchitis, and in tumours which compress the glandular tissue of the testis, also in compression of the spermatic cord and particularly of the epididymis and vas deferens, when the secretion of the sperm is prevented, by arrest of its expulsion.

II. Pathological Anatomy and Histology.

Inflammation. Experimental epididymitis.—Malassez and Terrillon have studied experimental inflammation of the vas deferens and the epididymis in the dog, by injecting a 1 per cent. solution of nitrate of silver into the former. They determined acute catarrhal inflammation, characterised by fall of the ciliated epithelium, the formation of one or more layers of indifferent epithelial cells, and by lymph cells accumulated in the lumen of the distended tubes. The globus minor of the epididymis was inflamed more acutely than the globus major; and at this spot the tunica vaginalis was also inflamed. In the less inflamed parts of the duct, club-shaped or round cells were seen interposed with the cylindrical cells. If the irritation was less marked, the cylindrical cells remained in situ but lost their cilia, and in their place small globes of mucus appeared which filled the lumen of the tubuli, where they became mixed with migratory cells. Later on, the inflammation was localised in the globus minor of the epididymis, where it was maintained by the products of secretion accumulated in its cavity. The duct of the epididymis, dilated in places, had the appearance of a series of small cysts. The connective tissue was also the seat of inflammatory foci, characterised by collections of lymph cells, or by small abscesses. Subsequently, fibrous sclerosis was observed, with disappearance of the muscular fasciculi of the walls of the duct, of which some segments had become cystic, while others were atrophied.

Acute orchitis.—Opportunity is rarely given to study anatomically the acute orchitis which is the sequela of gonorrhœa, mumps or wounds. It is probable that there is then œdematous infiltration of the connective tissue with all the consequences of this condition, namely, irritation of the cells of the connective tissue and inflammation of its lymphatics. The dominant lesion, that which can be best recognised during life, is *epididymitis* and *vaginalitis*. When the case is one of gonorrhœal orchitis, the specific inflammation and bacterial sepsis are propagated by way of the vas deferens, and are at first limited to the epididymis,

which is the first organ affected. It becomes large and hard; its vessels gorged with blood, the connective tissue of its various tunicæ infiltrated with fluid and leucocytes, and its mucous membrane is in a state of catarrhal inflammation. The lesions of epididymitis and orchitis are better known by experiments which have been made on the rabbit and dog (Malassez, Brissaud), than by anatomical observations in man, for acute orchitis always ends in recovery. According, however, to the observations of Gaussail, Marcé, Peter, Godard, &c., the vas deferens and epididymis are swollen, their walls thickened, inflamed, congested or infiltrated, and yellow in colour, and the dilated ducts are filled with a muco-purulent fluid of a grey or yellow colour. The inflammation simultaneously affects the tunica vaginalis, which shows the characteristic signs of inflammation of a serous membrane; that is to say, effusion of a fluid mixed with fibrin, lymph cells and extravasated red blood corpuscles, with proliferation of the endothelial cells. This is shown when puncture is practised to evacuate the fluid. Orchitis often leaves behind induration of the cellular tissue which surrounds the head and every other part of the epididymis. Nodules are formed of hard and refractive cicatricial tissue, which are lardaceous in appearance, and compress the excretory duct; whence result either partial stricture or complete closure of the duct, and consequently suppression of the function, and atrophy of one of the testicles. Sometimes also in the globus minor, cavities with purulent contents are found, which may be mistaken for abscesses, but which are probably nothing else than cystic dilatations of a segment of the duct of the epididymis. When these cicatricial nodules are developed simultaneously on both sides, the spermatozoa can no longer pass through the epididymis, and the subject becomes impotent (Gosselin). In consequence of inflammation of the tunica vaginalis, fibrous growths in the form of villi, plates or granulations are seen on its surface; they are prominent and will be described with hydrocele. Suppurative inflammation of the parenchyma of the testis is rather rare; it is, however, sometimes observed in local wounds and in pyæmia. The pus is formed in the cellular tissue of the gland, and sometimes there may be at the same time suppurative inflammation of the lymphatics and veins of the cord.

Chronic orchitis.—Chronic inflammation of the testicle varies. In one form, the testis and epididymis are simultaneously affected, and their size is increased throughout their whole mass. The lesion consists, according to Fœrster, in enlargement of the seminal

vesicles by cells which are found in greater numbers than in the normal condition, and in infiltration of the whole of the cellular tissue by inflammatory exudation; the fibrous septa are thickened, the testis and epididymis are indurated and tumefied, and on dividing them, thick fibrous septa are seen, between which there is a yellow caseous homogeneous mass (*caseous* or *apostematous orchitis*), in which only a few vestiges of the seminiferous ducts are found. This change somewhat resembles tuberculosis, for which it is sometimes mistaken. According to Virchow, it has no connection with tuberculosis, and is the result of traumatic inflammation, or the propagation of catarrhal inflammation from the urinary passages. Another variety of chronic orchitis consists in chronic inflammation of the interstitial tissue of the testicle. The organ is either increased, diminished or normal in size; atrophy of the substance of the testis is rarely observed. In some cases, this chronic inflammation is accompanied by suppuration which leads to the formation of one or more abscesses, which may remain stationary and become surrounded by a fibrous or calcified cystic membrane; at other times, they open spontaneously or are opened by the surgeon. A hernia of the testicle is then produced and it projects as a vascular and granulating mass, in which the more or less altered seminiferous tubes are surrounded by a granulating tissue. This is what has been called *benignant fungus of the testicle.* The mass gradually decreases by suppuration and a cicatrix is finally formed. It is found according to Moutier (Thesis, 1875) in acute purulent inflammation, in syphilitic orchitis and after opening of an abscess. The surface and connective tissue of the epididymis, as well as the serous membrane of the testis, may be the seat of chronic inflammation with an abundant production of embryonic tissue, which projects outside in the form of fleshy granulations, as in the fungoid growths of the testicle. The embryonic granulations, which are formed on the tunica vaginalis after gangrene of the scrotum, must not be confounded with benignant fungus.

Chronic syphilitic orchitis.—This lesion, the histology of which has been well described by Virchow, consists in the new formation of connective tissue between the seminiferous tubuli. These then become separated from one another by embryonic or fibrous connective tissue, and more or less atrophied by pressure. At places, they are reduced to their collapsed membranous envelope, which is fibrous or homogeneous in appearance, and they contain

only a few atrophied or fatty degenerated cells. This lesion may affect the entire testis or only some of its lobules. At the same time, thickening of the tunica albuginea and the tunica vaginalis is observed, and they show either vegetating growths or adhesions. This form of orchitis is coexistent with syphilitic gummata, but it may also be observed without them. This one of us observed with Coyne, at Bucharest, at the post-mortem of a syphilitic child. There were no gummata, but all the connective tissue between the seminiferous tubuli was abnormally thickened, and was infiltrated with newly formed round or fusiform cells.

Hydrocele. Hydrocele of the tunica vaginalis.—Though hydrocele of the tunica vaginalis is considered to be a true dropsy, it may with greater justice be looked upon as a chronic imflammation. It is, in fact, a rare lesion in general dropsy, and on the other hand, the fluid found in the tunica vaginalis contains a more or less considerable quantity of fibrin, which occurs in all inflammation; fibrous growths, new membranes and excrescences are often formed on the internal surface of the serous membrane. This disease, which is characterised by a serous or fibrinous effusion into the tunica vaginalis, is either caused by acute inflammation, or by suddenly induced chronic inflammation of the serous membrane, or by a variocele. The quantity of fluid effused varies from a few ounces to many pints; it is generally clear, sometimes stained yellow by a few red blood corpuscles, and it occasionally contains cholesterin, or tumefied endothelial cells and lymph cells in sufficient numbers to render it cloudy. In some cases, when a cyst of the epithelium has ruptured forwards into the tunica vaginalis, spermatozoa are found in the fluid of the hydrocele. In recent cases, the internal surface of the tunica vaginalis is smooth, but the connective tissue of the membrane is always thickened; in hydrocele of old standing, unmistakable signs of chronic inflammation are constantly found; more or less vascular false membranes are then found, superimposed in leaf-like layers on the parietal or visceral surface of the tunica vaginalis. These growths are composed of connective tissue, which is generally hard and dense, and similar to that which lines the surface of the spleen in chronic circum-splenitis. Here, as on the surface of the spleen, these tough fibrous growths are in the form of projecting plates which are cartilaginous in appearance, or of flattened or projecting nodules. They are composed of lamellar connective tissue with parallel layers separated by flat cells. According to Malassez,

effusions of blood and ecchymoses are often found beneath them, at the junction of the normal connective tissue and the fibrous growth. These round prominent growths have the form, semi-transparency, and hardness of a small pearl, and may become pedunculated and free in the serous membrane, in the same way as foreign bodies are formed in the joints. These inflammatory growths often become infiltrated with calcareous salts; the indurated tunica vaginalis cannot collapse, and the testicle, surrounded by a serous membrane which is equally thickened and contracted, becomes more or less atrophied. Hydrocele of the tunica vaginalis is often complicated, either with cysts, or other varieties of hydrocele, or with scrotal hernia; it is sometimes the point of departure of suppuration, and it may be complicated with hæmatocele, that is to say an effusion of blood into the tunica vaginalis.

Congenital hydrocele.—The portion of peritoneum which passes with the cord and testis into the scrotum, may, instead of becoming obliterated above the testicle to form the tunica vaginalis, remain patent, and the serous membrane surrounding the testicle then communicates during life with the peritoneal cavity. The fluid contained in the peritoneum passes then into the tunica vaginalis and *vice versâ*; this condition is frequently complicated with inguinal hernia.

Encysted hydrocele.—Sometimes the peritoneum which accompanies the cord is not obliterated throughout its whole length, but remains patent at some point of its course, being obliterated above and below. If this portion becomes filled with fluid, an encysted hydrocele of the cord is produced. Sometimes many cysts are superimposed one above the other along the cord. It may also happen that an old hernial sac becomes obliterated, and the peritoneal prolongation which composed it instead of remaining collapsed fills with fluid; dropsy of the hernial sac is the consequence, which must not be mistaken for an encysted hydrocele. These different varieties, encysted hydrocele of the cord, and hydrocele of a hernial sac, often complicate simple hydrocele of the tunica vaginalis. Another series of cysts were long confounded with simple hydrocele, they are the *spermatic cysts* (*spermatic hydrocele*), which are generally found in the upper part of the testis near the epididymis. These cysts, which are sometimes very large, are filled with a cloudy fluid containing living or altered spermatozoa, and epithelial cells resembling those of the normal spermatic ducts. They sometimes open into the vaginal cavity, which is often the seat at the same time of a hydrocele: they

may also be ruptured or injured by the trocar in opening a simple hydrocele. Their mode of formation has given rise to a hypothesis regarding the new and independent formation of cysts (Paget). According to Gosselin, Luschka, &c., they are considered to be caused by the dilatation of previous ducts. Their seat is precisely the spot where the ducts of the testicle and of the epididymis, separately developed in the embryo, afterwards unite; it is here also that are found the tubes, no longer used, which are derived from the Wolffian body, and which now constitute the organ of Giraldès. Besides all these various cysts met with in hydrocele, œdematous infiltration of the connective tissue of the vas aberrans of Haller and of the organ of Giraldès, or an actual cystic dilatation of its ducts, is often found.

Hæmatocele.—We have already said that the tunica vaginalis may be the seat, in chronic hydrocele, of vascular pseudo-membranes arranged in thick or superimposed fibrous layers, and which may sometimes show ecchymoses. As the result either of friction or contusions of these tumours, blood is often effused into the tunica vaginalis. Gosselin has made out the pathogeny of this affection ('Arch. Gén. de Méd.,' 1851). The tumour formed by this effusion of blood is hard and non-fluctuating; the thickened fibrous tunica vaginalis is filled with a chocolate-coloured fluid, the brown colour being caused by the decomposed red blood corpuscles. On the surface of the serous membrane are blood clots and coagulated fibrin. Under the microscope, the fluid is found to contain fibrin, red blood corpuscles, swollen endothelial cells containing blood pigment and fat granules; crystals of cholesterin are also often present. If the hæmorrhage occur in a tunica vaginalis which was previously affected with hydrocele, the fluid is blood-stained, but the fibrin does not coagulate. The testicle is then generally atrophied under thick layers of false membranes. An effusion of blood may also take place in a cyst of the cord. Infiltration of blood may sometimes, though very rarely, be observed, in the testicle itself, *intratesticular hæmatocele.* We examined with Coyne two cases in which the following conditions were present. There was in the tunica vaginalis an old and very large hæmatocele. In the centre of the testicle an old clot was found, it was partly decolourised and the size of a small apple; this clot was traversed by vessels with thickened walls. In its peripheral layers seminiferous tubuli were found. The tissue of the testicle which was immediately contiguous showed the lesions

of parenchymatous or interstitial orchitis, characterised by an abundant development of round embryonic elements.

Tumours of the Testicle.

Chondroma.—Chondroma of the testicle is not very rare; it is generally the result of contusions and wounds. Hyaline cartilaginous tissue is easily recognised, from its naked-eye and microscopic characters, in the form of more or less voluminous nuclei, or as a diffuse infiltration. It is usually seated in the gland itself, but it may also invade the epididymis, either primarily or subsequently. The testicle is increased in size; in some cases, it may be very large, but the cartilaginous tissue is then found in the midst of fibrous or sarcomatous tissue which is riddled with cysts; chondroma is, in fact, often a complex tumour. From a number of cases collected by Paget, L'Honneur and others, and analysed by Virchow, it has been shown that cartilage may be developed inside the lymphatics of the testicle and take the ramified form of these ducts. In one of these cases, reported by Paget, the growth extended along the spermatic cord, the iliac glands, the lymphatics and the inferior vena cava, into which a cartilaginous mass projected, as far as the pulmonary artery and the lung. In secondary tumours of the same kind the latter were found.

Fibroma.—Besides the hard and frequently calcified fibromata which are developed on the parietal surface of the tunica vaginalis or on the surface of the thickened tunica albuginea in hydrocele, fibroma of the testicle is rarely met with. Fœrster, however, quotes a case, observed by himself, in which a fibrous tumour, developed in the tunica albuginea, projected into the substance of the testicle. Similar cases are rare and are not of any great interest.

Sarcoma.—Simple sarcoma with cystic formation is rare. Virchow ('Treatise on Tumours') gives a description based on a small number of cases. It is seated either in the testis itself or in the epididymis; the gland is uniformly increased in size; the tunica albuginea is unaffected, and the tunica vaginalis contains a little fluid. On dividing the tissue, it appears to be soft, fleshy, vascular, homogeneous, and often shows extravasations of blood. Examined under the microscope, the tumour seems sometimes to resemble myxoma by its ground substance, which is disseminated with fusiform cells, and sometimes encephaloid sarcoma by reason of its small round cells. Fatty degeneration, and extravasation of

blood often give a caseous appearance to more or less extensive masses of the tumour. In a case reported by Lebert, there were secondary growths in the lymph glands, as far as the glands of the neck and pleura. In another form of sarcoma which is often combined with chondroma, the tumour is riddled with cysts of different sizes. This is **cystic sarcoma**, which after remaining localised, breaks through the tunica albuginea, is propagated like a malignant tumour and forms secondary growths. Cystic neoplasms, described under the names of cystic disease of the testicle (Astley Cooper), cystic disease (Chassaignac and Richelot, Gosselin and Peter), belong to this variety of tumour by their nature, structure and prognosis. In reference to a case of cystic disease of the testicle, which has been very well analysed and which had nothing in common with sarcoma,[1] Malassez concludes that this was a case of a peculiar form of epithelioma, to which he purposes to give the name of *myxoid epithelioma*. In a large cystic sarcoma, the fibrous or sarcomatous tissue, which is fasciculated in places, embryonic in others, and with islets of chondroma often disseminated through it, is interposed between the seminiferous tubuli and cysts. The latter vary in size from that of a millet seed to that of a small nut, and they are filled with a serous or colloid fluid. The tumour is at first limited by the tunica albuginea, within which are found unaltered parts of the testicle. More rarely, it commences in the epididymis. According to the histological descriptions given by observers and by Fœrster in particular, the cysts are caused by enlargement of the seminiferous tubuli; they are lined internally by an epithelium undergoing mucoid degeneration, which becomes detached and fills the cystic cavity. The cysts then contain a homogeneous and mucoid fluid. On enlarging, their contents sometimes become quite fluid. Their walls give origin to papillary excrescences lined by an epithelium. The contents of the cyst, instead of being mucous or serous, may approach the caseous contents of dermoid cysts. The epithelium of serous cysts is sometimes formed of flat cells and sometimes of cylindrical cells, which may be ciliated. Finally a new formation of striated muscle fibres may be found in the stroma. In many cases of simple chondroma and of cystic sarcoma complicated with chondroma, Nepveu has traced the process of enlargement of the seminiferous tubuli, and has noted the existence of small pearl-like globes in the cavity of the enlarged tubuli. These globes are composed of horny epithelium.

[1] *Archiv. de Phys.*, 1875, p. 122.

It is probable that under the name of cystic sarcoma, tumours which do not resemble one another by their structure and course have been confounded, and that a stricter analysis will doubtless establish important differences between them. This is what Malassez has already done. In a case which he has published, cystic growths, located in the centre of the testicle, were completely isolated from the parenchyma of the testis, which was pushed against the tunica albuginea in the midst of a sclerotic connective tissue. These cysts were of the size of a pea or small nut and were situated in a connective tissue which was almost normal, but which contained, however, a few lymph cells between its fibres, also a few smooth muscle cells. The internal surface of the cysts was smooth or showed prominent villosities, and was lined with cells varying in form, polygonal or flat, cylindrical or caliciform, or ciliated cylindrical. These various cells were united into groups in the same cavity. The cells, contained in the mucous or serous fluid of the cysts, were of the same various forms as the parietal cells; many of them were, however, round, and in a state of fatty degeneration. At no spot was Malassez able to find indications of the change of normal seminiferous tubuli into cysts. On the contrary, the cysts showed no analogy with the seminiferous tubuli, whence he concluded that there is here a new formation of epithelium and of cavities filled with mucoid epithelium, and he proposes to give the name of *myxoid epithelioma* to this and to similar cases.

Tubercle.—Tuberculosis of the testicle may be the first manifestation of tuberculosis of the genito-urinary organs, when there are as yet no pulmonary lesions. It may commence in the testicle, but most frequently it is the epididymis or the vas deferens which is the first affected. Very small miliary granulations, hardly visible to the naked eye, are sometimes seated in the tunica vaginalis or in the testicle itself, or they surround the spermatic ducts. These granulations, which are semi-transparent at first, finally become caseous at their centre. It cannot be doubted that the granulations develop at their commencement around the spermatic ducts. In one case, Malassez withdrew the spermatic ducts and found that they showed a swelling at certain points, a little nodule which surrounded them entirely, and that this nodule was nothing else than a tubercular granulation. On examining the ducts at these nodules, he found that the lamellæ of the proper membrane of the duct were separated by an abundant deposit of small lymph cells, so that the membrane was much thickened.

At the same spot, the lumen of the tube was enlarged and not diminished as might have been thought *a priori*; the epithelial cells were granular and were united to one another by a granular substance. On section of a testis infiltrated with these tubercular granulations undergoing development, an accumulation of small lymph cells was seen forming a circular zone around a seminiferous duct, the enlarged cavity of which was full of epithelial cells undergoing caseous change. The lymph spaces and blood vessels comprised in the tissue of the granulation were filled with a fibrinous coagulum including lymph cells and endothelial cells. The connective tissue of the intertubular septa also contained lymph cells around the granulation, the tissue of which was imperceptibly lost in the neighbouring parts. On dividing larger sections, a central caseous part could still be recognised which corresponded to the lumen of a canaliculus full of cells, while in the peripheral zone of proliferation, the seminiferous tubuli were atrophied by compression and narrower than in the normal condition. Tizzoni and Gaule, in a more recent work on tubercle of the testicle, conclude that the affection commences by a new formation of the epithelium of the tubuli. Giant cells are generally observed in the tubercular masses of the testicle, where they show the same arrangement as in all other tubercles. They often originate in the lumen itself of the tubuli of the testicle. When the tubercular masses of the testicle become larger and unite into groups, their centre becomes caseous and softens. This softened and suppurating central part always corresponds, at the commencement, with the lumen of an enlarged seminiferous tubule; but when this cavity extends by ulceration, all the tissues, which become caseous at the centre of the tumour, indistinctly undergo molecular disintegration. It is not rare to see many caseous centres unite to form a single cavity. The bacilli are sometimes very few in number in tubercles of the testicle which have existed many years. Tubercles, such as are described above, do not, however, always commence in the testicle itself; generally they are localised first in the epididymis, the *rete testis* or in the vas deferens. In the latter and the epididymis, they are found in the form of numerous nodules along the duct. These large nodules, which double or triple the diameter of the canal, are oval or spherical in form, and consist of an infiltration of the proper wall of the duct by small lymph cells, at the same time that the epithelial lining of the mucous membrane proliferates, and granular cells fill the detached lumen of the duct. Thus is produced in a larger duct the same lesion as in the seminiferous tubuli. The

yellow caseous contents of the duct soften, and at a given moment its walls show suppurative destruction with caseous ulceration. At the same time, chronic inflammation of the neighbouring connective tissue takes place, by means of which adhesions are produced between the diseased parts and the skin. Thus open cutaneous fistulæ are established in the scrotum, communicating either with the epididymis and the cord or with the testicle. Tubercle of the epididymis and the cord are often complicated with tubercle of the seminal vesicles, the prostate and bladder, in fact, with the whole of the genito-urinary system. The lesion is often propagated to the neighbouring lymph glands, and finally to the lungs, which are generally attacked consecutively.

Syphilitic gummata.—We have already described syphilitic orchitis on p. 567; it remains to us to speak of gummata of the testicle which always accompany interstitial orchitis, or peri-orchitis, that is to say, fibrous thickening of the tunica albuginea and the tunica vaginalis, frequently with close union of the two layers of the serous membrane. The syphilitic testicle, such as is observed in the adult, is in section of pinkish-grey colour, and shows fibrous tracts and white spots. It is firm, fleshy, and the tubes cannot be drawn out. Yellow caseous masses are seen moreover of the size of a pea or small nut, irregular in form, with sinuous or eroded edges, which cannot be torn with the finger nail. These gummata are often surrounded with a fibrous zone. They are never softened nor changed into a cavity full of detritus and pus. According to the classic description of Virchow, the fibrous fasciculi which form the tissue of the testicle are the centre of development of gummatous growths. Malassez and Reclus have recently shown the anatomical relation between a certain number of syphilitic testicles ('Archiv. de Phys.,' 1881), in which they studied the way in which gummata developed. Between the fibrils of the newly formed connective tissue which separates the tubuli of the testicle are small round cells, and others which are large and granular and contain one or more nuclei. From place to place there are small inflammatory nodules, some of which are composed of round cells (lymphoid nodules) and others of large granular cells (epitheloid nodules). Many contain both large and small cells. These nodules, which constitute so many small gummata, are similar to those already described in the syphilitic liver. By their union they form conglomerate nodules. According to Malassez and Reclus, they implicate the surrounding tissue and cause a more or less marked sclerosis.

The seminiferous tubuli are compressed and atrophied; the external part of their membrane thickens and becomes fibrous, blends with the neighbouring connective tissue, and contracts, while the internal basement membrane thickens and becomes wrinkled and folded. Their diminished lumen only contains a few epithelial cells in a state of fatty degeneration. This atrophy ends by changing the tubuli into fibrous cords. At the same time the capillaries, arteries and veins become surrounded by connective tissue and their calibre diminishes. The small arteries and veins near to the gummatous islets are affected with chronic inflammation of their middle and internal coats with narrowing of their vascular lumen. The disturbance of the circulation resulting from this state of the blood vessels and the insufficiency of the blood supply are the cause of more or less extensive necrosis of the gummatous growths, necroses which may be compared to syphilitic necroses of the bones. The yellow mortified parts become encysted in a fibrous shell. According to Malassez and Reclus, gummatous nodules are the point of departure and the cause of interstitial fibrous orchitis. If we compare the genesis of tubercle with that of gummatous nodules, we see that the former surround the tubuli of the testicle and cause their dilatation and suppuration, while the latter never have, on the contrary, a seminiferous tubule in their centre, and they cause atrophy which ends in changing the tube into a fibrous cord. Tubercles produce foci which have a tendency to soften, suppurate, and open by means of fistulæ, while gummata tend to caseous induration, and a mummification which shows no tendency to soften. Gummata, moreover, are found much more often in the epididymis and cord, than in the testicle, while the contrary is observed in tubercle. Syphilis of the testis may be present in new-born children. Hutinel[1] has described syphilitic nodules or gummata similar to those described above, but in which caseous degeneration was not present. Syphilis of the testicle, by reason of the complete closure and atrophy of the seminiferous tubuli by connective tissue, entirely destroys its functions.

Lymphadenoma.—The first case of lymphadenoma of the testicle was made out by Malassez; since then many similar cases have been published. The tumour is formed of typical retiform tissue, the meshes of which are filled with lymph cells. This tissue, which replaces the connective tissue of the testicle, forms thick bands around the seminiferous ducts. The walls of these ducts

[1] *Revue mensuelle de Méd. et de Chir.*, 1876.

themselves are changed into a close adenoid tissue, and their lumen is more or less contracted. In their centre may, however, be distinguished a narrow lumen, in which one or more layers of indifferent cells are found replacing the epithelium (*n*, fig. 225).

FIG. 224.—SECTION OF LYMPHADENOMA OF THE TESTICLE.

a, *a*, lumen of the seminiferous tubuli. All the tissue belonging to the wall of these tubuli and the connective tissue proper of the testicle are changed into a retiform tissue, as is well shown in fig. 225 drawn under a higher power. Magnified 40 diameters.

Carcinoma.—Carcinoma is one of the most common of the tumours of the testicle; it is developed primarily and is scarcely ever secondary. The tumour only occupies one testicle. It commences either by disseminated nodules or by a diffuse infiltration, which extends rapidly and attains a considerable size, which may vary from that of a fist to 4 or 5 lbs. weight or even 9 lbs. (Boyer). The tumour generally commences in the testicle, but the epididymis is almost always altered at the same time. The new tissue first appears around the seminiferous ducts, in the connective tissue of the gland which is changed into carcinomatous stroma. In the diseased part, the seminiferous tubuli are atrophied and choked by the new growth. At the centre of the tumour, in the part which has been the longest and the most diseased, not a trace of them is found. When the tumour commences in the centre of the testicle, in the *rete testis* or in the corpus Highmori, at a point at its periphery under the tunica albuginea, a grey and opaque layer is generally seen, which may

be pinker than the carcinomatous tissue, and which is formed by crowded and compressed seminiferous tubuli. These tubuli are

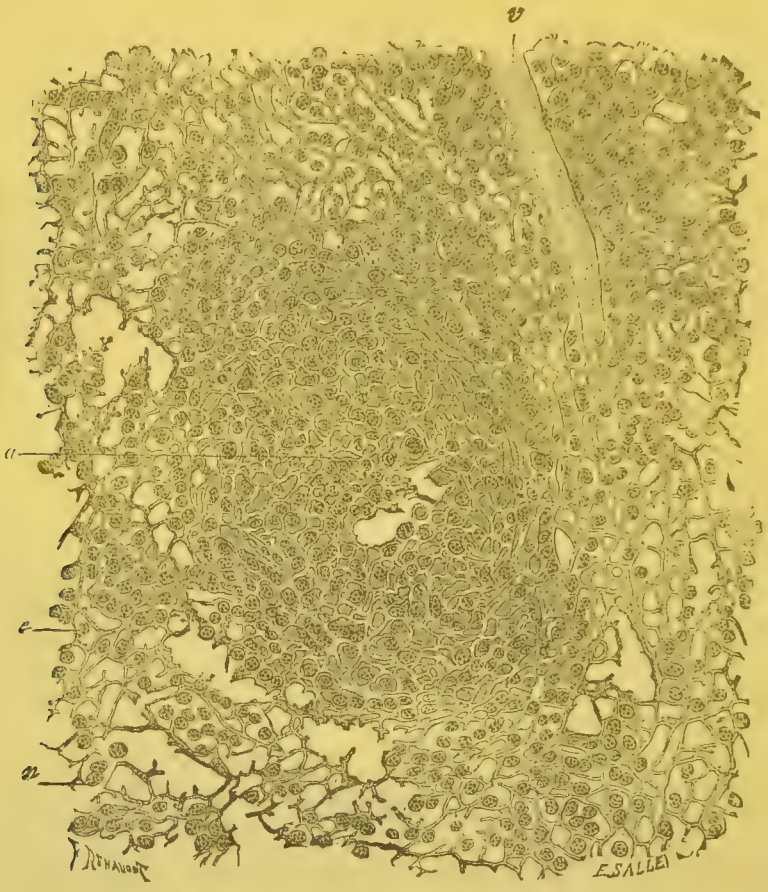

FIG. 225.—SECTION OF LYMPHADENOMA OF THE TESTICLE, PASSING THROUGH A SEMINIFEROUS DUCT.

a, section of a seminiferous duct the wall of which is thickened and changed into adenoid tissue; in its narrowed lumen are a few lymph cells; *c*, fibres of the retiform tissue; *n*, lymph cells. (After a preparation by Malassez.) Magnified 300 diameters.

themselves atrophied and are surrounded by a highly vascular connective tissue, from which they cannot be detached. The tunica albuginea is generally preserved intact, but is distended and thinned by the new growth which it encapsules. At a certain moment, however, the tunica albuginea is invaded by the neoplasm, and on the tunica vaginalis are seen excrescences of the same character; at the same time the epididymis, the cord and the pelvic and retro-peritoneal lymph glands are affected. Though, according to our own observation, it seems to us that the seminiferous tubuli are never the starting point of carcinoma, yet we must say that Birch-Hirschfeld has isolated, by means of a 15

per cent. solution of hydrochloric acid, seminiferous tubuli which showed nodular swellings, and which rapidly become enlarged on penetrating the morbid mass. According to this author, carcinoma of the testicle develops by means of a new formation of epithelial elements inside the seminiferous tubuli. We have not observed this mode of development, and we believe that carcinoma is developed in the testicle by swelling of the connective tissue cells and the new formation of large cells which fill the lymph spaces. The most common variety of carcinoma of the testicle is the encephaloid. On section its surface is seen to be white, pasty, and soft, and it yields on pressure or by scraping a large amount of milky juice. It is impossible to mistake the naked-eye appearance of such a tumour with sarcoma, which gives no milky juice except when in a state of cadaveric decomposition. There is also a marked development of the capillaries in an encephaloid tumour, so that it is sometimes called hæmatoid carcinoma, in which case it is very friable and its connective tissue slight. Scirrhus is extremely rare, so much so that its presence in the testicle has been denied by some authors. Nepveu has examined and published a case of this kind. Melanotic carcinoma has been observed as a secondary growth in the testicle. In many cases of tumours published some years ago under the name of cancer of the testicle, with insufficient histological details or even without microscopic examination, the presence of cysts has been mentioned; in other more recent cases, the coexistence of carcinoma with cystic sarcoma has been described, and it has been admitted that sarcoma may be transformed into carcinoma.

The testicle may be the seat of **dermoid cysts**, but they are pathological rarities here. Coexistent with sarcoma, striated muscle fibres have also been found (Schuh, Billroth, Rokitansky, Sanftleben, Nepveu) and smooth muscle fibres (Rindfleisch, Malassez, &c.) There are also a few rare cases recorded of **hydatid cysts** with echinococci developed in the epididymis and the tunica vaginalis.

CHAPTER IV.

THE PROSTATE.

I. Normal Histology.

The prostate is an organ composed chiefly of smooth muscular fibres and connective tissue; in the latter are situated glands which open on the sides of the verumontanum, in the radiating folds of the urethral mucous membrane. At the lower part of the prostate, along grooves in the gland, are conducted the ejaculatory ducts which open into the lower part of the prostatic portion of the urethra. The verumontanum, or crest-like projection directed from above downwards in the middle of the prostatic portion of the urethra, has a slit-like median depression which leads into a duct situated under the verumontanum, and which has received the name of the prostatic utricle or the male uterus. The glands of the prostate, which open by ten or twelve ducts on each side of the verumontanum, are remarkable for the length of their ducts and the small number and tenuity of their saccules. These glandular vesicles are lined by a layer of cylindrical or polygonal epithelial cells which contain brown pigment granules. The prostate has been compared to the uterus. It resembles it in its muscular structure, but it differs from it in that the glands are situated in the muscular tissue itself. It would be more logical to compare the prostatic utricle to the uterus, in which the fibro-muscular tissue is distinct from that of the prostate, and gives passage to the vasa deferentia, which may justly be compared to the oviducts of the female.

II. Pathological Histology and Anatomy.

Inflammation.—Inflammation of the prostate occurs most frequently in hæmorrhagic catarrh of the urethra and neck of the bladder, but it may also be spontaneous or traumatic. It is acute or chronic, often with the formation of abscess. It is the latter

variety which is seen in autopsies, for patients do not succumb to non-purulent prostatis, and hence we are obliged to formulate hypotheses as to its nature. It is supposed that the gland is congested and œdematous, and that it secretes a rather considerable quantity of mucus mixed with pus cells, and that the glandular ducts and saccules take an active part in the inflammation. Prostatic abscesses, which are the most frequent sequelæ of chronic inflammation of the mucous membrane of the genito-urinary organs, are sometimes small and more or less numerous, but sometimes they are large. The whole prostate may be changed into a large sac full of creamy, thick caseous pus, if the lesion has lasted some time. These abscesses may remain pent up in the prostate for rather a long time ; they may even become surrounded by a dense cystic wall infiltrated with calcareous salts. At other times, they open into the urethra, which is what generally happens ; but they may also open into the bladder, vesiculæ seminales, or the peritoneal cavity.

Tumours.—Myoma.—The increase in size of the prostate is a physiological fact due to the progress of age. The veins of the prostate and of the whole of the perineum dilate; the fibro-muscular tissue of the gland becomes thicker and denser, the glandular vesicles hypertrophy and multiply, and the prostate enlarges, either throughout its whole mass and regularly, or in some of its parts, in its right half or lobe, or in its left lobe, or in its middle part which is improperly called the median lobe.

Calculi.—Prostatic concretions or calculi are often met with in old persons. They are formed inside the glandular saccules and ducts. In diameter these calculi vary from 4 to 5 μ to $\frac{1}{2}$ and even 1 mm. The smallest of them are round or oval in form, refractive, and colourless, and they are composed of a hard colloid substance which is crushed with difficulty. On applying tincture of iodine, or iodine and sulphuric acid, they show the same reactions as amyloid bodies, so that Virchow describes them as the products of amyloid degeneration. The larger calculi are more resistant, yellow, or black or brown yellow in colour. They show concentric layers, and to the central nucleus layers of oxalate or phosphates of lime may be added, and they then become much larger. The glandular saccules and ducts, dilated by the presence of calculi, are filled with a mucous fluid, so that when the prostate is the seat of a large number of calculi, which is not unusual, it is at the same time changed into a collection of cavities. The dilated

saccules of the prostatic glands are then lined with a polygonal and cylindrical epithelium forming many thick layers, as is the case in the principal ducts and in the urethral mucous membrane. These calculi remain *in situ* and cause no symptoms, or they are evacuated by the dilated excretory ducts, thus causing inflammation of the prostatic ducts or of the urethra.

General or partial hypertrophy of the prostate may be classed among myomata. It is due to the new formation of a very dense, grey or pinkish white tissue, which consists of smooth muscle fibres and of newly-formed connective tissue. The prostatic glands are, however, also increased in size, and their cellulo-muscular tissue is increased and new glandular saccules are formed, so that these tumours may be looked upon as mixed tumours or adeno-myomata.

Hypertrophy.—General hypertrophy of the prostate, resulting from the formation of new fibro-muscular tissue, is usually irregular. It produces elevations and projections on the surface of the gland, which often raise the urethra, and are an obstacle to micturition and catheterisation. The increase in size is not always symmetrical, and hence a lateral displacement of the urethra may be produced. Partial hypertrophy is characterised by the projection on the surface of the prostate of one or more protuberances of the same nature as the preceding. They are formed of connective and muscular tissue, which is generally developed around hypertrophied glandular acini.

Tubercles.—Tuberculosis of the prostate accompanies that of the genito-urinary organs. The granulations are developed in the connective tissue, near the ducts of the glandular saccules; they are discrete or grouped and do not differ from those of other organs. The caseous softening and ulceration of the glandular ducts, and the central suppuration which result, produce large cavities, which sometimes open by means of fistulous passages into the bladder or rectum.

Carcinoma.—Carcinoma of the prostate is very rare, whether it be primary, or secondary to a primary tumour in the rectum. It is most frequently of the encephaloid variety. The diseased prostate projects on the side of the urethra, and raises the neck of the bladder as occurs in simple hypertrophy. The walls of the bladder may be also subsequently attacked and degenerated at a corresponding spot. According to O. Wys, carcinoma commences by the new formation of cells derived from the epithelium of the glandular tubules, the stroma remaining almost passive.

CHAPTER V.

THE OVARY.

I. Normal Histology.

In the ovary two substances are distinguished, the cortical and the medullary. The cortical substance consists superficially of a single layer of small cylindrical cells, and a connective-tissue layer containing a great number of small cells. The latter, described under the name of the tunica albuginea, envelopes the entire organ and accompanies the vessels which penetrate at the hilum. It is continuous, without line of demarcation, with a layer of less dense and greyish connective tissue, which is absent at the hilum; it contains the primordial follicles. These latter, which are present in children and young women in considerable numbers, are composed of a proper membrane lined with an epithelium; each one of them contains an ovule. The smallest of these follicles or vesicles are represented solely by the ovule surrounded by a layer of cells which are in immediate contact with itself. But on approaching the medullary substance, the follicles enlarge, become filled with a fluid and form larger capsules, visible to the naked eye and which are called the **Graafian vesicles.** These vesicles are always present in large numbers in young children, as well as in girls at puberty and in women. They have a wall formed of two layers; the external fibrous layer blends with the ovarian stroma; the internal layer is formed of a retiform tissue containing in its meshes numerous cells varying in form. The internal surface of the vesicle is lined with an epithelium (Slavjansky), which serves to support the numerous layers of pavement epithelium which constitute the *membrana granulosa.* There is a thickened spot in the membrana granulosa called the *discus proligerus*, in the midst of which the ovule is found. The ovule is situated in that part of the vesicle which is farthest from the ovarian surface. The rest of the cavity of the vesicle is filled with a fluid holding a few cells in suspension.

The **ovule**, isolated from the cells of the discus proligerus, appears as a large spherical cell, measuring from 0·1 mm. to 0·2 mm. in diameter, and hence is visible to the naked eye. It is surrounded by a capsule, the vitelline membrane, which is very thick and is traversed in some animals by plainly marked porous ducts. The viscous mass of the cell, called the vitellus, contains proteic and fatty granules. The nucleus of the germinal cell or vesicle (Purkinje's vesicle) is also perfectly spherical, from 20 μ to 48 μ in diameter, and it contains many nucleoli called germinal spots. The Graafian follicle, when it is completely developed, that is when it has attained a centimetre, for example, in diameter, projects on the surface of the ovary, when it bursts and throws its contents into the Fallopian tube. It is, however, an error to suppose that every Graafian follicle opens thus on the surface of the ovary, for a number of follicles undergo involution and atrophy, both before and after menstruation; while on the other hand it appears to be proved that the discharge of an ovule may take place without menstruation, in consequence of ovarian congestion caused by an acute fever (typhoid fever, variola, &c.), and also that impregnation and pregnancy may take place in certain cases without menstruation, or after the menopause, or without there being any return of menstruation. In spite, however, of these exceptional cases, it is an established fact that menstruation generally corresponds with the passage of an ovule by the Fallopian tube into the uterus. The primordial follicles, containing the ovule, are derived from peculiar glandular cords (the tubes of Pflüger or Valentin), which are present in the ovary in the fœtal state. These cords are formed from the germinal epithelium on the surface of the ovary, and at the moment of birth their communication with the germinal epithelium can still be made out. They are composed of small epithelial cells, which represent the membrana granulosa of the Graafian follicles, and in their centre are a number of rudimentary ovules. In consequence of the development of these cells, which are continuous with one another and with the surrounding connective tissue, these cords become divided into very small isolated segments. Each segment contains an ovule surrounded by its zone of epithelial cells, which constitute the ovisac.

When the Graafian follicle has emptied its contents into the oviduct, it undergoes a new series of changes, in consequence of which it becomes a yellow body or a **corpus luteum**. These bodies vary according as it is a case of an impregnated ovule or one of

simple menstruation. The corpora lutea of pregnancy undergo change very slowly and attain a considerable size. They project on the surface of the ovary, where the cicatrix and rent caused by rupture of the follicle can be seen. On cutting across the ovary at this spot, a circular or oblong cavity may be seen, which attains its largest size two or three months after impregnation, and which is filled with coagulated blood or with a blood-stained mucous fluid. It is bordered by a yellow or white wrinkled zone, which is thick and very vascular; more externally, at the junction of the corpus luteum with the stroma of the ovary, there is a white and very delicate fibrous membrane. The crumpled and yellow cortical layer is produced by considerable thickening of the internal or reticulated layer of the Graafian follicle. This thickening, in which the epithelium takes no part, is produced by a large number of connective-tissue cells. Most of them become actual giant cells, containing one or more large nuclei and a great number of fat granules. It is the latter which give the corpus luteum its yellow colour and its opacity. The new formation of cells is continued during the whole of the pregnancy, at the same time that the blood and the fat granules are reabsorbed.

Finally the corpus luteum diminishes in size and becomes denser. It measures at least 9 mm. in diameter at the time of parturition. Later it atrophies more and more, and forms a fibrous cicatrix which is white, yellow or black, but it does not disappear entirely. The various tints which it takes are due to changes in the hæmoglobin which it contains and which infiltrates its wall. When the corpus luteum coincides with simple menstruation, it is generally small from the commencement. The phenomena which take place in the follicle are the same as in the preceding case, but they are evolved more rapidly, so that the corpus luteum disappears entirely in the course of a month or two.

The medullary substance is formed of a dense fibrous tissue which is continuous with the round ligament, and which sends prolongations into the fibrous capsule of the organ. It contains blood vessels and large lymphatics, which pass into the ovary at the hilum. The arteries, which are helicine, intersect the central connective tissue, then pass to the surface of the ovary, following the fibrous fasciculi; the veins and lymphatics are solidly united to the connective tissue. The external fibrous membrane of the Graafian follicles contains a close network of lymphatics. The connective tissue of the medullary substance is provided with a very small number of smooth muscle cells. The nerves are derived

from the ovarian plexus and penetrate the organ, following the course of the arteries. Their terminations are unknown. The broad ligament is traversed, beneath the ovary, by ramifying and undulating tubes. These ducts contain a proper membrane and an epithelial lining. They are looked upon as vestiges of the Wolffian body from which the ovary was developed, and are known by the name of *the organ of Rosenmüller*.

II. Pathological Histology of the Ovary.

Hyperæmia. Hæmorrhage.—Congestion and hæmorrhage of the ovary are physiological mensual facts; menstruation and the dehiscence of a Graafian follicle are, in fact, accompanied by acute congestion followed by hæmorrhage. Ovarian congestion is also often present in the first period of acute fevers (Gübler). Congestion of the ovary is related to all the causes of congestion of the genital organs in the female, excessive coïtus, pregnancy, parturition and its sequelæ, metritis, &c. Traces of chronic congestion are observed in venous stasis from cardiac disease, and in the same cases, induration of the ovary may result from a new formation of connective tissue. Extravasation of blood may occur in very acute congestion of the ovary, during menstruation or between the menstrual periods, in diseases such as purpura, scurvy, typhus, variola, scarlatina, measles, &c. These hæmorrhages have been divided into follicular and parenchymatous. The former are seated in one or more Graafian follicles at the same time. The ovary remains large, and, on dividing it, many follicles are seen filled with coagulated blood in the midst of an indurated parenchyma. These follicles vary in size from that of a pea to a cherry, but they may be as large as a walnut or an egg. The coagulated blood, which distends them, is of a brown or blackish colour. These pathological productions are easily distinguished from the corpora lutea; in the normal condition there is never but one follicle which contains blood, that of the last menstruation, and its cicatrix is easily recognised on the surface of the ovary. Pathological hæmorrhage occurs, on the contrary, in two or three follicles of the same ovary or in both ovaries, and in the deeply seated follicles as well as in those on the surface. Follicular hæmorrhages often coincide with adhesions of the ovary with the peritoneum in chronic circum-ovarian peritonitis, and with the Fallopian tube, thus preventing the normal dehiscence of the

follicles. Callous thickening of the ovary is observed at the same time in such a case, and abnormal retrogression of the Graafian follicles, which are sometimes filled with a mucoid tissue (Slavjansky), and at others they become dropsical. When the ovary is free from adhesions, and the hæmorrhage takes place in a superficial follicle, rupture of its wall may result, and a more or less profuse hæmorrhage into the peritoneum (hæmatocele). Parenchymatous hæmorrhage may take place under the same conditions, in the midst of the connective tissue of the ovary.

Inflammation of the ovary. Ovaritis (oophoritis).—Primary inflammation of the ovary, independently of pregnancy, pelvic peritonitis or pyæmia, is very doubtful, and is at least exceptional. Ovarian hyperæsthesia, which is met with in some women and particularly in hysteria, does not correspond to any appreciable material lesions. During pregnancy, the phenomena which occur in the ovary resemble those of inflammation. Its parenchyma is tumefied and circulation is more active; this is probably due to the fact that the corpus luteum of pregnancy acquires such an unusual size. The organ is disposed, in consequence of nutritive changes, to a more or less acute pathological inflammation after parturition or after abortion. Thus it is in women recently delivered that acute inflammation is almost exclusively met with, accompanying metritis and circum-ovarian peritonitis. In subacute inflammation, the ovary is soft and impregnated with fluid, and its tissue infiltrated with lymph cells. The large Graafian follicles contain a milky fluid, which is often blood-stained, and contains a large number of epithelial cells and lymph cells. In more acute inflammation, in pelvic peritonitis after delivery, for example, severe congestion is found, and fibrinous new membranes are seen on the surface of the ovary with a number of lymph cells, collected into white lines or as small abscesses, in the stroma of the ovary. The fluid in the Graafian follicles simultaneously becomes sero-purulent. Finally, in the most acute puerperal metro-peritonitis, the ovarian tissue is highly congested and its follicles are generally filled with pus. When ovaritis is together with peritonitis limited to the lower part of the pelvis by fibrinous and connective-tissue adhesions, the ovary may be found in the midst of an abscess, which is either reabsorbed, or opens into the rectum, bladder, &c.; later on, the ovary may become closely united by fibrous membranes or filaments to the neighbouring organs, to the Fallopian tube or uterus, and its function may be destroyed. One of the sequelæ of chronic

interstitial ovaritis is the formation of hard and dense fibrous tissue, which is caused by repeated ovarian congestion and the retrogressive evolution of the Graafian follicles, which may be in fact changed into cicatricial tissue even after the menopause. In old women, the ovary is almost always hard and callous, its surface uneven and cartilaginous in appearance, its capsule is thickened and indurated like the fibrous capsule of the spleen, the cortical layer is absent and the Graafian follicles, or the corpora lutea of previous pregnancies, are only seen as cysts with fibrous, hard and contracted walls. These ovaries are either normal in size or atrophied.

Tumours.—Chondroma of the ovary has been observed twice by Kiwisch; in one of these cases, the right ovary was as large as a fist and was changed into a hard and hyaline cartilaginous mass. Scanzoni has seen a case of chondroma in the midst of a fibrous tumour.

Tubercles are very rare in the ovary; they are sometimes present in tuberculosis of the genito-urinary organs, particularly in children. The peritoneum which covers the ovary is often the place where they are found; tubercular granulations on the parenchyma are far less frequent. They show their usual characteristics, namely a semi-transparent granulation with a caseous centre.

Syphilitic gummata are equally rare. Lancereaux has, it is true, reported two cases, but without histological details, and he treats as syphilitic a dense fibrous condition of the ovary which he has several times observed in women who are still menstruating.

The secondary growths of **lymphadenoma** have been observed once by one of us.

Fibro-myoma is much less frequent in the ovary than in the uterus. It is sometimes seen in the form of small round tumours seated either on the surface or in the depth of the organ, or as large hard tumours the size of a fist or more, in which the ovary is changed entirely into a homogeneous mass. The fibrous tissue dominates, and smooth muscle cells are not numerous. In section, the connective-tissue fasciculi are seen to be irregularly arranged and do not radiate, as in fibro-myoma of the uterus, from one or more centres. Cystic cavities are sometimes found containing a clear or blood-stained fluid; their surfaces are often calcified.

Sarcoma.—Many cases of sarcoma, primarily developed in the ovary, have been of recent years brought before the *Société Ana-*

tomique. The tumour varies greatly in size ; sometimes the ovary remains stationary, at others it acquires an enormous size. In a case reported by Villard ('Soc. Anat.,' 1870, p. 195) the tumour, composed of an embryonic sarcoma with hæmorrhagic cysts, weighed 14 pounds. In other cases, serous cysts have been developed in the sarcomatous tumour. These ovarian sarcomatous tumours are generally oval and smooth. The two ovaries may be attacked simultaneously. If the disease lasts long enough, metastases may be observed in the peritoneum, pleura, intestine &c.

Carcinoma.—Among old cases of carcinoma of the ovary, there are certainly some which would be now classified among cysts and epithelioma. But carcinoma of the ovary exists nevertheless. It may be primary or secondary ; it may, in fact, be consecutive to carcinoma of the cervix and fundus of the uterus, the rectum or an organ further removed ; the new growth is then generally small and nodular. We have, however, frequently seen diffuse infiltration of the entire organ by secondary cancer emanating from the uterus. Primary ovarian carcinoma may attain a great size ; in some cases, for example, the tumour may be the size of a man's head or larger ; most frequently, it belongs to the encephaloid variety. Generally only one ovary is the seat of the tumour, but the other ovary may also be affected in a less degree. Medullary ovarian carcinoma forms a soft tumour, which is, however, generally firmer in texture than in other organs, in consequence of the fibrous structure of the ovary ; it yields on scraping a rather large quantity of milky juice, and on section its surface is white or greyish white and opaque. The fibrous capsule of the ovary is more frequently affected when the carcinoma is not quite recent, and on its surface growths and fleshy granulations are found composed of carcinomatous tissue. The peritoneum always participates in the degeneration of the ovary, and the tumour invades the pelvic cavity, the great omentum, and the appendices epiploicæ of the intestine. The tumour corresponds generally to the encephaloid variety of carcinoma ; the septa of the alveoli often contain smooth muscle cells ; the epitheloid cells are arranged without order in the alveoli, or they are implanted perpendicularly on their surfaces. The blood vessels sometimes acquire a considerable size in encephaloid as well as in hæmatoid carcinoma. In carcinoma of the ovary, as well as in other ovarian tumours, cysts are found ; they may be present from the commencement of the carcinoma or have preceded it. Buds, composed of the tissue of the tumour, project then into the cavity of the

cysts. Primary carcinoma is sometimes seen in the form of a colloid or scirrhous tumour. Secondary tumours of the ovary resemble the primary tumours in structure; thus, for example, cylindrical-celled or pavement-celled epitheliomata are consecutive to similar tumours developed in the uterus. The former may, according to Rindfleisch and Klebs, be developed primarily in the ovary. In a case reported by Klebs, the tumour having been extirpated, it recurred in the skin near to the wound.

Cysts of the ovary.—Of all the new growths and diseases of the ovary, the most frequent and the most important, both from their mode of development and their consequences, are cysts. The ovary and the kidney are the organs in which these growths show the greatest tendency to develope. We have already mentioned the cysts found in the tumours described above; it therefore remains for us to study cysts, properly so called; they vary greatly both as regards their nature and their development.

1. Dropsy of the Graafian follicles.—Rokitansky has shown that the Graafian follicles may become distended by a limpid serous fluid, so as to form small cystic cavities the size of a haricot bean or small nut. In an ovarian tumour composed of cysts of this size, Rokitansky found an ovule in each of them. Cysts produced by distension of the follicles are generally small; the ovarian tumour is then seldom larger than a closed fist.

2. Unilocular cysts.—Sometimes a single ovarian cyst is met with of large size; its wall is then formed simply by the peritoneum, a layer of lamellar connective tissue, and an internal epithelial lining. It might be thought that these tumours are caused by extreme dilatation of a Graafian follicle; but there is nothing to prove this; on the contrary, everything tends to show that these cysts are formed by the union of many pre-existing cysts and that they are developed by a peculiar cystic degeneration of the ovary, the description of which is given in vol. i. p. 299.

3. Proliferous cysts; gelatiniform or multilocular cysts; myxoid epithelioma.—Multilocular or areolar cysts generally contain a mucous fluid. They vary in size, but are usually large. They are more or less regularly spherical in shape, the secondary cysts making slight projections. These tumours are generally pediculated, the pedicle, which is rather thick, is formed by the retro-ovarian ligament which is enlarged and vascular, the ovarian artery being in particular very large. On dividing a tumour of this kind, it is seen that it is composed of many large cysts,

or loculi varying in size. When there is one large sac and the cyst seems to be unilocular, a thickening will always be observed at a point in its wall, generally near the pedicle, where small secondary cysts will be found in process of growth. Not a vestige

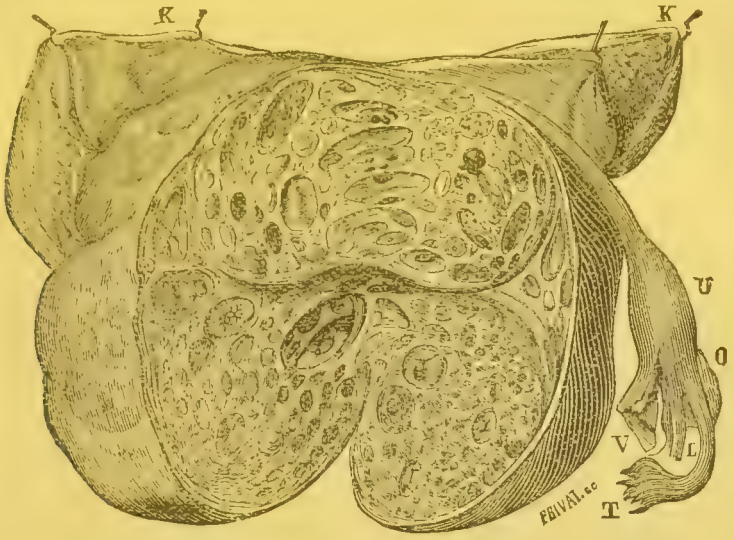

FIG. 226.—AREOLAR CYSTS OF THE OVARY (after Cruveilhier).

K, K débris of the walls of the principal cyst, which contained an areolar mass; U, uterus altered from pressure continuous with the right Fallopian tube, which is attached to the tumour; O, left ovary; L, left round ligament; T, left Fallopian tube; V, neck of the uterus and upper part of the vagina laid open.

of the normal ovary can be found. There are three distinct layers in the walls of the old cysts; the external and internal are fibrous; the middle layer, which is absent in places, is composed of loose connective tissue. The arteries, which are often helicine, are, as well as the veins, situated in the middle coat; the latter are, however, also found in the external coat. The veins are very large and have thick muscular walls, by reason of which they are often mistaken for the arteries. Their arrangement is similar to that of the sinuses of the dura mater. The lymphatics are numerous and are continuous with those of the broad ligaments. They have been studied by Malassez and Sinéty, by means of nitrate of silver injections. The muscular fasciculi are sometimes highly developed in the wall of a cyst. Externally the cysts are lined with a layer of low cylindrical epithelium, quite different from that of the peritoneum. The internal membrane of the cystic cavities, which is almost always the seat of papillary or warty growths, is lined also by an epithelium. According to Malassez and Sinéty,[1] from whose works we borrow most of the histological

[1] Sinéty, *Traité Pratique de Gynécologie*, 2nd edit. 1884. O. Doin, publisher.

details concerning these tumours, this epithelium is implanted on an endothelial layer, and its cells often undergo mucoid degeneration either partially or entirely; some become caliciform with a nucleus at their root, and their cavity contains and constantly

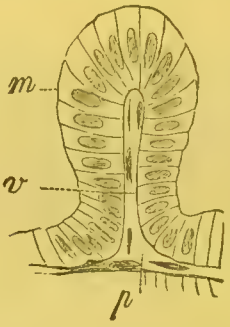

Fig. 227.—Granulation from the Internal Surface of a Cystic Cavity.

v, blood vessel and connective tissue of the papilla, *p*; *m*, cylindrical epithelium. Magnified 300 diameters.

secretes mucus; others become spherical and hollowed by cavities containing mucus. On falling into the sac of the cyst, they become destroyed and the quantity of mucus is thereby increased. Ciliated cells are also sometimes met with. On staining the internal surface of a cyst with nitrate of silver, the open ends of the caliciform cells are plainly seen, and after brushing away these cells, the endothelial cells which are beneath them may be stained in the same way. By this process also, the epithelium of the capillaries of the wall of the cyst may be shown, and the superficial position of these vessels made out. The cysts contain a mucous or gelatinous fluid which is coagulated by alcohol, and afterwards swells and becomes again transparent by the action of water. The cells found here are arranged without order in the midst of a colloid mass, or they are found in parallel lines; these latter are either caliciform cells which have been desquamated in groups, or round cells, or branched cells with multiple processes resembling those of mucous tissue, though mucous tissue is not produced in the interior of cysts. Masses of cells are also found in a state of fatty degeneration. According to Méhu, this fluid contains large quantities of albumen, meta-albumen and para-albumen, and it is the latter substance which gives it its gelatinous consistency. Eichwald states having found albuminous peptone, mucin and mucous peptone. These different substances are the product of the filtration of albumen from the blood, and the peculiar elaboration of the caliciform cells. Exceptionally, sugar and urea may be found. The contents of cysts, the walls of which are lined

with highly vascular villosities, are often mixed with blood, which gives them a brown or chocolate colour; a great number of lymph cells may be present or actual suppuration, particularly after puncture or a wound. Cysts may communicate by a circular opening at the spot opposite that at which the principal arteries enter, that is to say where the wall is originally thinner and less vascular. There is nothing to prove that a cyst originally single may divide; on the contrary, adjoining cysts open into one another in consequence of thinning and rupture of the septa of separation. In tubo-ovarian cysts, described particularly by Richard, the cyst opens into the Fallopian tube which was previously attached to it by adhesions. The connective tissue which separates the cysts is itself usually the seat of small cysts in an

FIG. 228.—SECTION OF AN OVARY CYSTIC FROM A NEW EPITHELIAL GROWTH.

a, epithelium on the surface of the ovary; *b*, epithelial depressions; *c*, epithelial tube opening on to the surface of the ovary; *d*, cystic cavities varying in form and size; *e*, vessels; *f*, ovarian stroma. (Figure borrowed from Sinéty's 'Traité de Gynécologie.') Magnified 25 diameters.

early state of development; they resemble the large cysts in structure and project into the cavities of the latter on increasing in size. Fatty degeneration of the epithelium or walls is sometimes seen

in places. In none of the smallest of the cysts which are undergoing development, neither ovules nor discus proligerus are met with, which fact negatives the theory that these cysts are formed by distension of pre-existing Graafian follicles. We have already in vol. i. p. 301 described the growths on the walls of these cysts; we have also indicated (vol. i. p. 299) the mode of development of cysts which are first produced in the tubes opening on to the surface of the ovary (*c*, fig. 228), and those which are afterwards developed in their walls; these, according to Waldeyer, Malassez and Sinéty, are a peculiar form of epithelioma, myxoid epithelioma. When these cysts are old, or even during the period of growth, they may, in consequence of peritonitis, become closely united to neighbouring parts, the omentum, intestines, uterus &c., and it is this which renders the operation of ovariotomy more difficult. Generally only one ovary is affected, and constitutes the entire tumour; but at the same time the other ovary may already contain a few small cysts in a state of development, so that when the largest ovary has been removed, the other becomes in its turn the seat of a large cystic tumour. In very old tumours there is fibrous or cartilaginous thickening of their walls; the connective tissue is then encrusted with calcareous salts, and the cyst contains a white soft mass formed of cells in a state of fatty degeneration, calcareous granules and crystals of cholesterin. Tumours of this kind do not give origin to secondary growths. There have been, however, some exceptional cases in which they have shown the characteristics of malignant tumours with secondary growths in the uterus, rectum and peritoneum.

Dermoid cysts.—The ovary is the seat by predilection of Lebert's third variety of dermoid cysts; they are sometimes as large as a man's head, and contain hair, teeth &c. They have been already described in vol. i. p. 295. We have twice seen the wall of a dermoid cyst become the starting point of lobulated pavement epithelioma.

CHAPTER VI.

THE FALLOPIAN TUBES AND UTERUS.

I. Normal Histology.

The Fallopian tubes.—The two Fallopian tubes or oviducts serve to conduct the ovule, which they seize by covering the ovary when menstruation occurs, from the ovary to the uterus. These ducts have a peritoneal covering which surrounds them, a layer of fibrous and muscular tissue which forms their wall, and a central canal. The Fallopian tube consists of a funnel-shaped, fimbriated end which is connected with the ovary, and an inferior narrow part which pierces the muscular tissue of the uterus at the cornua of that organ, and opens by a duct so narrow that a bristle can hardly be passed into it. In its free part this duct is rather wide, and its mucous membrane is folded into rugæ, like that of the vas deferens; from the fimbriated extremity to the uterine orifice it is lined with a ciliated cylindrical epithelium. The motion of the cilia aids the passage of the ovule from the ovary to the uterus, but hinders that of the spermatozoa. The mucous membrane of the Fallopian tubes contains no glands.

The uterus.—The uterus is divided into the fundus or upper part, and the neck or cervix which opens into the uterus. A central passage passes from the apex of the fundus to the orifice of the cervix, which passage becomes narrower at the union of the fundus with the cervix. The uterus has very thick walls composed of small muscular fibres and connective tissue. It is difficult to follow and isolate the muscular fibres; the superficial layer is composed of longitudinal and transverse fibres. The former form a delicate layer which extends over the base and anterior and posterior surface of the organ; the latter, which are in thicker layers, are continuous with the round ligaments, the ligaments of the ovary and the Fallopian tubes. The middle layer, which is the thickest of all, is composed of longitudinal oblique and transverse

bundles intersecting one another. The internal layer, which is delicate like the external, contains intersecting fibres and bundles, which form the rings around the orifices of the Fallopian tubes. The transverse fibres of the cervix form an actual sphincter; in the cervix also very superficial fibres are found in the arbor vitæ. The muscular fibres of the uterus and Fallopian tubes are short during the period of inactivity; they are separated by a large quantity of dense connective tissue containing oval cells. The uterine mucous membrane is closely united to the muscular layer, from which it can, however, be distinguished by its lighter colour. Its corium is formed of connective tissue, and contains smooth muscle cells without elastic fibres. Its epithelial lining consists of a single layer of ciliated epithelial cells. The motion of the cilia is from without inwards. The glands of the mucous membrane of the fundus are simple tubes, like the glands of Lieberkühn. They are lined by a ciliated cylindrical epithelium and open on to the mucous membrane, either alone or two or three united together. According to Léopold, the glands and vessels of the uterine mucous membrane are surrounded by lymphatic sheaths which communicate with lymph spaces and they intercommunicate between themselves by cleft-like spaces. All these vessels open into a subperitoneal network, which covers the whole of the external surface of the uterus, one part of which is conducted into the larger lymph vessels of the broad ligaments. The mucous membrane of the cervix uteri, instead of being smooth like that of the fundus, shows granular rugæ which unite in the arbor vitæ; these rugæ are, like the rest of the mucous membrane of the cervix, covered with villi between which utricular depressions are found on the surface of the folds; between the folds are pits which contain, like the whole of the cavity of the cervix, a transparent and viscid mucus. Into these pits open rather large acinous glands (Sappey), which resemble sebaceous glands in shape; their saccules are lined with caliciform cylindrical cells and they are filled with a viscid mucus. The cervical mucus is produced by a peculiar elaboration and secretion of the cylindrical cells of the cervix itself and of its glands. Here, as in the intestine, the cells which secrete mucus are generally chalice-shaped, and are chiefly found in the flexures of the membrane, in the crypt-like depressions and in the glands. In the cervix, in the normal condition in young subjects, but more frequently in old women, the glands may be found to have undergone cystic dilatation, and to be full of a mucoid fluid, when they are called ovula Nabothi.

These bodies contain mucin and rods which might be mistaken for fibrils. The cervical mucus also contains mucin and rods as well as cylindrical oval, long or round cells in a state of mucoid degeneration. These cells may be found parallel to the rods or irregularly arranged; branched cells are also found. The vaginal portion of the cervical mucous membrane is changed both in appearance and structure; its connective tissue contains papillæ, which are pushed up into a stratified pavement epithelium. The hard excrescences, found on the surface of the vagina, are of the same structure, being nothing else than large papillæ covered by a stratified epithelium. The arteries of the uterus ramify in the muscular layers and in the mucous membrane, forming networks of capillaries. The veins are without valves; they are large with thin walls and follow the same course as the arteries. The lymphatics are very numerous; they spring probably from the mucous membrane and form close networks on the surface of the uterus under the peritoneum; they pour their contents into the pelvic and lumbar ganglia. The cellulo-vascular tissue of the broad ligaments contains smooth muscular fibres independently of the vessels (Rouget).

During **menstruation**, the marked increase in size of the uterus is due to the greater afflux of blood to its muscular tissue and mucous membrane. It undergoes, in fact, considerable enlargement some days before menstruation commences; it becomes softer, and utricular glands, measuring from 200 μ to 600 μ in length and 70 μ to 90 μ in width, can be easily isolated; swollen fixed cells, and even at some places giant cells, and numerous migratory lymph cells are found in the connective tissue of the œdematous mucous membrane. The blood vessels of the mucous membrane are also dilated and very numerous. The menstrual blood flows from the superficial network of the mucous membrane, for neither ecchymoses nor deep infiltrations of its tissue are found. It was thought for a long time that the whole of the surface, or at least the most superficial part of the mucous membrane, was eliminated. But the researches of Kundradt, Léopold and Sinéty have shown that the muscular coat of the mucous membrane is never denuded in menstruation, and that the whole of the mucous membrane remains intact. Cases in which glands and flakes of exfoliated mucous membrane are eliminated during menstruation are pathological. We have often examined these expelled products, which coincide with the condition known as *pseudo-membranous dysmenorrhœa*. They vary; sometimes they are simply

fibrinous clots which have been expelled with difficulty owing to a narrow os cervicis. This is frequently the case in nullipara; under the microscope, the fibrin is seen to be fibrillar, and to contain in its meshes a large number of lymph and epithelial cells; sometimes there are white irregular false membranes, composed of coagulated mucus and mixed with a certain number of lymph and epithelial cells. In other cases, however, irregular membranes are found containing capillaries with embryonic walls situated in a connective tissue infiltrated with lymph cells. Fragments of uterine glands or the entire glands are also frequently present at the same time. There is here an actual expulsion of a partly exfoliated mucous membrane. This elimination may be complete, which is, however, very rare, though M. Guyon has reported cases.

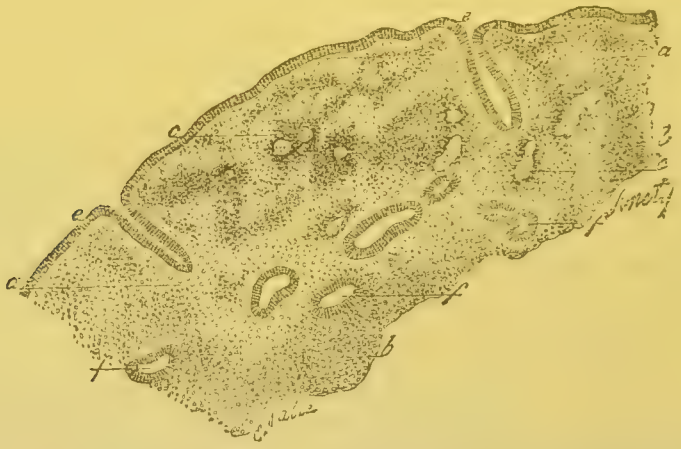

FIG. 229.—SECTION OF A FLAKE OF MUCOUS MEMBRANE EXPELLED DURING MENSTRUATION IN A CASE OF MEMBRANOUS DYSMENORRHŒA.

a, a, hæmorrhagic spots; *b, b*, parts infiltrated with embryonic elements; *c, c*, vessels filled with red blood corpuscles; *e, e*, epithelium on the surface of the mucous membrane dipping at places into the depth of the tissue to form the glands; *f, f*, glands lined with their epithelium cut across. (After Sinéty.) Magnified 40 diameters.

There is a third and less frequent series of cases connected with the débris of the decidua at the commencement of pregnancy. This form is easily recognised by the villi of the chorion of the ovum, which are very characteristic. The surface of the discharged membrane is villous, as may be easily seen under water with the naked eye; the villi are formed of branching cylinders containing blood vessels and lined with epithelium. If the membrane be discharged entire, a smooth part will be found or a cavity containing the ovum. We are convinced that villous dysmenorrhœa is always connected with the products of conception and the membranes of an embryo two or three weeks old. The changes which the uterus undergoes during *pregnancy* bear chiefly on the smooth

muscular fibres, the blood vessels and the mucous membrane. The marked hypertrophy of the muscular layer is caused by the increase in size of pre-existing muscular fibres, and by the growth of new fibres. The former become ten times longer and five times broader than they are normally. The production of new fibres takes place, chiefly during the first months of pregnancy, in the internal layers of the muscular coat. After conception, the mucous membrane also thickens and becomes smoother and redder, and the rugæ more prominent; it becomes infiltrated with embryonic cells at the same time that the glands hypertrophy (decidua vera). Near the ovum it becomes changed into the *placenta*. This placental portion of the mucous membrane gives origin to fleshy granulations, which extend all round the ovum and constitute the decidua reflexa. The epithelium of the fundus disappears entirely in the deciduæ. The mucous membrane of the cervix takes no part in these changes; it preserves its epithelium and secretes a mucous plug which fills the cervical canal during pregnancy. The smooth muscular fibres of the blood vessels hypertrophy, similarly to those of the muscular walls of the uterus. After delivery, the decidua vera is eliminated; the expulsion of the placenta leaves an open granulating surface which degenerates and is also expelled. On the internal surface there is then not a vestige of mucous membrane; it is a soft pulpy tissue, in which hypertrophied muscle cells, blood vessels and cells are found in the midst of an embryonic connective tissue. The cells found here are tumefied connective-tissue cells; they are flat, round, oval or branching, sometimes very large and granular, containing one or more nuclei, and are often in a state of fatty degeneration. The histological phenomena of regeneration of the mucous membrane have not been hitherto sufficiently studied; it probably takes place slowly, for the wound left by the placenta can still be recognised many months after parturition, by its fungoid appearance or by the grey infiltration of its tissue. Three months after delivery, Slavjansky has described papillary fleshy granulations and lymphatic infiltration of the superficial layer of the mucous membrane of the projecting part where the placenta was inserted. Both the mucous membrane and the papillary growths had no epithelium. The utricular glands were well formed and normal in arrangement, but in the most internal part of their course they were filled with round cells. The muscular fibres rapidly return to their normal size after being infiltrated with fat granules. It is probable that some of them are destroyed by fatty degeneration.

II. Pathological Histology and Anatomy of the Fallopian Tubes and the Uterus.

Congestion and hæmorrhage of the Fallopian tubes.—Hyperæmia, of the Fallopian tubes, simultaneously affecting all the different tissues of which it is composed, is observed in menstruation, after sexual excesses, and in acute affections of the uterus. Hæmorrhage into the mucous membrane of the Fallopian tubes, and effusions of blood into their cavity, are sometimes observed under the same conditions and in a series of other diseases. Thus Rokitansky reports two cases of hæmorrhage into the Fallopian tubes in typhoid fever, another in a woman just delivered who had died of pleurisy and hepatitis, and a fourth in retroversion of the uterus. Barlow has noted it in hæmorrhagic purpura; Scanzoni in menstrual congestion; Puech in a young girl ill of measles, who died from the hæmorrhage into the Fallopian tube having made its way into the peritoneum and set up general peritonitis. To these cases, quoted by Fœrster, we may add those of Royer and Godelle, analysed by M. Bernutz, which appear to him to be cases of rupture of the Fallopian tube in intratubular gestation. (See Peri-uterine Hæmatocele.)

Inflammation of the Fallopian tubes. Catarrhal salpingitis.—Catarrhal inflammation of the Fallopian tubes is very common, as the result of inflammatory or catarrhal affections of the genital passages after parturition, or when the uterus is empty. The tubes are distended and tortuous with irregular dilatations. This lesion is often accompanied with congestion of the ovary, and almost constantly with irritation of the adjoining peritoneum, an actual chronic or subacute adhesive pelvic peritonitis, and sometimes with acute and purulent peritonitis. The Fallopian tube is then generally fixed to one of the neighbouring organs; it almost always adheres to the uterus, to the lower part of the fundus or rather to the upper part of the cervix. The tumour, formed by the hypertrophy and adhesion of the Fallopian tube, can generally be felt by vaginal digital examination. In acute inflammation of the Fallopian tube, it may become as thick as the little finger or larger; its mucous membrane is very red, congested and thickened; its longitudinal folds are effaced, the infundibulum being blocked, and it is filled with mucopurulent or opaque fluid. On examining this fluid under the microscope, it is found to contain a large

number of granular cylindrical epithelial cells, which are more or less deformed, and are mixed with lymph cells. In sections of the wall, the cylindrical cells are found to be desquamated almost everywhere; the connective tissue of the mucous membrane is infiltrated with lymph cells, which are particularly numerous around the blood vessels. They form tracts around the muscular fasciculi, which do not, however, show any marked changes. Inflammation of the Fallopian tube reaches its maximum in puerperal metritis; it is then always complicated with phlebitis, lymphangitis, and general or partial peritonitis with false membranes infiltrated with pus and purulent effusion. In chronic inflammation, the Fallopian tubes always adhere to the adjacent organs, and the connective tissue of the mucous membrane is thickened and indurated; the contained fluid is sometimes clearer and serous, sometimes more opaque and caseous than in the preceding case. Dropsy of the Fallopian tubes ought to be looked upon as a form of chronic inflammation; the organ may attain the size of a child's head, and the canal may contain sacs or cysts placed one after another, the duct between the cysts being obliterated. It occasionally, though rarely, happens that the fluid in the Fallopian tube is evacuated by a large opening between the duct and the uterus, and is drained off by the vagina.

Tumours of the Fallopian tubes. Tubercles.—Tuberculosis of the Fallopian tubes is coincident with that of the genital organs in the female; tubercular granulations are found in the peritoneum covering the tubes, and in the submucous connective tissue. Acute catarrhal inflammation of the mucous membrane occurs at the same time. The duct dilates and becomes filled with pus, which is at first mucoid or muco-purulent, but which soon becomes caseous. Both in the mucous membrane and in the submucous tissue, the tubercles, and the embryonic tissue which unites them, undergo caseous degeneration. The tissue of the tube which is situated between the tubercular peritoneum and the thickened submucous connective tissue is itself infiltrated with lymph cells. These lesions cause considerable thickening of the walls of the Fallopian tube, and so much rigidity that it gapes on being cut across. The tube is enlarged and irregular, and is often folded on itself, and adherent to the uterus or the neighbouring organs. Cases, collected by M. Bernutz, Siredey, and Brouardel, most of which are published in the 'Recueils de la Société Anatomique,' prove that tuberculosis may commence in the Fallopian tubes.

Carcinoma.—Carcinoma of the Fallopian tubes is never primary, and generally follows that of the uterus. When carcinoma is limited to the cervix, the Fallopian tubes are nearly always intact. In a case of secondary carcinoma of the Fallopian tubes, we have seen the organ greatly enlarged, and its infundibulum, infiltrated on the side of the peritoneum with cancer, open and filled with milky juice. Peritonitis was also present, from which the patient succumbed. It was evident that carcinoma of the Fallopian tubes was the cause of the peritonitis; a few other cases of this kind have been reported. Generally, however, carcinoma of the Fallopian tube is induced by direct propagation of uterine carcinoma, complicated with that of the ovary. Rokitansky has observed cancerous growths in the lumen of a Fallopian tube filled with fluid.

Cysts of the Fallopian tubes.—Cysts developed around the opening of the tubes are very frequent, but they are generally small. Their mode of development is still unknown. There is, however, one which is found so often at the end of the fimbria of the tube, that it is looked upon as developed in the cæcal extremity of Müller's duct, a fœtal organ from which the duct of the Fallopian tube is developed. Another cyst which is often found beside the preceding, and which is inserted in the broad ligament, represents, according to Virchow, a vestige of the primitive excretory duct of the Wolffian body. These two cysts may sometimes grow as large as a cherry. Besides these cysts others are found developed in the tubes of the body of Rosenmüller, and some seem to originate simply in the subperitoneal connective tissue of the Fallopian tubes and the broad ligaments.

Peri-uterine inflammation.—There is no occasion to describe again localised peritonitis (*vide* p. 415); but peri-uterine inflammation plays such an important part in the pathology of the uterus, that we must give a short description of it. It may be localised: 1st. In the peritoneum of the true pelvis, or more particularly in those prolongations of the peritoneum which constitute the recto-vaginal pouch. This is **perimetritis** or **pelvic peritonitis.** The inflamed pelvic peritoneum is lined with false membranes, and covered by a sero-purulent effusion which is divided by fibrinous bands. The ovary and Fallopian tubes are also surrounded by false membranes, and are adherent to one another and to the uterus; later, the false membranes become organised, the

Fallopian tube often becomes dilated and its orifice obliterated. The muscular fasciculi of the external layers of the uterus undergo fatty degeneration; and the uterine mucous membrane is affected with chronic inflammation. The lymphatics of the inflamed uterus often appear to be the starting point of the pelvic peritonitis. 2nd. In the connective tissue which is limited above by the recto-vesical pouch of the peritoneum and below by the levator ani muscle; in fact, around the upper part of the vagina and the cervix uteri. This circum-uterine inflammation is very rarely seen on the post-mortem table, for the lesion is not serious. The tumefaction of the tissue, which is perceptible on digital examination, often gives the feel of an isolated nodule, and A. Guérin and Martineau have considered this to be caused by an inflamed gland; but it is chiefly caused here by the circumscribed inflammation of a plexus of lymph vessels, for the presence of a gland in this region is doubtful, or at all events not constant. The swelling of the connective tissue is due to inflammatory œdema. 3rd. When the inflammation is more acute, it is not limited, as in the preceding case, to the circum-uterine tissue, but affects the broad ligament. We have, then, **phlegmon of the broad ligament** or **parametritis.** The importance of the lesions of the lymph vessels and glands in this disease has been shown by Cruveilhier, Siredey, Gueneau de Mussy, A. Guérin, Lucas-Championnière, &c. This form of lymphangitis is found chiefly, in fact almost solely, in pelvic peritonitis of puerperal origin. Serous or sero-purulent infiltration of the connective tissue, and collections of pus, which are either disseminated or in foci, are found in the circum-uterine tissue, the broad ligaments, the iliac fossæ, and may even be found as high up as the renal region. In most of the cases which prove fatal, pelvic peritonitis is also found.

Peri-uterine hæmatocele.—We have already seen that effusions of blood may take place into the peritoneum after rupture of a Graafian follicle (Laugier); but the quantity of blood is then very small; more extensive hæmorrhage occurs in consequence of the rupture of the large varicose veins of the broad ligaments (Chaussier, Olivier d'Angers, Richet), or by bleeding from the Fallopian tube in consequence of a menstrual flux, or in post-partum hæmorrhage, or from rupture of the Fallopian tube in tubular gestation. In the latter case, the hæmorrhage is caused either by rupture of the tubal varicose veins, or by rupture of the ovary, or by a solution of continuity of the tube itself, or finally by rupture

of the fœtal cyst. When the effusion is very abundant, it rapidly causes death, either by reason of the quantity of blood poured into the peritoneum, or by the acute peritonitis which results. If the intraperitoneal effusion of blood occur under less acute conditions, or if it be frequently repeated at the menstrual periods, the blood which is effused in small quantities collects in the most dependent part of the pelvic peritoneum, and there sets up peritoneal inflammation which surrounds the blood tumour with false membranes. This is peri-uterine hæmatocele, properly so called, and it is of great clinical importance. Bernutz, who has, by numerous and important publications on this subject, done more than anyone to clear up the history of this affection, thinks that the Fallopian tube plays an important part in the production of hæmorrhage into the peritoneum. The blood comes in fact from the Fallopian tube, whether the hæmorrhage occur first in the tube, or simultaneously in the tube and the uterus, or if there be retention in the uterus of the catamenial fluid for many months, as may occur in atresia of the vagina in young girls. It must, however, be remembered that it is not easy for fluids to pass from the uterus up the duct of the tube, particularly through its narrow uterine orifice; that this does occur has, however, been put beyond doubt by the observation of many cases. Bernutz has moreover published cases which show the possibility of effusions of blood into the cellular tissue of the broad ligaments; these effusions are situated under the peritoneum and strip off the connective tissue of the vagina, so that the tumour projects at the side of this passage. Virchow has remarked that new vascular membranes, caused either by primary or secondary inflammation, may be formed on the surface of the peritoneum; these new membranes are themselves the starting points of blood effusions on their surface, or in the loose connective tissue of which they are composed, just as occurs in the new membranes of pachymeningitis, whence the name of hæmorrhagic pachyperitonitis, which has been proposed by Besnier. Whatever may be the origin of the hæmatocele, it is characterised by a tumour located behind, on one side, or around the uterus, which tumour can be felt by vaginal digital examination. The sac of the tumour, which separates it from the peritoneal cavity, is composed of false membranes, which are fibrinous at first and afterwards cellular; it is limited below, and on the sides, by the peritoneum, and above, by the appendages of the uterus. It contains either liquid or coagulated blood, which varies in colour according to the age of the effusion and the

various chemical changes which it has undergone. The blood is finally reabsorbed, and the sac contracts by reason of the organisation of the surrounding connective tissue. At the same time that the blood is effused, inflammatory and even purulent foci are sometimes seen, so that peri-uterine phlegmon and hæmatocele, which are somewhat analogous from their seat and symptoms, may complicate one another.

A. Lesions of the Uterine Mucous Membrane.

We distinguish between pathological lesions of the uterus according as they are localised in the mucous membrane, in the muscular parenchyma, or on its surface, or in the serous membrane; we should remark that such a lesion of the mucous membrane or the submucous connective tissue causes either increase or decrease in the size of the fibro-muscular wall of the uterus, and that in certain forms of inflammation and in certain tumours the whole of the tissue of the uterus is affected.

Congestion. Hæmorrhage.—Congestion of the uterus, due to venous stasis, is very common in cardiac and pulmonary disease with asphyxia. The mucous membrane of the fundus uteri is of a violet red colour, and contains a variable amount of blood-stained mucus. This lesion is very frequent in old persons. It occurs in compression of the uterine venous plexuses by tumours, particularly by fibrous tumours of the uterus and its appendages. The physiological hæmorrhage of menstruation cannot be considered here, but we must say one word on menstrual effusions of blood into the uterus, which cannot be expelled quickly enough, or which are retained in consequence of complete obliteration of the cervix, or by an imperforate lumen. In such cases, the Fallopian tubes are also filled with blood, and blood is sometimes exuded from the tube into the peritoneum (*vide* Peri-uterine Hæmatocele, p. 603). We need only mention here the uterine hæmorrhages which occur after parturition or abortion.

Metritis.—Inflammation of the uterus may affect either its mucous membrane or its fibro-muscular tissue, whence the division of metritis into internal or catarrhal, and parenchymatous. Metritis is acute or chronic. Catarrhal metritis varies also according to its situation in the cervix or the fundus; puerperal metritis presents quite peculiar characteristics. The

various inflammatory and ulcerative changes in the cervix uteri are often also classified, so that the varieties of metritis become very numerous. Inflammation of the mucous membrane and parenchyma are, however, rarely isolated. We follow the classification, adopted by Sinéty, of acute and chronic metritis.

Acute metritis.—Acute metritis is rarely seen except in the puerperal state; hence post-mortem examination of the disease is uncommon. It is chiefly characterised by congestion and repletion of the blood vessels, redness of the mucous membrane, and a catarrhal secretion from the cervix and fundus of the uterus. It supervenes after gonnorrhœal vaginitis, or a local eruption on the cervix, in certain general acute diseases such as typhoid fever, or which is more frequent, in a number of pathological conditions, scrofula, tuberculosis, syphilis, &c. In many cases the cause may be found in chloro-anæmia, or in menstrual disturbance, or it may be the sequela of parturition which has occurred some time previously. In catarrh of the mucous membrane of the cervix a mucoid fluid is exuded which resembles the cervical mucus, but which, instead of being transparent, is more or less purulent. Catarrh of the fundus uteri is most frequently characterised by an abundant secretion of a more serous fluid than that of the cervix, but equally opaque and purulent; the exudation is composed of free desquamation of epithelial cells, and of lymph cells extravasated from the vessels, and it is often blood-stained. Turgescence of the blood vessels of the mucous membrane, and infiltration of its tissue with serum, are concomitant phenomena. In sections of the mucous membrane, the superficial cells of the epithelium will be seen to have almost completely disappeared, and the glands are found to be located in the midst of embryonic tissue. The vaginal surface of the os uteri is often red, eroded and papillary. The uterus is increased in size, its walls are softened, infiltrated with embryonic cells, and its vessels are dilated. Abscesses are found here quite exceptionally.

Chronic metritis.—The lesions of chronic metritis being better known and more frequent than acute metritis, it is better to treat internal metritis and parenchymatous metritis separately, though they are often united.

a. **Internal chronic metritis.**—The uterus is increased in size, which is not due to thickening of its walls, but to dilatation of its cavity. It is softened, and on incising the dilated cavity of the fundus, it is found to contain a purulent or blood-stained fluid. The mucous membrane, which is considerably thickened,

is of a red or grey colour. It is rarely smooth, but is generally covered with villi, granulations and fungoid growths varying in size from a pea to that of a strawberry. These growths, which are generally found in the posterior wall, become pediculated and form actual polypi. In the cervix, the rugæ of the arbor vitæ are exaggerated, and hypertrophied papillæ, numerous ovuli Nabothi, and polypoid growths are found formed of vascular connective tissue; they are sometimes mucoid and take the elongated shape of the cavity of the cervix, or they remain small and sessile. The former often project from the os uteri and may attain many centimetres in length. Among these small polypi, some contain ovuli Nabothi either in their substance or at their extremity. Fibro-mucoid polypi are much rarer in the cavity of the cervix; they may, however, be found here; they are generally small and sessile. Small ovuli Nabothi may sometimes be seen spread throughout the whole surface of the mucous membrane of the fundus. In severe chronic catarrh of the mucous membrane of the fundus, it becomes of a brown red colour and on pressing it between the fingers a purulent fluid is squeezed from the glandular openings. Occasionally in old women, chronic metritis is found with obliteration of one of the orifices of the cervix, generally the os internum; whence it results that the cavity of the fundus is separated from that of the cervix; the former contains a considerable quantity of sero-purulent or purulent fluid, and the fundus is dilated, pyriform or round. In the cavity of the cervix there is a thick, transparent mucus, and the mucous membrane contains a large number of ovuli Nabothi. The granulations and fungoid growths of the mucous membrane of the fundus in chronic metritis were long ago pointed out by Récamier and Aran. The histology of these growths and the changes in the mucous membrane have been carefully studied by Sinéty. The mucous membrane is denuded of its cylindrical cells, and its surface is only covered by a layer of lymph cells infiltrated in the connective tissue. Contrary to what certain observers have stated there are no tesselated cells. The fungoid growths take three principal forms: 1. In some of them the dilated glands are observed to have become hypertrophied and flexuous; their epithelium is preserved (*vide* fig. 230). 2. Less vascular growths, formed of embryonic cells; only traces of glands and degenerated epithelial cells are found (fig. 231). 3. Fungoid growths which are formed almost entirely of blood vessels and which may attain a considerable size (fig. 232). These three varieties of growths may be seen in the

same uterus; the first giving origin to a mucous effusion, the second to a purulent secretion and the third to hæmorrhage. In

FIG. 230.—TRANSVERSE SECTION OF A GRANULATION FROM A CASE OF INTERNAL METRITIS.

a, stroma; *b*, section of dilated glands lined with epithelium; *c*, section of vessels. (After Sinéty.) Magnified 40 diameters.

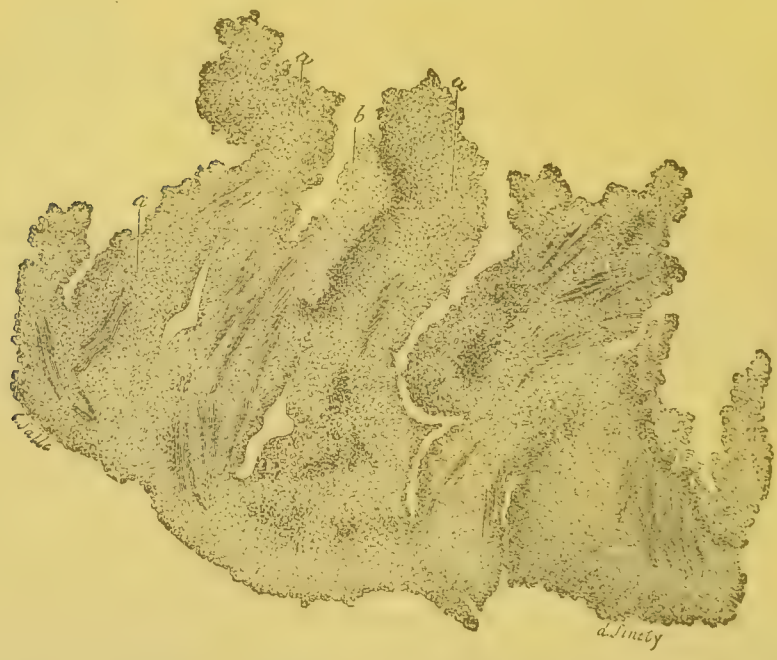

FIG. 231.—LONGITUDINAL SECTION OF A GRANULATION FORMED OF EMBRYONIC ELEMENTS WHICH ARE DEGENERATE AT CERTAIN POINTS, FROM A CASE OF INTERNAL CHRONIC METRITIS.

a, embryonic tissue; *b*, parts which have undergone fatty degeneration. (After Sinéty.) Magnified 40 diameters.

consequence of these various pathological conditions, the mucous membrane of the vaginal portion of the cervix is always more or less altered. Thus in catarrh of the fundus or cervix, when a

large amount of secreted fluid is exuded through the os uteri, it remains in contact with the lips of the os externum, particularly

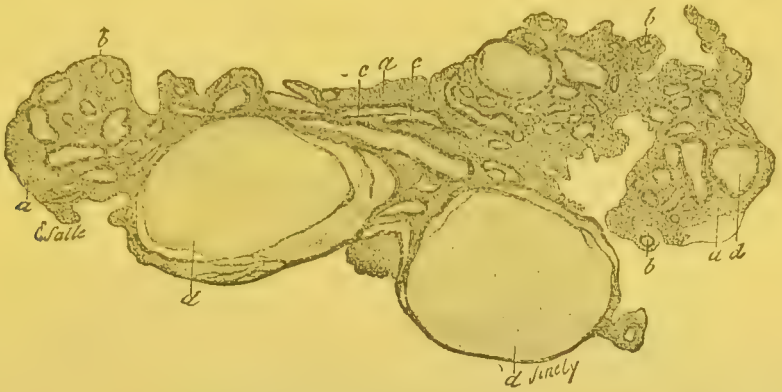

FIG. 232.—TRANSVERSE SECTION OF A GRANULATION COMPOSED OF DILATED VESSELS FILLED WITH BLOOD CORPUSCLES, FROM A CASE OF CHRONIC INTERNAL METRITIS.

a, embryonic stroma ; *b*, vessels cut across ; *c*, vessels cut longitudinally ; *d*, dilated vessels filled with blood corpuscles. (After Sinéty). Magnified 40 diameters.

with the middle of the lower lip, and a superficial erosion is first produced; then an actual ulceration which destroys all the epithelial lining. In chronic conditions, a budding of the papillæ of the mucous chorion is observed in the lower lip, and is seen in the form of small granulations composed of embryonic connective tissue supplied with blood vessels. These granulations are pink or red in colour. When they are cured, they become lined with epithelium and shrunken, and their embryonic connective tissue becomes fibrous. In cases in which their development can be easily studied, it can be made out that they are simply derived from productive inflammation of papillæ, which normally exist under the stratified epithelium of this part of the mucous membrane of the cervix.

Lesions of the os uteri.—The os uteri is the seat of various eruptions, namely of herpes vesiculosa such as is seen on the vulva and prepuce ; the bullæ of pemphigus ; the eruptions connected with the eruptive fevers ; simple or indurated chancre ; mucous patches ; the growths which spring from the surface of mucous patches ; the erosions which result from these various eruptions, &c. In secondary syphilis, redness of the cervix and uterine catarrh are almost constant, and are more marked in a cervix which has been the seat of mucous patches followed by erosions. Independently of these ulcerations of the cervix, there are other profound changes in the mucous membrane which

simulate ulceration, though a layer of epithelium is found on their surface. This epithelium is not, however, according to Sinéty, the usual stratified epithelium, which is almost completely destroyed, but a single layer of cubical or cylindrical epithelium; in sections, moreover, the epithelium will be found to be folded in, like glandular diverticula, lined with cylindrical or caliciform epithelium. The presence of these glands in the vaginal part of the cervix, where they do not exist normally, is due to the fact that the mucous membrane is everted like the conjunctiva in ectropion. In the diseased parts, a thick layer of embryonic elements and interstitial hæmorrhages will be seen beneath the preserved epithelium. This lesion, in the form of groups of small cells, dips deeply in places into the fibro-muscular tissue of the uterus; whence hypertrophic thickening of the cervix is the result. When the mucous membrane of the cervix is everted, the part seen through the speculum often contains the glands of Naboth.

b. **Chronic parenchymatous metritis.**—In chronic parenchymatous or interstitial metritis, the uterus is generally increased in size. It may become as large as the fist. This increase is generally regular; but when it is only partial, from hypertrophy of the cervix or one of its lips, a deformation results and the cervix becomes trumpet-shaped. The walls of the uterus, particularly at the base of the organ, may attain the thickness of two or three centimetres, and the cavity of the fundus is generally enlarged. As this affection is not mortal, it is only met with accidentally at necropsies. At the commencement of parenchymatous metritis, the uterine tissue is soft, red, gorged with fluid, and blood flows freely. Internal metritis and ulceration of the cervix are generally present at the same time. At a more advanced period, the parenchyma is indurated, resistant, white and of an almost cartilaginous hardness. On histologically examining parenchymatous metritis at the commencement, a large number of embryonic elements are found throughout the uterine wall. They are seen chiefly around the dilated vessels. Many observers, Virchow among others, consider that hypertrophy of the uterine wall consists, in its more advanced stages, in a new formation of muscular fasciculi, and they consequently ally partial hypertrophy of the cervix, lengthening of the cervix, prolapsus uteri &c., with parenchymatous metritis. Other anatomists, Rokitansky, Kiwisch &c., think that thickening of the walls is caused by the new formation of fibrous tissue. Considerable dilatation of the lymph spaces, and marked hyperplasia of the circum-vascular connective tissue, are,

according to Sinéty, observed in sections. This new connective tissue is formed of fibrous fasciculi and is poor in cells; it is a

FIG. 233.—SECTION OF THE UTERINE TISSUE IN A CASE OF CHRONIC METRITIS.

a, dilated lymph spaces; *b*, vessels; *c*, circumvascular connective tissue; *d*, section of muscular fasciculi; *e*, longitudinal section of muscular fasciculi. Magnified 40 diameters.

perivascular sclerosis distinct from atheromatous thickening of the external coat of the vessels. Its result is to narrow the calibre of the blood vessels and even to partially obliterate them. When inflammation of the mucous membrane is very marked, its chorion is found infiltrated with lymph cells and fibrin in such large quantities as to cause superficial mortification and ulceration; this may be observed, though very rarely it is true, in typhoid fever and in the serious eruptive fevers.

Puerperal inflammation.—Puerperal metritis, whether it occur immediately after delivery, or on the following days or many weeks afterwards (post-puerperal metritis), is never simple internal metritis, for it extends to the parenchyma, the venous sinuses, the lymph vessels, the peritoneum, the Fallopian tubes &c. The uterus is, in fact, as we have already seen, profoundly changed in all its parts by parturition, namely, in its mucous membrane, its muscular walls, and its blood vessels, and it is predisposed by this increased physiological activity of all its elements to acute inflam-

mation, which is nothing else than an exaggeration of its condition; thus all its parts participate in puerperal inflammation. The entire economy is profoundly altered, and it is more apt than in any other physiological state to allow of the entrance of bacteria which accompany purulent inflammation.[1] Effort, injury, the manipulations and operations undergone during delivery, the wound which results from the exfoliation of the placenta, fissures or rents in the vulva and vagina, are the media which give entrance to bacteria, and are the occasional and additional causes of inflammation. Putridity of the contents of the uterus, phlebitis, lymphangitis, the state of the blood which carries the infectious germs, are the causes of the febrile phenomena, which rapidly culminate in multiple metastatic abscesses, general peritonitis and death. At the necropsy of women who have been recently delivered and who have died of metro-peritonitis, the uterus is found dilated; its walls flaccid, infiltrated with fluid, and its venous sinuses generally more or less filled with pus or purulent fibrinous coagula. The mucous membrane of the uterus is of a purplish red colour, infiltrated with a blood-stained puriform fluid, and the decidua is pulpy and softened. Near the root of the placenta, a granulating surface is seen formed by the cotyledons of the mucous membrane, and at their most prominent parts, small fibrinous clots are found. The whole of the placental disc is infiltrated with blood mixed with a purulent fluid and of a fœtid odour. This part of the mucous membrane is often gangrenous, and of a dark brown colour, and on letting a stream of water fall on it flakes are detached. At other times, there is at this spot a grey pseudo-membrane which is detached in flakes, and under which the mucous membrane is seen to be of a reddish brown colour. This diphtheritic or gangrenous pseudo-membrane sometimes extends over the whole of the internal mucous membrane. On scraping the surface and examining the fluid obtained under the microscope, a large number of lymph cells are found, which contain both superficially and internally a quantity of diplococci, or round microbes in chains. On scraping the deeper layer of the mucous membrane and chorion, which is infiltrated with serum, lymph cells or large swollen connective-tissue cells in a state of fatty degeneration are found in the fluid. The cervix is softened, of a purple red, pulpy, and often covered with grey pseudo-membranes, under which the tissue is internally congested. The same

[1] Dolèris, *La Fièvre Puerpérale et les Organismes Inférieurs*, 1880. Thèse de Paris.

gangrenous lesion is found in places in the vaginal mucous membrane and on the vulva. The venous sinuses are free, or they contain a puriform fluid, or coagulated or semi-fluid softened fibrin, mixed with lymph cells or swollen and granular endothelial cells. Their walls show the characteristic signs of endo- and peri-phlebitis. The large veins are often filled with pus and fibrin, and the connective tissue of the broad ligaments always contains a more or less considerable quantity of pus, so that in sections of the broad ligaments, one or more small purulent foci are always found either in the connective tissue or the veins. The superficial lymphatics of the uterus are sometimes filled with pus, and in every case the peritoneum surrounding the uterus is the seat of acute inflammation with redness, vascularisation, the formation of fibrino-purulent false membranes on its surface, and with purulent infiltration of its connective tissue. If sections of the broad ligament be made at the spots infiltrated with serum and pus, stained with B methyl violet, then placed in a solution of iodine in iodide of potassium, and decolourised by alcohol and oil of cloves, a large quantity of migratory cells and swollen fixed cells will be seen interposed between the fibrous fasciculi. The fluid and cells contain quantities of microbes in chains or associated in couples. The fibrinous false membranes, examined in sections and stained in the same way, show a great number of lymph cells between the fibrinous fasciculi, covered and filled with the same microbes in chains. The Fallopian tubes and ovaries are affected in the same manner (see pp. 587, 601). The peritonitis becomes general with alarming rapidity, and metastatic abscesses are formed in the lungs, liver, kidneys &c.

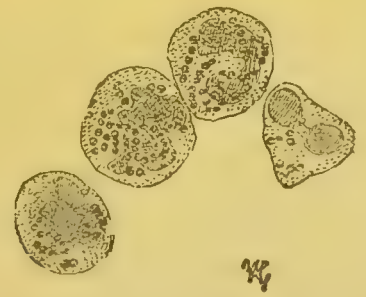

FIG. 234.—PUS CELLS, FILLED WITH MICROCOCCI IN CHAINS, FROM FIBRINOUS FALSE MEMBRANES, FROM A CASE OF PUERPERAL PERITONITIS. Seen under a homogeneous immersion lens, No. 12 of Vérick, eye-piece No. 2. Magnified almost 800 diameters.

In metritis which occurs some time after delivery, the phenomena are not nearly so acute; the uterus has already contracted, at

least it no longer contains large clots or fragments of the placenta; the venous plexuses have had time to contract, and the decidua has already been mostly eliminated. Often during the first months after delivery, grey, semi-transparent granulations, formed of slightly vascular connective tissue, are found at the spot where the placenta was inserted. All parts of the uterus and its appendages are less vulnerable. Metritis is, nevertheless, always more acute under these circumstances, than when the organ is in a state of quietude, and it is often accompanied with perimetritis, that is to say inflammation limited to the peritoneum covering the uterus, its appendages and the true pelvis. This limited peritonitis is circumscribed by false membranes containing a collection of pus, which may be reabsorbed if small in amount. At other times, there may be phlegmon of the broad ligament, or of the cellular tissue of the iliac fossa (parametritis), which may open spontaneously into the rectum or burrows in the inguinocrural region.

Phagedænic rodent ulcer, characterised by the progressive destruction and gangrenous appearance of the cervix, ends in a loss of substance of the lower part of the cervix, the fundus of the uterus, and the vaginal mucous membrane, and in certain cases in perforation of the bladder and rectum. This ulcer always seems to us to be related to carcinomatous or ulcerated epithelial tumours of the cervix (see p. 615).

Tumours developed in the uterine mucous membrane.—We have already described the *mucous cysts* which are produced by the retention of mucus in the glands known under the name of the glands of Naboth; we may, however, add that these glands may become as large as a small pea or even as a cherry. We have also mentioned the *villous growths* of the mucous membrane of the fundus, and the *fibrous polypi* of the cervix. These polypi are highly vascular and they generally contain, either in their substance or on their surface, Naboth's glands, which fact has given them the name of *mucous polypi*. We intend, however, to describe, when considering hypertrophy of the muscular walls of the uterus, the tumours or nodosities of the cervix which are produced by a new formation of muscular tissue.

Tubercles of the uterine mucous membrane.—Tuberculosis of the uterine mucous membrane is not entirely unknown. It is in every way comparable to that of the Fallopian tubes. The surface of the mucous membrane of both the fundus and the cervix is the

seat of a profuse catarrh with the production of thick, grumous, opaque and caseous pus. In the mucous membrane of the fundus are seen granulations which are semitransparent at the commencement, later on yellow and opaque centrally, and which unite to form more or less extensive patches. The subepithelial connective tissue is the initial seat of these lesions, but the deeper tissues of the mucous membrane are also invaded by an abundant new formation of embryonic connective tissue, and by tubercular granulations; whence results marked and general thickening of the submucous connective tissue. Identical lesions may show themselves in the cervix and even at the os uteri, but they are always very limited. The gelatinous mucous fluid secreted by the cervix contains yellow, opaque, grumous, semisolid particles, produced by the caseous degeneration of the pus derived from the tubercular masses. An eruption of tubercular granulations may quite exceptionally be seen in the vaginal portion of the cervix. They are semitransparent, often with caseous centres, and have a very characteristic appearance; the culs-de-sac of the vagina are affected in the same way. The mucous membrane of the vagina may also be the seat of ulceration and fissures, or even of tubercular recto-vaginal fistulæ. Giant cells and very long bacilli are found in them. **Syphilis**, which often manifests itself by chancre and mucous patches in the cervix, may also be seen here in the tertiary period in the form of indurations and deep ulcerations, which have, however, received little study hitherto.

Carcinoma.—Primary carcinoma of the cervix is almost always encephaloid. Thus in thirty-four cases examined histologically by one of us in 1863 and 1864, all were encephaloid. Authors mention, however, certain isolated cases of scirrhous or colloid carcinoma; but it must be borne in mind that carcinoma which seems hard at first, softens and looks like soft encephaloid as the tumour extends. Carcinoma of the cervix commences in one of the lips of the os uteri, which becomes indurated and hypertrophied, and soft vascular growths are soon seen beside the os or at the free edge of the lip. The opposite lip is affected in its turn, and this hypertrophy results in dilating the orifice, so that the finger can be introduced; its surface is granulating. This infiltration of the vaginal portion of the cervix, results in producing peripheral increase in size, so that the cervix projects into the vagina in the form of a mushroom. The cellular tissue, under the vaginal mucous membrane which surrounds the os, becomes indurated in its turn, blends with the adjacent portion of the cervix, and

nodules and granulations are developed on the vaginal mucous membrane. Carcinoma always seems to commence in the submucous connective tissue, so that the mucous membrane of the cervix and its vaginal portion appears for a time to be normal on the surface of the tumour; but it soon ulcerates, and cancerous granulations exude a fluid which becomes fœtid on mixing with the secretions of the vagina. The tumour extends to the muscular walls of the cervix, and simultaneously to the peripheral connective tissue and the subvaginal tissue. The ulceration, which accompanies moist gangrene of all the parts primarily attacked, is followed by a considerable loss of substance, which is limited by the preserved carcinomatous tissue. On examining this kind of cloaca under water, a number of white or grey thread-like loops are seen; they are the blood vessels of the part of the tumour which has been destroyed by ulceration. On microscopically examining the walls of these vessels, cells are seen which are inserted perpendicularly; they are in a state of fatty degeneration, and the walls of the vessels are infiltrated with a brown or black pigment due to the retrogressive metamorphoses of the colouring matter of the blood. On dissecting out these vessels they will often be seen to contain a clot of fibrin or a thrombus, formed of large cancer cells, at the spot where they enter the morbid tissue. The large veins frequently contain similar granulations and contents, which partly obliterate them. These thrombi are evidently the cause of the mortification of the pathological tissue, which is hastened by putrid decomposition of the fluid accumulated in the vagina. As the parts adjacent to the neoplasm become infiltrated, the walls of the cervix and a large part of the walls of the uterus, as well as of the bladder and even of the rectum, are affected, thickened, infiltrated, and softened by the milky juice of encephaloid cancer. Perforation from one cavity to the other may be the result. Vesico-vaginal fistula is a chief cause of rapid putrefaction of the parts infiltrated by carcinoma. The surface of the ulcer is then often covered with phosphatic and calcareous deposits derived from the salts of the urine. At other times, the ulcerating surface of the uterus and vagina is, at the time of death, formed of normal tissues, all the part affected by carcinoma having been destroyed by gangrenous ulceration. It might be thought that this was a case of rodent ulcer, if the villous or tuberous granulations were not found impregnated with milky juice and projecting on the surface of the perforated bladder or rectum. Before perforation is effected, the organs show cancerous infiltration of their

deep connective tissue, and their mucous membranes are in a state of acute catarrh. Destruction of the uterus may proceed so

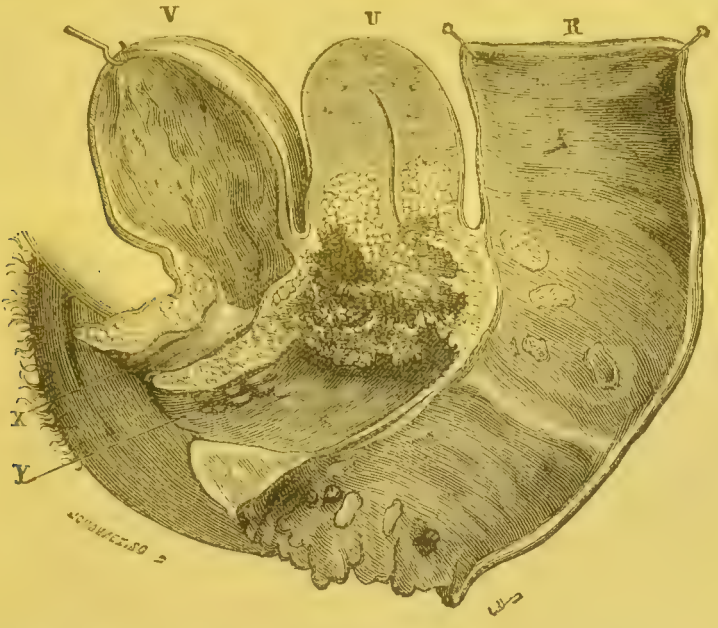

FIG. 235.—CANCER OF THE UTERUS WHICH HAS INVADED THE ANTERIOR PART OF THE VAGINA, THE BASE OF THE BLADDER, AND THE URETHRA.
(Drawing by Sinéty, after Cruveilhier.)
V, bladder; U, uterus; R, rectum; X, urethra; Y, vagina.

far that only the upper part of the fundus may be left; but the tissue which remains is normal and the Fallopian tubes are not altered. When, instead of commencing in the cervix, carcinoma occurs simultaneously in this part, and also infiltrates all the muscular tissue of the uterus, the cervix does not ulcerate in the same way. The uterine wall is thickened and infiltrated by the new growth, so that it may measure from 2 to 3 cm. or more in diameter, and it is then not unusual for the Fallopian tubes and the ovaries to be degenerated at the same time. In both these varieties of the same lesion, the subperitoneal connective tissue of the true pelvis is generally, in old cases, indurated and thickened, so that it has to be carved, as we may say, from the bony walls. This callous and fibrous tissue is particularly thick and hard on the posterior lateral wall; the sacral and sciatic nerves are also compressed and affected with the parenchymatous neuritis of carcinoma. Hence the pains radiating to the lower limbs, which are nearly always observed in cancer of the uterus. The cellular tissue itself is also often degenerated, as well as the pelvic and lumbar lymphatic glands. Metastases are found in the

lungs and liver. The ureters are affected with the bladder, whence retention of urine with urinous infiltration and anæmia of the kidneys. The cellular tissue of the broad ligaments and iliac fossæ is often the seat of purulent collections, so that general peritonitis may finally occur and cause death. We have also observed carcinomatous phlebitis and lymphangitis. On histologically examining the morbid uterine tissue, stroma and alveoli are seen, as in every other carcinoma, filled with polymorphous cells, which are generally arranged without order, though the parietal cells are sometimes regularly implanted on the septa of the alveoli. In the stroma, which is composed of connective tissue, smooth muscle cells are often plainly recognised.

Epithelioma.—Primary epithelioma is seen in the mucous membrane of the uterus in three distinct varieties: pavement-celled epithelioma with epidermal cell-nests, tubular epithelioma, and cylindrical-celled epithelioma. The first seems to us to be much more frequent than the others. According to what we know regarding the development of these tumours, they only originate in mucous membranes which have epithelial cells similar to those which form the tumour. The cervix normally contains stratified pavement cells in its vaginal portion, and cylindrical cells in its cavity. These various forms of epithelioma commence in the cervix, and cannot be distinguished during life from carcinoma by their seat, physical signs, colour, course or gravity. At the necropsy, it is very difficult, nay, even impossible to make a naked-eye diagnosis between these varieties of epithelioma and carcinoma. Cylindrical-celled epithelioma is generally a soft tumour, infiltrated with juice, closely resembling encephaloid; further, it contains lacunar cavities visible to the naked eye and full of milky juice. In three cases which we have seen, the alveoli contained cylindrical cells and pus, and from their walls sprang numerous looped capillaries which were themselves covered with cylindrical cells. The tumours extended to the adjacent parts, to the glands, bladder and uterus in one case, and to the sciatic and crural nerve in another. In one of them, the whole tissue of the uterus was affected, as well as the lymph vessels, which ramified on the peritoneal surface. Organs further removed were not affected, but there have been cases in which this has been observed. Pavement-celled epithelioma has certain characteristics by which it may be recognised by the naked eye at a necropsy. The parts of the tumour, which are only slightly vascular, have a semi-transparent, waxy and firm appearance, which contrasts with

their actual friability. On dividing the tumour, its surface is seen to be dry, and on scraping it small grumous particles are obtained, and white, opaque, vermiform filaments, composed of aggregated pavement epithelium cells. Under the microscope it will be seen that we have here either tubular epithelioma, or lobulated epithelioma with epidermal globes. The tubes found in epithelioma in the first variety are sometimes large, sometimes small, and the cells filling the latter are equally small. These tubes are

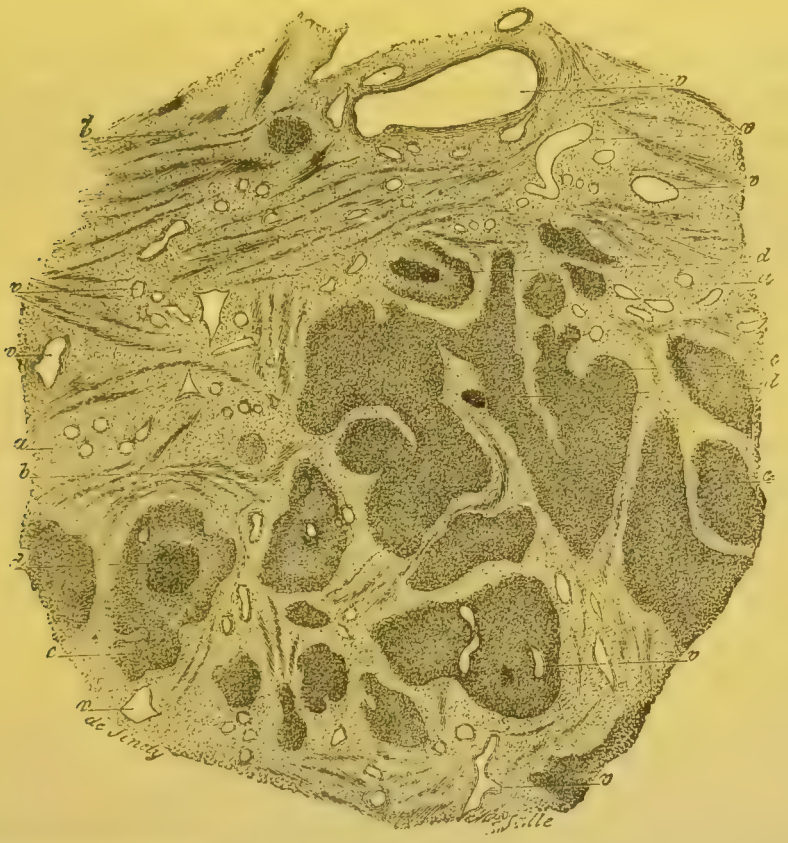

FIG. 236.—SECTION OF LOBULATED PAVEMENT EPITHELIOMA OF THE NECK OF THE UTERUS.

a, connective tissue; *b*, muscular fasciculi; *c*, epithelial masses; *v*, *v*, vessels cut across or lengthwise. (After Sinéty.) Magnified 30 diameters.

probably developed from the glandular saccules of the cervix, but of this we are not certain. The tissue separating them is formed of the fibro-muscular fasciculi of the uterus. These epitheliomata are reproduced in their characteristic form in the glands, and in the secondary nodules which are met with in the fibro-muscular tissue of the uterus, or on its peritoneal surface, and in the granulations which are developed in the different layers of the

bladder and finally on its mucous surface. But metastatic nodules, situated in organs removed from the uterus, are rare in epithelioma. We have observed them in the liver, and a certain number of cases reported, particularly by Virchow, prove the possibility of secondary growths occurring in pavement-celled epithelioma ('Gazette Méd. de Paris,' 1855). Ulceration with its various consequences, particularly gangrene of the morbid part, is absolutely identical in epithelioma as in carcinoma. In pavement-celled epithelioma particularly, the diseased part of the cervix may entirely disappear. The cervix or fundus, which is cut clean across, terminates by a surface which is horizontal to the upper part of the cloaca. As in such a case the adjacent organs are not as constantly nor as evidently infiltrated with the new growth as in carcinoma, it might be thought that this was a case of simple rodent ulcer. Any trace of epithelioma must then be carefully searched for on the vaginal surface of the ulcer, or in the sacral and lumbar glands. We have found parts showing the characteristic structure in all the cases we have examined. The different varieties of carcinoma and epithelioma of the uterus occur at the menopause or a few years afterwards; they have, however, been observed in young women of from twenty to thirty years old, and tumour of the cervix does not prevent impregnation, pregnancy or delivery. We have seen many cases of this. It must be added that after delivery the lesion increases rapidly.

Hypertrophy of the fibro-muscular walls of the uterus. Myoma.—This lesion consists in the new formation of smooth muscular and fibrous tissue; it sometimes causes general or partial hypertrophy of the uterus, it may be more or less isolated in the form of myomata, which are actual tumours of a round or oval form. The tissue of which these growths are composed may be of two kinds; one, by its softness, vascularisation, and abundant muscular fibres, recalls the state of the uterine walls a short time after delivery; the other is hard, compact, slightly vascular and very rich in fibrous fasciculi. Partial hypertrophy often follows delivery, particularly when the cervix has been lacerated. Inflammation then causes new formation of connective tissue, and an active nutrition which retards or hinders the fatty degeneration and atrophy of the muscles hypertrophied by pregnancy, and gives origin to fibro-muscular hypertrophy of the cervix. Simpson referred to changes in the muscular fibres, during and after pregnancy, as playing the chief part in general and partial hypertrophy and atrophy of the uterus; in the former, the smooth fibres, hypertrophied during

pregnancy, remain such, or their atrophy is at least arrested; in the second case, this physiological atrophy continues till a partial or total pathological atrophy is produced. This ingenious view is true in a certain number of cases, particularly in those of general or partial hypertrophy following pregnancy. It is certainly true that myomata previously existing in the uterus increase very rapidly after pregnancy; but, on the other hand, uterine myomata are observed in young girls who are virgins, and in women who have never had children. Dr. West even thinks that myomata result from the inactivity of the uterus, when this organ does not exercise its natural functions, as in the case of married women without children, in whom both partial and complete hypertrophy of the uterus is observed.

Partial hypertrophy of the vaginal portion of the cervix is frequent in multipara. The lips are large, irregular, and tumefied, so that to the touch it might be thought that a commencing car-

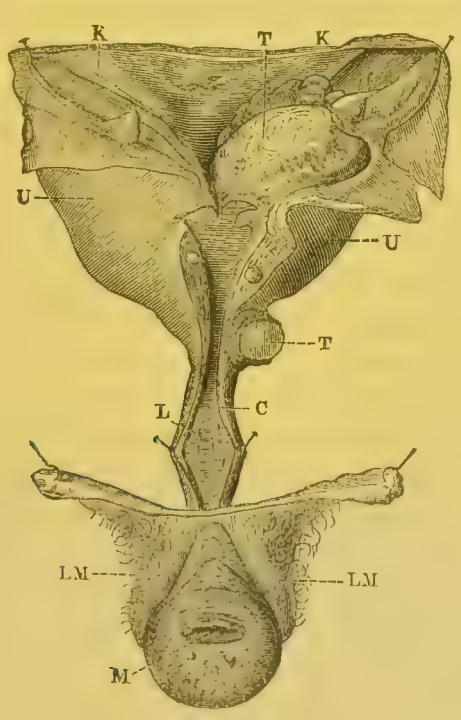

FIG. 237.—FIBROUS TUMOURS WITH SEROUS CYST OF THE UTERUS COINCIDING WITH EVERSION OF THE VAGINA. ELONGATION AND HYPERTROPHY OF THE UTERUS. (After Cruveilhier.)

U, uterus; T, T, fibrous tumours varying in size; K, K, walls of the cystic cavity; C, C, cervical cavity considerably elongated and showing lacunæ, L, which are probably dilated glands; LM, labia majora; M, os uteri.

cinoma was under examination. Such a cervix is called *tapiroid* by Ricord; the lips curve outwards and project like a mushroom.

The glands of Naboth, folds, depressions and crypts are generally seen in varying numbers. On the surface of tumours which spring from the cervix, the ground tissue of which is fibro-muscular, pouch-like depressions may be seen, and projecting septa which give them the appearance of hypertrophied tonsils (Virchow). Cases have also been observed of hypertrophy of the lips in the form of long fleshy projections from the os; they are covered with a delicate mucous membrane lined with pavement cells. The whole of the vaginal portion of the cervix may be hypertrophied, and the cervix may be prolapsed as far as the vulva. But prolapsus is more often caused by hypertrophy of the whole of the cervix uteri, the supravaginal as well as the vaginal portions. This form of hypertrophy is rather frequent, and has been described by Huguier. The cervix, which is very long, projects into the vagina either by an elongated extremity, or as a club-shaped mass (fig. 237). The uterus, normal in size or hypertrophied, may be in situ, or it may be displaced by the weight of the cervix. This hypertrophic elongation of the whole of the cervix has been observed in women who have never had children. General hypertrophy of the whole of the uterine wall is much rarer than partial hypertrophy.

Myomata are almost the only tumours which take their origin in the muscular walls of the uterus. They are formed of smooth muscle fibres intersecting one another in various directions (see vol. i. p. 232). The general description of myoma already given applies to uterine myomata, which are the types of this form of tumour. We need only give their peculiarities of development, their seat, and their anatomical consequences in the uterus. They commence in the thickness of the muscular wall; they are generally very vascular and soft at their commencement; later, they become indurated in consequence of fibrous organisation of their connective tissue. Certain interstitial tumours, which are small and round, are always very hard. At the beginning their fibres are directly continuous with the adjacent fibro-muscular fasciculi of the uterine wall. As they develop, they project either under the peritoneum, on the external surface of the uterus (subperitoneal tumours), or on the internal surface of the cervix, when they are covered by the mucous membrane. They frequently become pedunculated, so that they are united to the internal wall by a pedicle which is either large and vascular, or very thin. The myomata which project into the uterus are generally called fibrous polypi. The subperitoneal tumours, having nothing to impede

their growth, often attain a great size. They are generally multiple, even when they are very large; subperitoneal tumours, intraparietal tumours, and polypi, may be co-existent with them and project into the uterine cavity. The various forms of degeneration, which are described in vol. i. p. 234, may be found in subperitoneal myomata, where these changes are more frequent. In a case of peritoneal carcinoma, we once saw two very large myomata attached to the uterus, infiltrated with carcinomatous tissue, which appeared as sheaths around the blood vessels ('Soc. Anat.,' Juillet 1875). Virchow has also published a case of carcinoma in a myoma. The myomata, which project into the cavity of the fundus, are some of them hard and fibrous like the preceding, and others are composed of a soft, pink tissue which is vascular, and even large vessels may be found in them. Their removal may set up hæmorrhage which it is difficult to arrest. The first of these varieties of intra-uterine polypi cause repeated and violent hæmorrhage during life. It is rare for such a polypus to be developed in the wall of the cervix. When a polypus, which originates in the fundus, projects from the external os, its mucous membrane changes its character, becomes thickened and covered with tesselated epithelium. The projecting part, which is covered by the mucous membrane, is sometimes inflamed, red, and ulcerated, in a similar way to what occurs in the mucous membrane of the cervix when completely prolapsed. The mucous membrane is entirely destroyed at a certain point, which may be more or less extensive, and the muscular tissue is denuded. The mucous membrane around this solution of continuity is red, or of a reddish brown colour, and highly inflamed from contact with the irritating fluids of the vagina.

CHAPTER VII.

THE MAMMA.

Normal Histology.

THE mammary glands are composite racemose glands, and they are developed, like all other cutaneous glands, from the horny layer, and belong to the skin. They contain from ten to twenty ducts, the galactophorous ducts, which open singly at the apex of the nipple; beneath which they dilate into ampullæ; they then divide and subdivide and terminate in pyriform or spherical culs-de-sac. Both the smallest ducts and the saccules are composed of a homogeneous basement membrane, lined on its inner surface by an incomplete layer of endothelial cells, and by a layer of cubical cells which are 12 μ in diameter at least. The large galactophorous ducts contain cylindrical cells. Outside the basement membrane of the saccules, there is loose connective tissue containing a few round cells, fibrous tissue and fat cells. The nipple and its areola are contractile and contain smooth muscle cells. On the surface of the nipple, papillæ and various glands are found; namely sudoriparous and sebaceous glands, and small isolated mammary glands the ducts of which open on the nipple, the acini being more deeply seated (Sappey, De Briès). The mammæ, which are incomplete and consist of merely ramifying ducts during infancy, develop during puberty, when their terminal saccules increase. They do not attain their complete development till the first pregnancy, when these lobules enlarge and separate; their epithelial cells then contain the fat granules which are excreted to form the milk corpuscles. These epithelial cells are also desquamated and fall into the saccules, where they constitute the colostrum. The milk corpuscles are fat granules. Milk contains water, neutral fat, casein, lactose, and certain salts, particularly phosphate of lime. The mammæ of newborn infants secrete a milky fluid in which fat granules are present. The mammæ continue in a highly developed condition during the child-bearing period, after which they atrophy. The

saccules then elongate, become thinner, and either disappear entirely or contain only a few atrophied cells. The saccules are

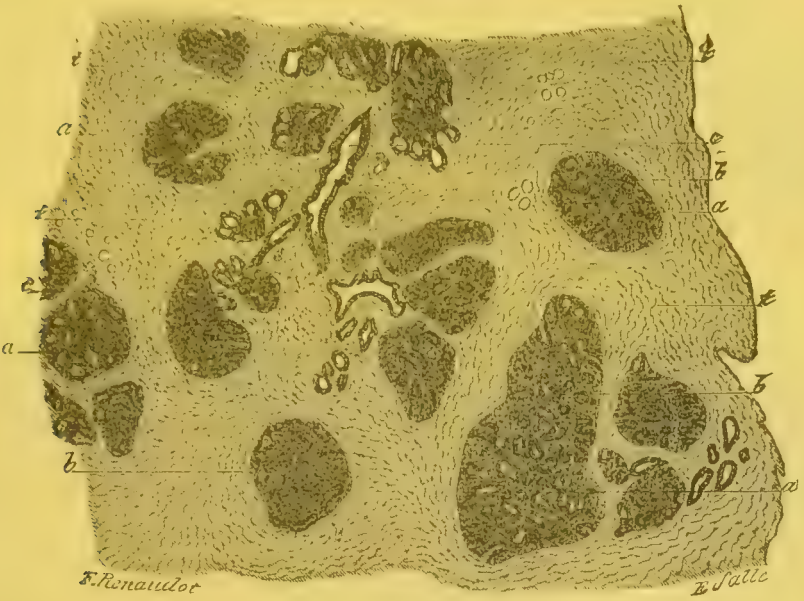

FIG. 238.—SECTION OF THE MAMMA OF A WOMAN DURING LACTATION.

a, lobules of the gland; *b*, acini lined by a layer of cubical epithelium; *c*, ducts of the glands; *t*, stroma formed of connective tissue. (After Sinéty.) Magnified 20 diameters.

normally surrounded by connective tissue, and the lobules are separated from one another by adipose tissue. The blood vessels form a network of capillaries around the saccules. The lymphatics are numerous. According to Labbé and Coyne,[1] the saccules are first surrounded by a layer of loose connective tissue containing a

FIG. 239.—ACINUS OF THE MAMMA OF A WOMAN DURING LACTATION.

a, epithelial cells; *b*, nucleus; *c*, nucleolus; *d*, milk globules; *e*, connective-tissue fibres; *f*, connective-tissue cells. Magnified 300 diameters.

few nuclei, and outside this by a layer of thick connective tissue. In the latter, large lymph lacunæ are found, which partly envelope the saccules from which they are separated by fibrous tissue. Coyne has remarked that this arrangement prevents the extension

[1] Labbé and Coyne, *Traité des Tumeurs Bénignes du Sein*. Paris, 1876.

of tumours to the lymphatic glands, as they then remain localised in the glandular saccules. In fact, the surrounding fibrous tissue must be infiltrated before the lymphatics become affected in their turn and convey to the glands the fluids and cells which subsequently infect the axillary glands. It should be added that Giraldès drew attention a long time ago to the large number of lymph vessels in the breast, particularly describing those at the base of the gland, where they form a kind of cavernous plexus. The mamma is attached to the fascia superficialis by loose connective tissue, which appears in some cases like a more or less complete serous bursa (Giraldès). The arteries of the mamma are derived from the external mammary, the aortic intercostal, and the internal mammary arteries. This latter may, during lactation, become as large as the radial. The deep veins accompany the arteries; the superficial veins often form a circle around the areola. The lymph vessels empty themselves into the glands of the axilla.

Pathological Anatomy.

Acute inflammation.—Inflammation of the mammary gland varies greatly. It is seen after delivery, during the first period of lactation, and as the result of contusions and tumours. Inflammation of the areola, cracks in the skin, and subcutaneous prominent abscesses of the areola, are rather frequent in the early days of nursing. Erysipelatous inflammation of the skin covering the gland is rather frequent, either during lactation, or as the result of ulcerating tumours, and in the latter lymphangitis is marked and is characterised by redness indicating the tracts of the subcutaneous lymphatics. This erysipelatous inflammation may be followed by actual subcutaneous phlegmonous abscess. Repeated lymphangitis, due to ulcerating carcinoma of the breast, often terminates by carcinomatous degeneration of the walls of the lymphatics, which are then changed into hard sinuous cords. Parenchymatous or glandular inflammation of the mamma is more deeply placed, and commences either by retention of milk, or by purulent inflammation of the connective tissue separating the lobules. Purulent inflammation is seen almost entirely in nurses and women recently delivered, and much more rarely in pregnant women. The abscesses which form then in the gland are sometimes numerous and persistent. They contain the elements of milk mixed with lymph cells. When they are opened surgically, a milk fistula may be produced if a large galactophorous duct, or the wound made by

the knife suppurates. Deep mammary abscess may be produced under the same conditions as the preceding, by the propagation of purulent inflammation to the loose connective tissue which separates the gland from the fibrous fascia. It follows inflammation of the lymph vessels and mucous bursæ, and it rapidly forms a sac full of pus beneath the gland, which is raised. Submammary abscess sometimes takes the same course as cold abscess. The cause is then, not acute inflammation of the breast, propagated to the deep connective tissue, but osseous lesions of the ribs and sternum, scrofulous or tubercular caries, or abscesses of the same nature developed on the internal surface of the ribs and sternum, which have perforated the intercostal spaces, and projected into the inflamed submammary connective tissue.

Chronic inflammation.—Abscess of the breast leaves as a sequela indurations composed of newly formed and organised connective tissue, which may increase and constitute a fibrous tumour. The causes of chronic inflammation, or general chronic mastitis, are much more obscure. In this case an abnormal quantity of fibrous tissue is formed and general induration takes place of all the newly formed tissue which separates the saccules. This anatomical alteration is often mistaken for hypertrophy, or for fibroma of the gland.

Tumours of the Mamma.

The structure of tumours of the breast was studied in the first volume when describing each variety of tumours. They are so common, and so frequently removed by the surgeon, that they have chiefly served for the histological study of tumours (*vide* vol. i. p. 176). Tumours of the breast are seen almost exclusively in women; but they may occur, though exceptionally, in males.

Complete hypertrophy of the breast.—It sometimes, though rarely, happens that the breasts hypertrophy considerably in young girls after puberty, or in young women after delivery. Either one or both glands may be affected, the left more frequently than the right, and it may attain the size of a man's head and weigh from four to six pounds or more. The breast is normal in consistency, but may be rather hard in young girls, or may be soft and pendulous in young women during pregnancy, when hypertrophy has existed for some time. On palpation, it gives the sensation of the lobules being displaced. The skin is normal or slightly thickened, but not adherent. The glands of the axilla are not hypertrophied. On section of the excised gland, the tissue is

seen to be grey with yellow lines or lobules. It yields no juice. Under the microscope, it is seen that the connective tissue, which is very abundant, is denser around each lobule of the gland. The ducts and saccules are sometimes lined, as in the quiescent state, with a single layer of small cells, and sometimes these cells are large and granular, as in the early months of pregnancy. In every case, the ducts are elongated to keep pace with the hypertrophy of the connective tissue, but fibrous thickening of the connective tissue is the principal lesion, and the epithelium is neither the first nor the chief part affected. This has been proved by Dufour, Cadiat, Ledouble and Labarraque.[1] Lobules of fat are also sometimes found in the tumour, but fat is generally absent. In a case reported by Manec,[2] the galactophorous ducts were so much dilated that the tip of the finger could be inserted. Here, as in other cases of hypertrophy, the ducts and saccules become dilated from the new formation of fibrous tissue; small cysts may also be formed by retention of the products of secretion when a galactophorous duct is isolated in the midst of fibrous tissue.

Galactocele.—This is a tumour formed by the retention of milk in a portion of the gland, either at its centre or circumference or near the axilla. It coincides with lactation and may disappear with the cessation of this function. The milk, which is almost normal, clotted or creamy, is contained in a sac which is either simple or divided by septa. The sac communicates with a certain number of secreting lobules by openings from which the milk may be squeezed. According to the clear descriptions given of cases of galactocele, that of Forget,[3] in particular, the sac of the cyst seems to be nothing else than a dilated galactophorous duct from which the milk cannot find exit by the nipple.

Sarcoma.—Sarcomata vary in size and do not at the beginning adhere to the skin, but such adhesion is shown later. The neighbouring lymph glands are rarely affected. The gland is sometimes invaded throughout its whole extent, when it is a case of massive sarcoma (vol. i. p. 139); or the tumour may be limited for a long time to a lobule of the gland. In the first case, the development of the tumour is uniform, the skin is tense above and is sometimes adherent; in the second case, there is one or more isolated tumours

[1] *Sur l'Anatomie Normale et les Tumeurs du Sein chez la Femme.* Thèse de Paris, 1875.

[2] *Gazette des Hôpitaux*, 1859, No. 12.

[3] *Etude sur l'Hypertrophie générale de la Glande Mammaire.* Thèse de Paris, 1875.

which give the gland a lobulated appearance. On cutting the tumour across, after removal, it is seen to be of a solid uniform grey mass with more highly vascular parts; other older parts are yellow in consequence of fatty degeneration. Many nodules may also be observed separated from one another by less diseased parts. In massive sarcoma, the glandular ducts and saccules are preserved and enlarged, but are not cystic; the glands are often entirely absent in parts of the tumours which have never been developed solely from connective and adipose tissue. When the entire gland is affected by the new growth, there may be an exaggerated formation of epithelial cells and even distension and plugging of the galactophorous ducts and sinuses by cells in a state of fatty degeneration; this gives the appearance of milk to their contents.

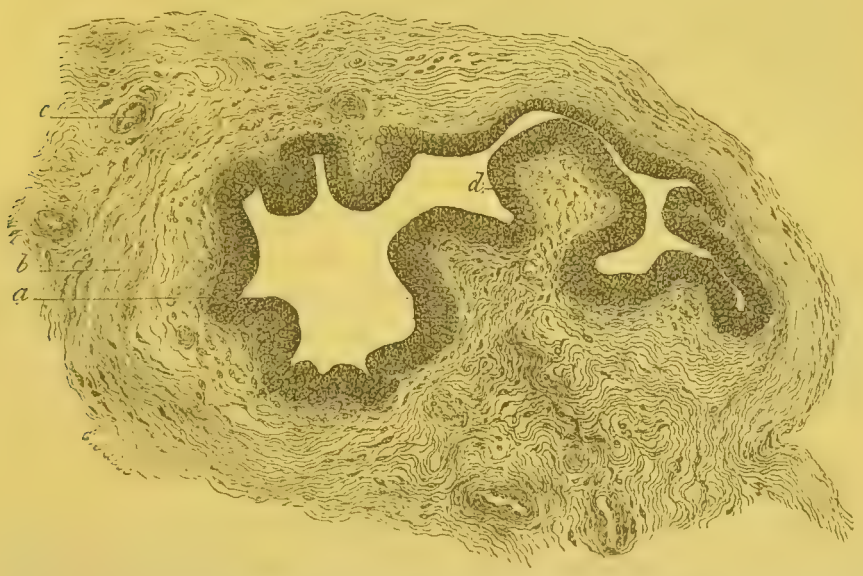

FIG. 240.—GRANULATING FIBROMA OF THE BREAST.

d, granulation projecting into a galactophorous duct; *a*, epithelial lining of this duct; *b*, connective tissue. Magnified 80 diameters.

More frequently a mucoid fluid is found in them. Cysts are often observed in similar cases, or branching fissures or slits which represent the cavities of ducts and saccules into which the sarcomatous tissue has granulated (vol. i. p. 139). On dividing sarcoma of the breast and examining it with the naked eye, normal fat is never seen, for it has been changed into sarcomatous tissue. The glands of the axilla are almost always intact, and it is these two characteristics which facilitate the diagnosis between sarcoma and carcinoma, for in the latter the glands are always affected, and lobules of fat are found in the mamma. Mammary sarcoma is most

frequently of the encephaloid variety, but is sometimes fasciculated. Sarcoma of the breast often recurs after removal. If the breast have been removed in a first operation, and sarcoma recur in the cicatrix, the mass is generally entirely sarcomatous without any cysts; this is easily explained by the fact of the glandular tissue having been removed in the first operation. Secondary sarcomatous nodules of the pleura, lung, bones and other organs are sometimes found at the necropsy of subjects who have been operated upon for recurrent and secondary sarcoma.

Myxoma.—Myxoma of the breast is rather frequent. It differs from sarcoma only in the tissue of which it is composed. Cystic myxomata are the most frequent (*vide* vol. i. p. 154 regarding myxoma in general, and p. 160 regarding myxoma of the breast). Myxoma of the breast is a tumour essentially benign, and adhesions are not contracted with the skin.

Fibroma.—Strictly speaking complete hypertrophy of the breast might be classified with fibromata, as the new tissue is fibrous; but fibromata also occur which are small and very hard. Virchow has reported a case of fibroma of the breast in a man. Instead of being general, fibroma of the breast may be partial, localised around part of the gland, forming a tumour varying in size though generally small, of almost stony hardness, and without close adhesion to the neighbouring tissues. Fibroma has the same relation as sarcoma and myxoma to the galactophorous ducts and saccules. (*Vide* vol. i. p. 161 and Fibroma of the Breast, p. 166.)

Tubercle.—There are a number of scattered observations of tubercle of the breast, which have been collected by Dubar.[1] The tubercles are found either disseminated or in confluent nodules. The former give no sign during life and are only discovered after death (case reported by Billroth). The second form tumours which increase by successive accesses, and may attain a considerable size. Their mass is hard, tuberous, and covered with small granular projections. Their centre is softened, and on cutting into them pus, containing caseous grumæ, escapes. They continue to suppurate and the pus is carried away by means of fistulæ with indurated and fungoid edges. The tubercular cavity remains surrounded with an indurated tissue. Caseous adenitis of the axilla is often present at the same time. On dividing the organ after removal, and on cutting across one of these fistulous tracts with granulating walls, it is seen to lead into an irregular cavity with numerous diverticula. The cavity is lined by a soft, velvety and grey membrane, which

[1] *Des Tubercules de la Mamelle.* Thèse de Paris, 1881.

may be yellow in places, and it contains a purulent mass and yellow grumæ. The peripheral tissue is indurated, of a greyish

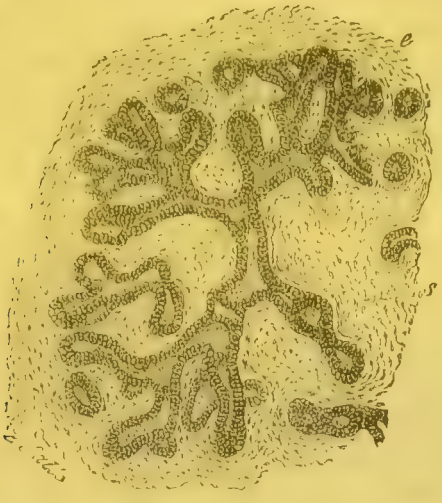

FIG. 241.—FIBROMA OF THE BREAST. THE GALACTOPHOROUS DUCTS AND ACINI ARE SURROUNDED BY FIBROUS TISSUE CONTAINING A LARGE NUMBER OF CONNECTIVE-TISSUE CELLS.

white colour, and contains groups of semitransparent or opaque nodules, which are yellow towards their centre. On examining these nodules under the microscope, they show all the characteristics of tubercles, with giant cells and obliterated blood vessels. Glandular saccules are sometimes seen in the centre of these granulations and giant cells may originate in the saccules.

Syphilis.—Syphilitic indurations may occur in the breast and be cured by antisyphilitic treatment. The histological appearance of these lesions is not known.

Carcinoma.—Primary carcinoma of the breast is either scirrhous or encephaloid and is rarely of the colloid variety. Fibrous or scirrhous carcinoma commences by a hard and generally small tumour, which behaves very differently in different cases. Thus, it may extend rapidly, and early in its course form adhesions to the skin, which is itself affected, thickened, rough and unequal; or it may be developed in the form of ramifying and anastomosing cords which are due to the subsequent alteration of the superficial lymphatics; at other times again small nodules are observed in the subcutaneous cellular tissue and in the derma. In the Salpêtrière we have seen two cases of very much enlarged lymph vessels, which were hard and prominent and passed from the tumour to the glands of the axilla. On examining one of the cases histologically, characteristic carcinomatous tissue with its

cells and alveoli was seen around the lymphatics throughout its whole extent. We have already in vol. i. p. 176 described the development of carcinoma in the breast, and the formation of large cells in the interfascicular spaces of the connective tissue. We need not recapitulate this here. It is unnecessary also to add that the glands of the axilla are always, early in the disease, indurated and degenerated, by simple fibrous induration or by carcinomatous change. In these fibrous carcinomata, which develop rapidly, the skin is indurated not only in the form of small granulations, but in dense patches and bands. The opposite breast is sometimes affected in its turn, and the morbid growth may extend to the pectoral muscles, the fibrous tissue of the axilla, the ribs, the intercostal muscles, the pleura, the lungs &c., and proceed step by step in a rapid manner. In a number of slightly different cases, observed particularly in old women, scirrhus may atrophy. The tumours remain small, the breast shrinks and the nipple is contracted. The glands of the axilla are, it is true, affected, but for many years, four, five or more, secondary nodules are not observed either in the skin or internal organs. It is, however, to these secondary growths that the patients finally succumb; the cancerous growths which are then found in all the organs and tissues are remarkable from their small size and their hardness,

FIG. 242.—TRANSVERSE SECTION OF AN ULCER OF A CANCER OF THE BREAST.

b, lobule of a gland from which passes an ulcerated galactophorous duct and opens into an ulcer; *c*, another glandular duct; *d*, a glandular acinus. Magnified 20 diameters.

from which they might be mistaken by a superficial examination for tubercular granulations. When atrophic scirrhus ulcerates, which it does frequently at a central contracted, pit-like spot, the

appearances already described in vol. i. p. 180 will be seen in a section which passes simultaneously through the ulceration, the edge and base of the mucosa. In the ulcerated and inflamed part a mass of embryonic tissue is found. At its edges and base are seen thick connective-tissue and carcinoma cells. This ulceration may be continuous by means of a galactophorous duct with the deep parts of the tumour, as shown in fig. 242. In completely developed scirrhus of the breast examined in sections, the large galactophorous ducts and sinuses are seen in the midst of a smooth, white and slightly succulent tissue, filled with a milky yellow juice, or opaque, yellow or brown caseous matter composed of granulo-fatty cells. The smaller ducts are equally filled with granular epithelial cells and are recognisable by the naked eye as branching lines, which may be traced to the periphery of the tumour. In sections examined in the fresh state, the glandular saccules may be seen filled with large cells, the nuclei and nucleoli of which are also large. In hardened sections of the

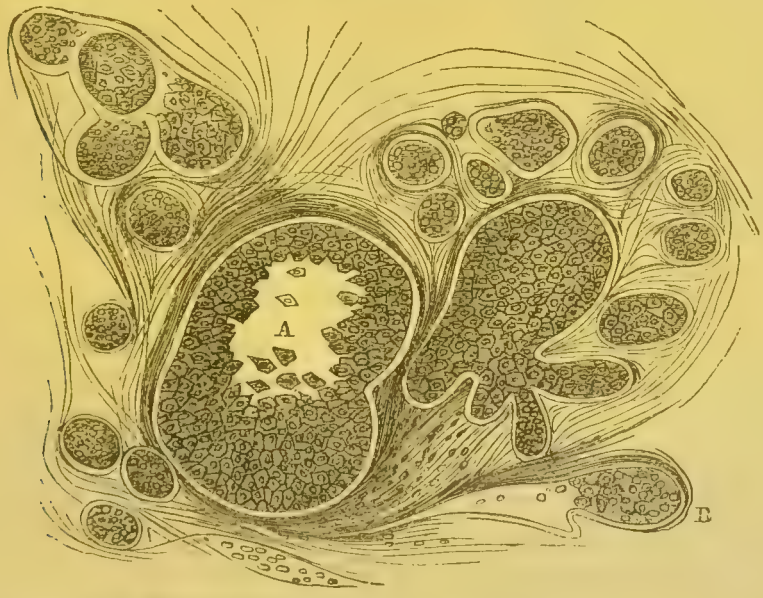

Fig. 243.—Section of the Breast in Carcinoma..

In the glandular saccules B the double contour of the membrane is plainly seen; they are filled with large cells. A galactophorous duct A is filled with the same elements. Magnified 80 diameters.

central and oldest part of the tumour, the ducts, which are easily recognised by their limiting membrane, contain epitheloid cells arranged in several layers, and in the centre of the duct is a collection of granular fatty cells which are distinct from those of the epithelial lining. The pre-existing glandular saccules and

the connective tissue are changed into carcinomatous alveoli containing large cells. At the edge of the tumour, at the parts more recently affected, the changes which occur in the glandular groups and the connective tissue may be followed. Thus, at the side of a normal glandular group, the cells of which are only a little swollen and the saccules a little larger than when empty, groups of saccules are seen distended by large and finely granular or transparent cells, which contain large nuclei and nucleoli. These saccules still retain their limiting membrane. The lobule which is thus altered is much larger than the lobules surrounding it. At the same time, the peripheral connective tissue contains swollen cells with nuclei undergoing proliferation, and the plasmatic spaces are filled with newly-formed cells and with lymph cells. The connective tissue is changed into carcinomatous tissue by the new formation of these cellular elements between its fibres. At a given moment the proper membrane of the saccules disappears, and all the pre-existing tissue is hollowed with alveoli filled with large cells. The lymph vessels are affected in their turn and contain the same elements. When scirrhous cancer is old, the fibrous tissue is much thickened and the alveoli small. In the centre of atrophic carcinoma fatty degeneration is present with atrophy of the cells; the dense fibrous tissue also contains fatty granulations. In this variety of carcinoma the glands of the axilla are always indurated and are often changed into fibrous tissue (*vide* vol. i. pp. 179, 180).

We should add that the connective tissue which accompanies the axillary nerves and vessels is also extremely hard, and contains carcinomatous alveoli at certain spots; it is also characterised by considerable new formation of dense fibrous tissue which compresses the vessels and nerves. The circulation is impeded in the veins, which are filled with organised thrombi, and in the arteries, the lining of which is folded lengthwise, and their lumen lessened, if not entirely obliterated; the result is œdema of the whole of the upper limb.

The compressed nerves show degeneration of their myeline in their peripheral course.

Encephaloid carcinoma of the breast is generally much larger than scirrhous, and increases much more rapidly. In the skin, which is easily affected and thickened by the new formation of embryonic tissue and by carcinomatous tissue in its deeper layers, the papillæ are hypertrophied and infiltrated with lymph cells, and their vessels greatly enlarged. These changes in

the derma precede the ulcerations, which are generally granulating. The highly vascular fleshy granulations of the ulcerating parts often give origin to repeated, continuous and sometimes considerable hæmorrhage. Such hæmorrhages may occur in scirrhous cancer, but are much more frequent and profuse in encephaloid cancer. On dividing the tumour the tissue is seen to be soft, vascular, of a greyish white, rich in milky juice, showing, in fact, all the characteristics of encephaloid. Its development and propagation to neighbouring tissues and glands take place as in scirrhous cancer, the new tissue showing the same characteristics as the primary tumour.

Colloid carcinoma is much rarer than the preceding.

Villous carcinoma.—We have frequently had occasion to observe a tumour of the breast which resembles carcinoma as regards its extension, the infection of the lymph glands, and secondary growths, but which differs, however, from the varieties already described by its histological characteristics. Its naked-eye appearances ally it to encephaloid; from its divided surface a large quantity of milky juice can be squeezed out; but cysts or cavities can be recognised from $\frac{1}{2}$ to 1 mm. or more in diameter, which are filled with a milky juice and contain dendritic filaments. Some of these cavities cut across longitudinally are found to be nothing else than galactophorous ducts filled with growths which could be easily detached with a needle. On spreading these dendritic growths on a glass slide, staining them with picrocarminate and examining them under the microscope they are found to present an elegant branching arrangement. The principal trunks divide to form long papillæ, which subdivide and terminate by free long or swollen extremities; all of them are covered by capillaries which terminate in loops at the extremities of the papillæ and are surrounded by a small quantity of connective tissue. They are everywhere covered with prismatic or cylindrical cells, forming one or more layers; the first layer is set perpendicularly on the surface of the papillæ, and the cylindrical cells, which are pressed together, are long, attenuated, clear, and provided with an ovoid nucleus. The cells, which are more superficial and become detached, are large, prismatic or polygonal, and transparent, and contain one large nucleus and one or more large nucleoli. These cells become free in the fluid of the cavities and then undergo fatty degeneration. On studying the preparations obtained after hardening the piece, these villous growths are seen to take origin from the fibrous wall of the

cavities and to develop in them. The internal surface of the cavities is lined with the same cells as the vegetations. Most of these small cysts are nothing else than dilated galactophorous ducts, filled with the growths described above, which spring from their walls, and follow the course of the duct, which they partly fill. The glandular saccules also undergo cystic enlargement; their walls contain epithelial cells arranged as in the ducts, and also often growths projecting from their surface. The walls of the galactophorous ducts are rather distinct; the neighbouring connective tissue is arranged in concentric fibres around them; but it is not so with the saccules, the hyaline membrane of which has disappeared, and they are surrounded by connective tissue changed into alveoli filled with large swollen cells containing large oval nuclei. These tumours might be looked upon as epitheliomata by reason of their probable origin from the galactophorous ducts, and the cylindrical form of the cells lining these ducts; but the infiltration of the neighbouring cellular tissue, changed into alveoli containing large cells, assimilates them to carcinoma more than to cylindrical-celled epithelioma, in which the epithelial growths, when they invade the cellular tissue, take the tubular form, containing cylindrical cells arranged in a regular manner. Hence we have classified these tumours among the carcinomata. We may add that in these tumours, as in many other kinds of mammary tumour, there are many points still to be cleared up; and we take this opportunity of impressing on those who intend to make researches on the classification of tumours of the breast, to pay especial attention to the examination of tumours which recur in situ, after the mamma has been completely removed. It is in the histological study of the recurrent new growth that the most important indications are given as to the nature of the primary tumour. It is also essential to keep the patient under observation in whom a tumour has been extirpated the first time and which has been analysed with care. Thus, for example, we may have a primary tumour riddled with cysts, and which we might hesitate to pronounce to be simple adenoma or an adeno-fibroma or adeno-sarcoma, recurring with all the characteristics of massive sarcoma, without cysts. In carcinoma also which recurs in situ after removal of the whole organ, it is important to note its histological formation, for here are found the best elements for scientific classification. Great attention must also be paid to the neighbouring degenerated connective tissue and the lymph glands. We have, in fact, seen hitherto that in fibroma, myxoma, sarcoma

and carcinoma, there is much analogy in the initial lesions of the glands and of the excretory ducts of the breast; that multiplication of the epithelial cells is always observed, and that the growths in all these tumours are developed inside the galactophorous ducts, and that cysts may result from the distension of the ducts and saccules. These cysts and growths are not therefore sufficient to characterise a given tumour.

Chondroma.—Chondroma of the breast is very rare; a few cases have been reported by Astley Cooper, Busch and E. Wagner. In the case of the latter, the cartilaginous masses were seated in a complex tumour and were combined with carcinoma. Bone-like indurations, constituted simply by calcareous infiltration or petrifaction, are found either in cartilaginous masses or in nodules of fibrous tissue. Velpeau reports many cases of this kind in his 'Traité des Maladies du Sein.'

Adenoma.—We have already in vol. i. p. 284 described adenoma of the breast. It was for a long time considered by Velpeau as synonymous with benignant tumour of the breast, in which were confounded fibroma, myxoma, sarcoma, and true adenoma.

Melanosis of the breast.—*Vide* vol. i. p. 317.

Epithelioma.—Pavement-celled epithelioma with epidermal nests is extremely rare in the breast. It is chiefly seen as a new growth taking origin in the skin and in that part of the nipple where numerous sebaceous glands are situated. It does not differ, either in its mode of development or growth, from epithelioma of the skin, particularly that of the lips. Tubular pavement epithelioma may also be met with in the region of the nipple. We have examined two small tumours of the nipple which were removed by Martel and which were cylindrical-celled epitheliomata ('Soc. de Chir.,' 1882). The new growths composed of epithelial cells, which occur in the glandular ducts and saccules of the breast, and which cause hypertrophy of the whole organ, might also justly be considered as epitheliomata. Such is the *mucoid epithelioma* of Malassez, whose views are set forth in the thesis of Deffaux.[1] As long as multiplication of the epithelial cells takes place in the middle of the ducts and saccules, the typical form of these cells is preserved, and the cavities are often changed into small microscopic cysts, when the name of adenoma or poly-adenoma may be applied to this form of tumour (Broca).

[1] *Contribution à l'Etude des Tumeurs du Sein d'Origine Epithéliale.* Thèse de Paris, 1877.

But when the epithelium loses its primitive form, when its nuclei enlarge, and acini are formed in the interfascicular connective tissue, and the membranes of the saccules are destroyed throughout a greater or less extent of the tumour, it may as well be called carcinoma, or, as many authors say, epithelial cancer. It should also be remembered that, in the most characteristic mammary carcinomata, the parts which are in process of development show evident participation of the glands in the formation of the tumour and the same changes as in the mucoid epithelioma of Malassez.

Under the name of **cystic disease** of the breast,[1] Reclus has described tumours which affect the whole organ. Cysts are found in them which are sometimes small and conglomerate, and sometimes as large as a cherry or even a pigeon's egg. They have viscous contents with thin walls and a smooth surface. Some of them contain a brownish fluid with drops of fat or a semifluid substance like that found in atheroma. This lesion affects both breasts simultaneously. On examining that part of the gland in which the cysts are formed, Brissaud found that the epithelial cells were increased in number and distended the ducts and saccules; the intermediate steps could be traced between this simple distension and the formation of cysts; hence he concludes that these growths are cystic epitheliomata similar to those which end by becoming ovarian cysts.

Cysts.—We have already spoken of the cysts of the breast which may be found in adenomata, sarcomata, fibromata, myxomata and carcinomata; but other cysts may be produced by retention of the secretion in distended galactophorous ducts and saccules. They are caused probably by the partial obliteration of one of the ducts following involutionary fibrous atrophy of the gland, or by cicatrices which are the consequences of operations on the breast. Generally, however, sero-sanguineous cysts coincide with tumours (sarcoma or myxoma), but they have been known to follow contusions. Many cases of dermoid cysts of the breast have been reported, particularly one by Velpeau, which may be included among the first variety of cysts (*vide* vol. i. p. 295); and another reported by Albers contained hair in the midst of a sebaceous mass. *Hydatid cysts* with echinococci, developed in the connective tissue of the breast, are very rare.

[1] Brissaud, 'Anatomie de la Maladie Kystique des Mamelles' (*Arch. de Phys.*, 1844, No. 1, p. 95).

Section V.—Pathological Anatomy of the Skin.

I. Normal Histology of the Skin.

The skin is divided into the epidermis and the derma. The nails and hair, and the sebaceous and sudoriparous glands, are included with the epidermis, being epidermal products. The epidermis, properly so called, is entirely composed of cells, arranged in two principal layers, called the Malpighian layer and the horny layer. The cells composing the Malpighian layer are soft, full of juice and of marked vitality, which is seen by the nutritive changes and active evolution they undergo. They all contain a distinct nucleus, with a double contour, and one or two nucleoli. These cells have a delicate structure which one of us has recently described. Striæ or fibrillæ may be seen in them which intersect one another around the nucleus, forming arcs. Between these fibrils, which are extremely numerous, an amorphous or freely granular substance is found, which corresponds to cellular protoplasm. These intra-protoplasmic fibrils pass out from the walls of the cell into neighbouring cells which they traverse to reach others. The cells do not touch one another; there are small spaces between them, which are traversed by the fibres just described, and which are called uniting filaments; in these spaces, between the uniting filaments, the nutritive plasma of the Malpighian layer circulates. These spaces are found as far as the derma; they exist, in fact, between the first row of cells which rests on the papillary body. The cells in this part are cylindrical and contain pigment granules. In them may be observed all the phenomena of the division of the nucleus and the multiplication of the cell. From their under surface spring simple or bifurcating teeth which penetrate the superficial layer of the papillary body and bring about a solid union between the derma and the epidermis. Lymph cells are often seen in the plasma which circulates between the cells of the Malpighian layer. These cells, which

are derived from the derma, stain a deep violet or even black in preparations treated by the gold method. Langerhans, who discovered them by means of this method, first looked upon them as

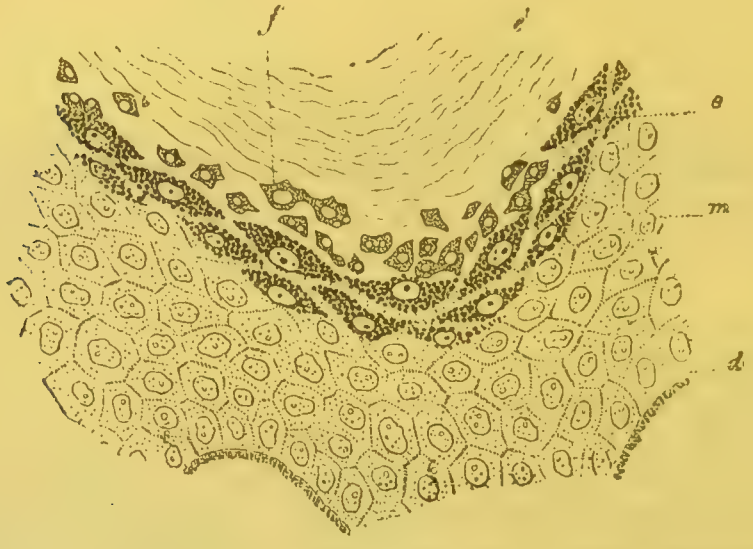

FIG. 214.—VERTICAL SECTION OF THE EPIDERMIS OF THE PULP OF THE FINGER, CUT AFTER HARDENING IN ALCOHOL; STAINED WITH WEAK PICROCARMINE AND PRESERVED IN GLYCERINE.

e', horny layer; *f*, stratum lucidum on the surface of which drops of eleidin are seen; *e*, stratum granulosum; *m*, Malpighian layer with cylindrical cells implanted on the papillæ by teeth. Magnified 300 diameters.

nerve cells. In these preparations they are often seen with a large process turned towards the derma, and a number of smaller peripheral processes. They are all amœboid in origin and their shape and direction are determined, up to a certain point, by the ducts and spaces in which the migratory cells find themselves. The **horny layer** is composed of dried cells, flattened perpendicularly to the surface of the skin; they are solidly united together, and no trace of a nucleus can be found. On subjecting them to a 35 per cent. solution of potash they separate, swell, become spherical and show a limiting membrane. Between the Malpighian and the horny layer there are two thin layers, the *stratum granulosum* on the side of the Malpighian layer, and the *stratum lucidum* on the side of the horny layer. The stratum granulosum is generally formed of two layers of cells, which appear lozenge-shaped in vertical sections of the skin which have been hardened in alcohol and stained with weak picrocarminate. When thus treated they stain deeply while the rest of the preparation is hardly coloured or of a yellowish tint. This peculiar staining of the cells of the stratum granulosum is due to the presence of

a peculiar substance which is seen inside them in the form of refractive drops, and which takes a deep stain with carmine. We have called it eleidin. It is not present in the Malpighian layer properly so called. It exists in the stratum lucidum in a diffused

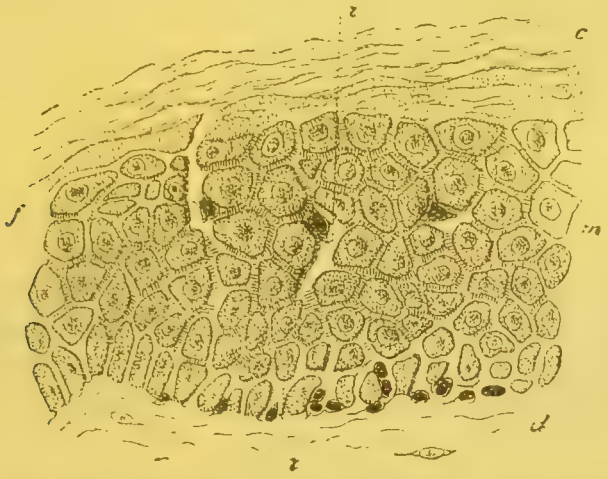

FIG. 245.—VERTICAL SECTION OF THE SKIN TAKEN FROM A LEG AMPUTATED FOR WHITE SWELLING OF THE KNEE. IN THE PART EXAMINED THE IRRITATION WAS NOT RECOGNISABLE BY ANY EXTERNAL SIGN, BUT IT HAD NEVERTHELESS CAUSED THE MIGRATION OF LYMPH CELLS INTO THE MALPIGHIAN LAYER.

d, connective tissue of the papillæ; *f*, intercellular spaces of the Malpighian layer; *m*, cells of the Malpighian layer; *r*, *r*, migratory cells. Magnified 300 diameters.

state, and it is recognised here in preparations in the form of drops or small masses with sinuous edges, which have about the same consistency and refraction as an essential oil. In the stratum lucidum, which is sharply defined, the cells are no longer granular; they are flat and are already joined together, and the spaces traversed by uniting filaments have disappeared. This layer may be considered as accessory to the horny layer, and it follows exactly the same course in any pathological process.

To recapitulate, the epidermal cells are constantly being formed in the deeper layer of the Malpighian layer, and they push towards the surface those which were previously formed; as they rise they increase in size, become regularly polygonal and their organisation is perfected. On arriving at the stratum granulosum, their structure becomes profoundly modified; they become slightly flattened, their fibrillation disappears as well as the uniting filaments, and in the place of the intra-protoplasmic fibrils drops of eleidin show themselves. A cavity is thus formed in their interior, the nucleus atrophies and disappears entirely, as well as the drops of eleidin, when they reach the stratum lucidum, where

being in contact with one another, they become intimately united, probably by means of a cement which the eleidin is instrumental in forming. The end of this cellular evolution is the formation of a horny layer, which, by its solidity and its resistance to chemical agents, gives an efficacious protection to the surface of the body. This evolution shows us how solid cells, without limiting membranes, like those of the Malpighian layer, may become scales, in which, however, by the action of potash, an enveloping membrane and a cavity may be discovered.

The nails.—The horny substance of which the nail is composed rests on a soft epithelial layer which corresponds to the Malpighian layer; only whilst in the epidermis proper the epithelial development is from the deep to the superficial layers, the nail, as everyone knows, grows from behind forwards, which indicates cellular evolution in the same direction. This is due to the fact that the nail does not grow equally from the whole of the Malpighian layer on which it rests. In this mucous structure two parts are distinguished; one, anterior, the bed of the nail; the other, posterior, the matrix of the nail and which corresponds to the external half-moon. At the bed of the nail, longitudinal ridges are seen, formed by the fusion of a number of papillæ; the cells of the mucous body of the bed of the nail fill up the depressions between the ridges. Towards the matrix the crests disappear, and are replaced by long papillæ buried in a mucous body which is much thicker than that of the bed of the nail. The mucous body of the nail does not differ essentially in structure from that of the epidermis; the first row of cells are cylindrical, and those next them polygonal; they are united to one another by the uniting filaments; but the striation which reveals their presence is much more marked than in the epidermis. When fully developed, they become full, both in the bed and the matrix of the nail, of granules which, acted upon by picrocarminate, do not stain a deep red like those of the stratum granulosum, but take a yellow stain. Hence we see that the stratum granulosum of the nail differs from that of the epidermis not only by the absence of eleidin, but by the presence of a peculiar substance called onychogen. It is thick in the matrix, where it is present in many rows of cells, but it is hardly found in the bed of the nail. The subunguial fold is lined by an epidermal layer in which the stratum granulosum, relatively thick, is characterised by the presence of large drops of eleidin. On subjecting the horny

plate of the nail to a 35 per cent. solution of potash it becomes decomposed into cells in which an atrophied nucleus may be found. We have here an important histological distinction between the horny substance of the nail and that of the epidermis.

The hairs.—If several be pulled out from any part of the body, two varieties will be observed among them; namely those which terminate in a full rigid bulb which does not change its shape on pressing it against a hard body; and others in which the end of the bulb is soft and flexible. The first are hairs with a full bulb, the second with a hollow bulb. We will describe the latter first, as the former are only hairs with hollow bulbs arrived at their full maturity. On making a section of the skin which passes exactly through the axis of the hollow bulb of a hair, its papillæ, sheaths, and all its constituent parts are easily recognised. From the body of the hair as far as the free extremity of the bulb, its surface is lined with a layer of imbricated cells covering it from below upwards like the tiles of a roof (the *hair-cuticle*). Around this is the root sheath of the hair, which varies in thickness and is composed of cells irregularly fusiform in shape, without nuclei, and in which pigment granules are found in coloured hairs. In the centre of the hair is a canal, full of cells distinctly polygonal in shape; here is the medulla of the hair, but its presence is not constant. At the bulb, the central medullary canal gives place to a cavity in which is lodged the papilla of the hair, which is formed of connective tissue, and derived from the derma. The cuticle and sheath of the hair are turned so as to cover the papillæ, and at its level and above it the horny cells, which compose the hair, are here soft and full of juice, as in the Malpighian layer. All these cells are derived from the surface of the papilla, those of the medulla from its extremity, and those of the sheath from its lateral surface, and those of the cuticle from its neck. The epithelial cells which take part in the formation of the medulla contain eleidin according to Waldeyer; but, contrary to this author, we maintain that the cells of the sheath and the cuticle do not contain eleidin at any period of their evolution. But it is quite otherwise with the three rows of cells which constitute what is called the internal root sheath, which, derived from the neck of the papilla immediately beneath the hair cuticle, accompanies it within the follicle as far as the orifices of the sebaceous glands. These three rows of cells form from within outwards the three layers which are called the *cuticle of the inner root sheath*, *the*

layer of Huxley and *the layer of Henle.* The evolution of these cells is really from below upwards, and not from without inwards, as most authors teach. Up to a certain spot above the neck of the papilla they all contain granules of eleidin; then, this substance becoming utilised in the formation of keratin, it completely disappears, and the cells which contained it become as homogeneous and transparent as glass; their nucleus atrophies and finally disappears. The entire internal root sheath is then carried with the hair into the interior of the hair follicle. As it passes upwards, it passes under an epithelial layer which fills the rest of the follicle and which is called the external root sheath. This latter has the same structure as the Malpighian layer; its epithelial cells are united by filaments, and between them are spaces in which migratory cells are found. Between the external root sheath and the fibrous coat of the follicle there is a delicate, transparent, amorphous layer, in which is implanted the first row of cells. This layer is called the *vitreous membrane* of the hair follicle; a similar membrane, but much finer, is present around the sebaceous and sudoriparous glands and on the surface of the papillæ of the derma. Eleidin is not present in the external root sheath as far as the orifices of the sebaceous glands, but above, in that part called the neck of the hair follicle, this sheath, which is no longer lined with the internal root sheath, undergoes complete epidermic evolution, and possesses from here a stratum granulosum and stratum corneum. The natural extremity of the hair is conical, which indicates that the papilla on which it is formed was originally small but has progressively increased in diameter, which fact can be verified in studying hairs undergoing development. The papilla preserves the same diameter as long as the hair which is formed on it remains cylindrical; then, at a certain moment, which in man varies according to the kind of hair, that of the head, beard, and other parts of the body, or in a great number of animals according to the season, the papilla begins to atrophy. The hair then diminishes in diameter, and ceases to grow, that is to say that fresh hair-forming cells are not formed. The hair becomes detached from the papilla, the hollow space which it formed inside the follicle is gradually effaced and finally disappears; the hair with a hollow bulb thus becomes a hair with a solid bulb. Acted on by the elevator muscles of the hair follicles—at least that is our explanation—the hair is gradually raised to the spot where this muscle is inserted into the follicle, that is to say,

immediately opposite the opening of the sebaceous gland. As it moves upwards it leaves behind it the cells of the external root sheath, which form a solid mass called the epithelial ligament. At the base of this ligament the papilla, more or less atrophied, is still found; it disappears entirely in the case of alopecia; but in the healthy condition the papilla may become active again and take part in the formation of a new hair with a hollow bulb, to take the place of the hair with the solid bulb. When the latter becomes separated from the papilla, the internal root sheath which accompanies it becomes detached with it and follows it through the hair follicle; but it becomes used up, gradually rubbed away as we may say, as it reaches the opening of the sebaceous gland; whence it results that the hair with a solid bulb has no internal root sheath when it has reached its final stage of evolution.

Sebaceous glands.—Generally only one of these glands is attached to each hair and is placed on the side of the hair follicle in the obtuse angle which is formed by the surface of the skin with the follicle, and it is always inserted more or less obliquely. It may be added that the sebaceous gland is contained in a triangle limited by the epidermis, the follicle and the elevator muscle of the follicle. This smooth muscle is inserted below into the follicular wall and above into the superficial layers of the derma. When it contracts, it raises the hair and favours the excretion of sebum (Hesse). The acini of the gland open freely into one another, and empty themselves by a common excretory duct which opens into the hair follicle at the lower border of its neck. Each acinus is surrounded by an extremely fine membrana propria, beneath which may be observed a layer of polygonal cells, which do not generally contain fat granules. They each contain a very distinct nucleus. To this first row others are added in which the cells become progressively charged with fat drops, which are larger and more numerous as the centre of the acinus is approached. The nuclei undergo at the same time progressive atrophy and at length completely disappear. The cells then become separated and are destroyed to form sebum, which passes into the excretory ducts and thence around the hair, thus facilitating its movement in the neck of the follicle.

The sudoriparous glands are originally solid epithelial cylinders which, springing from the rete mucosum of the embryo, penetrate the derma more or less deeply. They may thus be looked upon as appendages of the epidermis. When completely developed they form a long tube which may be divided into an epidermic

or spiral portion, and a rectilinear or slightly sinuous dermal portion, and a glomerulus, which is seated in the deep layers of the corium in the midst of or beside adipose lobules. In the glomerulus, the sudoriparous tube is folded on itself in an extremely varied manner and terminates in a cul-de-sac. In its intra-epidermal portion, the sudoriparous tube is formed solely of two layers of epithelial cells which undergo epidermal evolution. They have no membrana propria. In other parts, the tube has an external connective-tissue membrane lined by a structureless layer, which may be compared to the vitreous membrane of the hair follicles. The part of the tube which is between the epidermis and the glomerulus is lined with two layers of small polygonal epithelial cells solidly united together. There is a cuticle on the free surface of these cells which limits exactly the lumen of the gland. The epithelial lining has the same characters in a part of the tube of the glomerulus; but inside this body and quite abruptly the epithelium is changed and is continued the same to the end of the saccule. It is then formed of a single layer of cells which are distinctly granular, large and prismatic in shape, and in which the protoplasm contains radiating series of granules (rods) like the cells of the convoluted tubes of the kidney; these cells have no cuticle; between them and the membrana propria there are long fusiform smooth muscle cells, the long axis of which is obliquely to the direction of the sudoriparous tube. The part which contains the smooth muscle cells and the single layer of epithelial cells is the secreting part of the gland. One of us has called it the secreting tube, while the rest of the gland may be called the excretory duct. It must be added that the muscle cells of the secreting tube have on their external surface a series of longitudinal ridges by means of which they fix themselves firmly to the membrana propria. It is thus seen that, owing to their oblique position, the muscle cells bring about on contracting a diminution both of the length and the calibre of the secreting tube.

The derma or corium.—The derma is composed of connective tissue and contains the blood vessels, the lymphatics and the nerves. It forms the papillæ which are buried in the epidermic covering, so that the surface of the epidermis does not at all correspond to that of the corium. The ridges which are seen on the pulp of the finger are produced by a large number of papillæ associated together and covered by a common epidermal lining.

The connective tissue of which the papillæ and the superficial parts of the interpapillary derma are composed, is formed of small interlacing connective-tissue fasciculi, which are firmly pressed together; but in the deeper layers of the derma the connective-tissue fasciculi are much larger and are not so close together. Lastly, near the subcutaneous cellular tissue, the fasciculi separate at a number of points to give place to the glomeruli of the sudoriparous glands and the lobules of the adipose layer. These lobules are composed, as is well known, of fat cells. The connective-tissue cells of the corium have no special structure: they are flat and broad in the deep layers, where the fasciculi are large, and in the papillæ, placed between numerous small delicate fasciculi, they take various and unexpected forms, and show ridges from compression. There are always between the connective-tissue fasciculi a certain number of elastic fibres, which anastomose together and form a network. In the papillæ they are much finer and form a closer network. A similar and well-defined network may be seen in the connective-tissue envelope of the hair follicles and the sudoriparous glands (Balzer).

The vessels of the skin.—The arteries of the skin, after traversing the adipose layer, in which branches are given off to the lobules of fat cells and the sudoriparous glands, continue to subdivide till they reach the papillæ. Each papilla receives a small artery which gives origin to one or more capillary vessels; when the papilla only contains one capillary, it turns, on reaching the apex, and forms a loop and empties itself into a small vein. The point of juncture is indicated solely by a sudden swelling which corresponds to the origin of the vein. When the arteriole gives off several capillaries, the vein terminates in the same way by a swelling which is generally situated in the centre of the papilla, and into which the capillaries open. Some capillaries, however, reach the vein below this swelling. The different papillary veins form a plexus with narrow meshes at the base of the papillæ. From this plexus spring veins which go to form a deeper plexus, the branches of which are larger and the meshes wider than in the superficial plexus. In each papilla of the palm of the hand and the sole of the foot a lymph vessel is present, which seems to terminate in a cul-de-sac which is always placed below the blood vessels. The papillary lymphatics lead into a plexus which is below the superficial venous plexus.

The nerves of the skin are extremely numerous; some of them are motor or centrifugal: they are supplied to the blood vessels, the elevator muscles of the hair and the sudoriparous glands; others are centripetal and their function is general sensibility and the special sensation of touch. The nerves of tact terminate in special bodies, called the corpuscles of Wagner or Meissner, or on the surface of the derma immediately above the Malpighian layer, by peculiar meniscus-shaped swellings called tactile menisques In man, small terminal nervous apparatuses are found in the connective-tissue sheaths of the neck of the hair-follicle; they are comparable to the tactile menisques. We will not describe their structure, for nothing is known of the lesions of these different nervous bodies. The same may be said of the intra-epidermal terminations, the existence of which may be demonstrated very clearly by the gold method of staining. The nervous fibres in the papillæ will then be seen to pass through the surface and to enter the Malpighian layer, where they divide and subdivide to terminate in buds situated between the epithelial cells. Quite recently the termination of the nerves in the epithelial cells has been described first by Pfistner in the batrachians, and then by Unna in man. Each of these cells contains two terminal buds. We have tried to verify the assertions of these authors by employing the same objects of study and the same methods, but we have failed entirely to find a single intracellular nervous termination in the epidermis. We may add that the corpuscles of tact, properly so called, are small oval organs which are found isolated or grouped two or three together in certain papillæ, which have been called nervous papillæ. Into each of these corpuscles passes a medullated nerve fibre which reaches the interior after a more or less long and sinuous course on its surface. It then loses its myeline, and divides and subdivides to form a great number of branches. Each of these branches, the course of which is somewhat complicated, terminates by a bud flattened parallel to the surface of the skin. Between these different nerve branches and the buds in which they end certain cells are found in which in the adult the nucleus is always pushed towards the periphery.[1]

[1] For a detailed description of the structure of the skin, and the histological methods by means of which they may be studied, and for a bibliography of these interesting questions, see Ranvier's *Traité Technique d'Histologie.*

II. Pathological Histology of the Skin.

Elementary lesions of the skin.—We propose to consider in the skin, as we have already done in other organs and tissues, congestion or hyperæmia, hæmorrhage, œdema, acute and chronic inflammation, gangrene and tumours strictly from the pathological point of view. In the skin, many of these lesions are limited to the surface, as for example in the exanthemata, measles, variola, scarlatina, general and contagious diseases in which the evolution is by the successive stages of incubation, invasion, eruption and desquamation. The eruption, or cutaneous efflorescence, which is characteristic in each of these diseases, is nothing else than the manifestation on the surface of the skin of the lesions caused by the elimination of the micro-organisms which seem to be the cause of the general disease. Erysipelas, zona &c. may be grouped with the exanthemata. Other lesions, extending over a more or less extensive surface of the skin, are characterised by macular eruptions which are called *spots* or *macules*, *squamæ*, *papules*, *vesicles*, *bullæ*, *pustules* and *tubercles*. These various lesions which constitute the elementary lesions of the skin, are due in a general way to various modes of inflammation (congestion, exudation, simple inflammation, whether artificial, traumatic, or constitutional, bacterial neoplasms). We will describe these elementary lesions together with the dermatoses in which they are found and which they serve to characterise, and we will follow, as far as possible, the order of the elementary lesions in the description of various cutaneous diseases. Thus we hope to be able to give a succinct anatomical definition.

Spots or macules are generally pink or red in colour; they are generally caused by congestion, repletion and distension of the superficial blood vessels of the derma and papillæ. They disappear on pressure when they are recent, but if diapedesis of the red blood corpuscles has taken place, they become successively yellow, brown, and slate-coloured, and pressure with the finger does not modify their colour.

Hæmorrhagic spots, which are caused by extravasation of the blood into the connective tissue (petechiæ), are of the colour of blood and are not changed on pressure. The blood here undergoes the changes which are always seen when effused from the vessels. Such are the spots in purpura. Scales are nothing else than the shedding of the horny epidermis in the form of lamellæ.

Papules are characterised by limited swelling of the surface of the derma and of the papillary network in consequence of œdematous congestion, or inflammatory œdema of these parts. This takes place in erythema papulosum and nodosum. The papules are white, pink, red or ecchymotic, according to the fulness of the vessels and according as extravasation is present or not. In papules of old standing, such as those of syphilis, the papillæ and the whole of the derma are infiltrated with round cells. **Vesicles** are formed by raising the epidermis, generally by an effusion of serum into the Malpighian layer as the result of congestion or superficial œdema of the papillæ. The transparent serum which fills the vesicles is located in the middle of the epidermis. They terminate rapidly by desiccation or by the formation of a crust, and they rarely cause a permanent cicatrix. Such are the vesicles of herpes, zona, varicella &c. **Bullæ** are produced by the same process as vesicles, but the amount of fluid which raises the epidermis is much more considerable. The transparent serum is located between the corpus granulosum and the Malpighian layer, or in this layer near the papillæ. Such are the bullæ of pemphigus, erysipelas &c. **Pustules** are nothing else than vesicles in which the large quantity and the granular state of the migratory cells render the fluid thick and give it the physical characters of pus. They always open externally after the fall of the epidermis and become covered with a crust formed of pus elements. The suppuration often destroys the surface of the corium at the spot, whence results a small white and depressed cicatrix. Such are the pustules of variola and ecthyma. In **tubercles** there is infiltration not only of the papillæ but of the whole corium and the subcutaneous connective tissue, with round cells. Small tumours are thus produced the evolution of which is slow; they are hard, deeply placed, and blend with the derma, so that when they ulcerate they leave deep cicatrices behind them. Such are the tubercles of lupus, syphilis &c. After these elementary lesions we will describe tumours and finally animal and vegetable parasites.

Congestion and hyperæmia of the skin.—With simple congestion of the skin is included all those troubles caused by repletion of the superficial vessels of the derma and the papillæ. This congestion is characterised to the naked eye by patches of erythema (simple erythema) or by pink or red maculæ, which disappear completely on pressing them with the finger. The congested parts are hardly elevated at all, and the spots and

erythema become pale after death, so that it is impossible to find them in the cadaver. The most simple type of cutaneous congestion is seen in *emotional roseola*, which occurs on uncovering the neck of some young women. But if the spots have existed some days, as, for example, the spots of syphilitic roseola, or the lenticular spots of typhoid fever, effusion of blood often takes place into the connective tissue with diapedesis of the red blood corpuscles, so that though they may pale on pressing them with the finger, a yellow or slightly ecchymotic tint is observed. On examining sections of these spots at their commencement under the microscope, the dilatation of the vessels of the derma is first observed, particularly those of the papillary plexus, which are filled with blood; but it will be noticed at the same time that the migratory cells are present in much greater number than normally. These cells are found between the papillæ and in the Malpighian layer. A few red blood corpuscles are also found outside the vessels in the most superficial layer of the papillæ, and if the maculæ have already existed some days, blood pigment will be found in the place of the red corpuscles, between the surface of the papillæ, or at the base of the rete mucosum. The spots of syphilitic roseola last for a variable time, while some of them pass into the papular state. They often leave a pigmentation of the skin in their place, which is particularly marked on the neck. They form irregularly disseminated patches of a yellow or brown colour, which may be very slight but are still quite characteristic and which alternate with places in which the skin has preserved its natural colour. These characteristics enable us to distinguish syphilitic roseola from other varieties of roseola, such as estival or spring roseola, copaic roseola &c.

The eruption of measles is also a cutaneous congestion. It is seen in the form of reddish yellow spots, which are either flat or slightly acuminated and pale under pressure; or as small red papules corresponding to the orifices of the follicles. The spots have sometimes irregular edges and are in the form of semicircles. We have had the opportunity of examining a fragment of skin removed from a living subject the second day of the eruption at the time it was most marked. We found the vessels full of blood, and a few migratory cells in the papillæ and in the Malpighian layer, and yellow pigment granules also in the superficial layer of the papillæ. In sections stained deeply by allowing them to remain twenty-four hours in a partly aqueous and partly alcoholic solution of safranin, we discovered the presence of small micrococci

which were stained red. They were isolated or united into small irregular groups, situated along the vessels in the connective tissue at the base of the papillæ or inside them. The third day of the eruption, the macules begin to pale, become of a brownish yellow colour and disappear entirely at the end of the fourth day at least. A yellowish or grey discolouration of certain parts of the body may still be observed. The epidermis is desquamated in the form of a fine white powder.

The eruption of scarlatina is characterised by an erythema in the form of fine red points, which seen at a certain distance blend into a uniform red or scarlet tint. The erythema disappears on pressure. The eruption, which varies much in its dissemination, varies still more in its duration, which may last for some hours only or may even pass unnoticed, or may, on the contrary, last a very long time. The skin, which may sometimes remain tumefied and œdematous, is the seat of epidermic desquamation by large squamous plaques ; this may continue for fifteen or twenty days after the commencement of the eruption. Pohl-Pincus states that he has found small bacteria in the desquamated skin.

We may compare these eruptions in man to that called *measles in pigs*, which is characterised by diffused superficial redness of the skin accompanied with a general febrile condition. According to Klein, the micro-organisms which cause this disease are bacilli, while Pasteur and Thuillier have only found micrococci in the blood. We have found the same circulating in the dilated vessels of the papillæ without causing thrombi.

Œdematous congestion of the skin.—When hyperæmia is accompanied with nervous paralysis and distension of the blood vessels, serum is effused into the connective tissue. Thus œdema is produced accompanied with congestion and limited swelling of the skin in the form of round, circumscribed patches or nodules, varying in size. The part played by the nerves and vessels in the production of this congestive œdema is easily understood. In some nervous women, drawing the finger-nail across the skin causes red lines from the dilatation of the capillaries; these become afterwards œdematous, white and projecting, as the nervo-paralytic dilatation of the vessels favours the extravasation of serum into the cellular tissue. Around the raised part, which is white and distended, a red or pink zone is observed. By a similar mechanism, white papules, surrounded by a zone of congestion, are sometimes produced by the nail on scratching the painful spot caused by

the bite of a flea or mosquito, and papular eruptions accompanied with irritation are seen from various causes. Among congestive and œdematous dermatoses may be included *papular erythema*, *multiform* or *polymorphous exudative erythema* of Hebra, *urticaria*, *erythema nodosum* and *pityriasis*.

Papular erythema.—This lesion, which is generally seated in the uncovered parts of the body, is characterised by papules which may be flat or round, isolated or grouped, pink or purple red in colour. The relief and colour disappear entirely or partly on pressure with the finger, and the papules undergo sudden and spontaneous cure. We have examined sections of these papules removed from the living subject and hardened in alcohol. The epidermic layers were intact, and the migration of cells into the Malpighian layer is rare here, if we may judge from our own experience. A few cylindrical cells of the Malpighian layer are found undergoing indirect division. The papillæ are swollen as well as the derma. All the connective tissue of the derma is infiltrated with serum, and a great number of migratory cells are seen accumulated around the vessels at the base of the papillæ and around the hair follicles and glands.

Multiform exudative erythema of Hebra is an acute affection characterised by the multiplicity and variety of the eruption. It is seated by preference on the dorsal surface of the hands, the fore arm, legs, face and forehead. The eruption is generally symmetrical. Sometimes disseminated spots are seen, varying in size from that of a pin's head to a lentil, of a dark red colour paling under pressure, flat or projecting slightly above the level of the skin. These spots rapidly extend and become cyanotic; or they become pale centrally while the edges remain red (annular erythema); or in the middle of the white centre a red spot is seen (erythema iris). These spots often turn into the papules of papular erythema or urticaria. Sometimes actual vesicles are developed upon the papules (vesicular erythema, herpes iris), or bullæ (erythema bullarum). The eruption may last from one to six weeks.

Erythema nodosum (dermatitis contusiform) shows itself by deep and prominent tumefactions or nodules the size of a small nut and sometimes even of a filbert; the nodules are hard, generally seated on both legs or on the dorsal surface of the feet, and more rarely on the fore arm and thigh. The colour of these nodules changes rapidly from pink or red to blue, yellow or green tints, and the swellings diminish at the same time in size. They are sometimes accompanied with ecchymoses or even with a sub-

cutaneous effusion of blood. From the anatomical point of view, they consist in a serous infiltration of all the layers of the corium and the subcutaneous connective tissue, diapedesis of the red and white blood corpuscles, and stasis of blood in the vessels.

Urticaria consists of flattened elevations of the skin which may be red or white centrally with pink edges; they are round or irregular in shape, and are often united in rings. They are ephemeral in duration and are caused by congestive œdema similar to that of preceding eruptions.

The pink pityriasis of Gibert, pityriasis rubra (Bazin), desquamative papular erythema (Vidal), erythemato-desquamative pseudo-exanthema (Besnier), is characterised by superficial papules, which occur in successive crops. They are surrounded by an erythematous zone, and form by their confluence various discoid and crescent-shaped groups, and they end in a furfuraceous desquamation. We have examined a fragment of a papule removed from the living subject, and we found the same lesions here as in papular erythema. The papillæ and derma contained a few migratory cells, and in the cylindrical cells of the Malpighian layer the nuclei were seen undergoing indirect division, and a small number of migratory cells were found between the cells of the Malpighian layer.

Hæmorrhagic spots. Purpura. Petecchiæ.—There are various kinds of purpura, such as simple purpura, rheumatismal purpura, apyretic hæmorrhagic purpura or Werlhoff's disease, febrile purpura, which constitutes a rash such as that which follows certain affections of the spinal cord and nerves (Faisans) or certain forms of cardiac cachexia (Rigal and Cornil), and cachectic purpura; they are all essentially characterised from the anatomical point of view by an effusion of blood into the superficial layers of the derma and the papillæ. Purpura manifests itself by blood-coloured spots, which are not raised above the skin and which do not disappear on pressure; they pass through the successive changes of colour of ecchymoses. In a section of one of these purpuric spots which has been hardened in osmic acid or Müller's fluid, the blood vessels in the derma and papillæ are seen to be dilated. A large number of red blood corpuscles are found between the connective-tissue fasciculi of the derma immediately below the papillæ; they are less numerous in the papillæ themselves, where the delicate fasciculi are close together. Later on, only blood pigment is found instead of recognisable blood corpuscles.

In recent hæmorrhagic spots of cachectic purpura, we have sometimes seen (Jardet[1] and Leloir) the blood vessels of the papillæ and derma dilated in a really remarkable manner, so that it might be supposed that small angiomata were under observation. The capillaries of the papillæ were, for example, from ten to twenty times larger than normally and were filled with blood. Very few red blood corpuscles were effused into the connective tissue around these dilated vessels. In other purpuric spots which were rather older, we found migratory cells around vessels which were equally dilated and filled with blood, a certain number of which were filled with blood pigment. In fact, the function of the migratory cells is to take up and preserve in their protoplasm the molecules of pigment when interstitial hæmorrhage is undergoing resolution (see vol. i. p. 408). Sometimes actual proliferation of the endothelium of the vessels (Hayem) and capillaries (Leloir) has been observed. The patches of purpura terminate by resolution when the bundles of fibres are not separated by too large a quantity of blood and when the circulation has not been entirely arrested in the compressed vessels. But if this should occur, mortification of the infiltrated connective tissue may take place. The hæmorrhagic spots are then changed into gangrenous patches; their surface is black; the epidermis is raised by transparent or russet-coloured serum, and the bullæ which are thus formed contain a variable number of blood corpuscles; they burst, and the fluid escaping the superficial part of the derma is left exposed; it is of a blackish colour and either dries or ulcerates. In sections, the mortified part is seen to be infiltrated with the colouring matter of the blood, and altered red blood corpuscles are found between the fasciculi of connective tissue (see vol. i. p. 59).

Hæmatidrosis or blood sweat is chiefly related to hysteria, as Parrot has shown. This is the lesion of the stigmata. The skin reddens at a certain point, swells and the blood escapes in small red or pink drops. This phenomenon seems to result from hæmorrhage into the sudoriparous glands rather than from an anomalous secretion of these glands.

Pigmentary spots.—Pigmentary spots are frequently, as we have already seen, the result of papules or spots into which blood has been extravasated. There are other affections of the skin in which the formation of pigment is exaggerated; such are the

[1] *Société Anatomique*, 1883.

ephelides, the *spots of pregnancy*, and *melasma*, which are seen in the form of small grey or black spots. At the level of these spots a large number of brown or black granules are found in the cells of the Malpighian layer. In certain forms of cachexia, in some patients affected with chronic tuberculosis of the peritoneum and intestine, in malarial and saturnine cachexia, a deep discolouration of the skin may be observed in places or over a great part of the body. This discolouration, which may be seen in patients suffering from lead poisoning at the edge of the lips and gums, is due to a deposit of sulphate of lead in the fixed cells of the connective tissue, in the papillæ and around the blood vessels. In the meshes of the corium there are found at the same time a certain number of migratory cells full of grains of sulphate of lead (Renaut). The black discolouration of the skin which occurs in patients who have been subjected for a long time to the internal administration of nitrate of silver, is also due to the deposit of silver in the connective tissue and not in the epidermic cells. A similar discolouration is seen in the internal organs, in the glomeruli of the kidney, for example. In Addison's disease (see p. 452) the skin is more or less of a slate or olive colour, like the skin of a negro. It is, moreover, spotted over with points blacker than the rest, more particularly on the face, hands, breast, lips, inside of the cheeks and in the axilla. In vertical sections of the skin cut after hardening in alcohol, and examined without staining in glycerine, the whole of the Malpighian layer is seen to be pigmented, which pigmentation is more marked in the cylindrical cells in contact with the papillæ; this is also observed in the negro. Pigment granules are also found in the fixed cells of the connective tissue of the papillæ and superficial part of the derma, and principally around the blood vessels.

In **tattooing**, various coloured substances, such as indigo, vermilion and gunpowder, are inserted in the skin by means of needles. The colour is indelible and can only be removed by cauterisation of the derma. The coloured granules may, however, be partly carried away by migratory cells, for they are found in the glands to which the lymph vessels pass from the tattooed part.

Achromic spots.—The pigment of the skin, instead of being abundant, as in the normal condition, may be wanting in places and over a great part of the body. Thus in superficial cicatrices, in the patches of *Alopecia areata* and in certain patches of anæsthesic lepra, the colour of the skin is absolutely white, or less coloured

than the neighbouring parts. Albinism also constitutes a more or less marked and general form of achromia.

Dischromic spots.—**Vitiligo** presents a very remarkable example of unequal distribution of the pigment of the skin. This lesion consists in the appearance of decolourised patches, varying in size, slow or rapid in growth, and varying in number. They commence singly, and finally blend together; they are always surrounded by a zone of skin where the pigment accumulates. This hyperchromia at the edge of the decolourised patch induces us to think that the pigment leaves the patch of vitiligo and accumulates in its circumference. On a white patch, which is thin and dry, the hairs are always white. On examining hardened vertical and unstained sections of the skin, which comprise both the patch and its border, it will be seen that the epidermis of the neighbouring skin is highly pigmented. The entire Malpighian layer contains brown or black granules which are chiefly accumulated around the nuclei of the cylindrical cells implanted on the papillæ. The

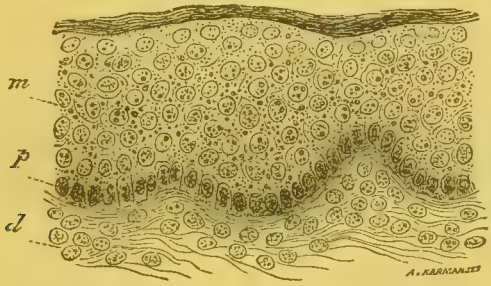

FIG. 246.—SECTION OF THE BORDER OF A PATCH OF VITILIGO.

d, connective tissue; *p*, layer of cylindrical cells of the Malpighian layer; *m*, polyhedral cells of the Malpighian layer infiltrated with black pigment. (After Leloir.)

papillæ themselves are well developed. In the central patch, the epidermis is, on the contrary, entirely without pigment; its various layers are, moreover, thinner; the horny layer is present, but the granular layer is wanting (Leloir). The cylindrical cells of the Malpighian layer are also often absent, and the Malpighian layer itself consists of two or three layers of pavement cells; the papillæ of the derma are flattened and project slightly; the derma itself is limited by a line which is almost horizontal, and it is itself thin, as in old persons. On examining the nerves which are distributed to these patches, after subjecting them to the action of osmic acid, they are often seen to show the lesions of parenchymatous neuritis, characterised by fragmentation of the

myeline, its more or less extensive disappearance from the nerve tubes, multiplication of the nuclei of the outer sheath, and even the disappearance of the axis cylinder. These lesions, which have been described by Leloir,[1] have been verified by Déjerine, Schwimmer and Pitres. The glands of the skin are more or less atrophied, as well as the hair follicles.

Cutaneous Œdema.—We have already in vol. i. p. 410 fully described œdema of the connective tissue from the histological and pathological point of view; so that we need not now reconsider the general condition. When the skin is the seat of general or limited œdema, of whatever cause, it, as well as the adjacent connective tissue, is tense, white, and thick, and it often has a kind of semitransparency. It pits easily on pressure with the finger, and the indentation persists for some minutes or longer (soft œdema), or indentation is more difficult, and the depression is quickly effaced (hard œdema). When the œdema is very marked there are seen transparent mammillated or linear projections, which sometimes seem to be united together by prolongations, so that at first sight it might be thought that they were caused by distended lymph vessels; but their appearance is simply due to

FIG. 247.—SECTION OF ŒDEMATOUS SKIN.

e, epidermis; *p*, Malpighian layer covering the papillæ; *d*, derma infiltrated with leucocytes; *v*, blood vessels; *l*, intradermic dilated lymphatics surrounded with white corpuscles.

more or less marked œdema of the papillæ. On examining sections of œdematous skin under the microscope, after hardening in

[1] *Recherches Cliniques et Anatomo-Pathologiques sur les Affections Cutanées d'Origine Nerveuse*, Paris, Lecrosnier, and *Progrès Médical*, 1881.

Müller's fluid, gum and alcohol, the capillary blood vessels are very apparent and are gorged with blood, though to the naked eye the skin appears to be white and anæmic. The bundles of connective tissue are separated from one another by a small quantity of serum, in which a small number of free lymph cells are generally found. This œdema is sometimes very marked at the level of the papillæ. The fibrils of connective and elastic tissue which enter into their composition are bathed in a transparent fluid containing a variable number of migratory cells; the papillæ have greatly increased in size while retaining their form. In the derma, the thick fasciculi of connective tissue are also separated by serum containing migratory cells. These cells often form masses, or irregularly disseminated islets. The lymph vessels are dilated (Renaut), and instead of being seen as in normal skin in the form of narrow slits they show large gaping stellate spaces, which on

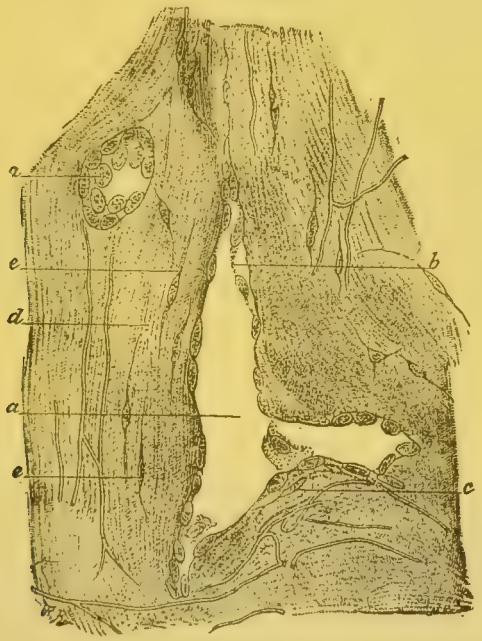

FIG. 218.—DILATED LYMPH VESSEL OF THE DERMA IN ŒDEMA.

a, cavity of a blood vessel; *b*, its endothelium; *c*, elastic edge of the lacuna; *c*, cells and *d*, fasciculi of connective tissue in the midst of which is hollowed the capillary lymphatic.

section are seen to be larger than the largest blood vessels of the derma. This dilatation of the lymphatics is constant in œdema. Young has described the dilated interfascicular spaces of the derma,

[1] Young, 'Zur Anatomie der œdematosen Haut' (*Wiener Akad. Sitzungsber.*, lvii. p. 951, 1868).

which are filled with fluid like the lymphatics; but the interpretation given by this author is incorrect.

Dermatitis. Diffuse inflammation of the skin.—The different forms of diffuse inflammation of the skin, that is to say those which implicate a more or less extensive surface, are very common. They include œdematous dermatitis caused by an irritant, such as heat or cold, burns or frost-bites; by chemical agents, and by bacteria, as in erysipelas; and deep suppurative dermatitis, such as in lymphangitis and phlegmon. We will commence their study by describing artificial inflammation of the skin.

Experimental dermatitis caused by bacteria.—We will take as our example the result of the injection into the cellular tissue of the guinea pig of a few drops of an infusion of jequirity.[1] The bacilli contained in this infusion multiply at the spot inoculated, and inflammatory œdema extends for a more or less considerable distance to the surrounding skin and cellular tissue. Twelve or twenty hours after the injection, the derma appears, on a vertical section, to be infiltrated with serum containing myriads of bacteria in active movement. Sections of the altered skin, cut after hardening in alcohol and stained with methyl violet, show a considerable quantity of small short rods, everywhere interposed between the elements of the derma. At the point where the lesion commenced, the fixed cells of the connective tissue are hardly swollen, but diapedesis of the lymph cells soon begins at the same time that there is infiltration of serum between the fasciculi of connective tissue. The bacilli, in large numbers, are situated in the interfascicular spaces and along the fasciculi, and are generally lying in the same direction as the fibres themselves. They are also seen between the fibres of the papillæ, as well as between the fasciculi of the derma, or between the adipose cells. The migration of lymph cells is at its maximum in the derma, in its deeper layers and in the subcutaneous cellulo-adipose tissue. The papillæ are infiltrated with serum, and a large number of small rods or spores are seen on their surface, between them and the Malpighian layer. The microbes penetrate between the cells of the epidermis and the sheaths of the hair. The epidermis softens and the hairs fall spontaneously or at the least touch; the surface of the skin is infiltrated with fluid which contains a number of small rods and spores. The hair follicles aid by becoming detached to eliminate the bacteria. This œdematous inflam-

[1] Cornil and Berlioz, *Archives de Physiologie*, 1884.

mation may terminate by superficial mortification of the derma, or by abscesses containing caseous pus. Œdematous dermatitis, similar to the above, may be obtained by injecting under the skin, or into the muscles of the guinea pig, the blood of an animal which has died of symptomatic anthrax.

Erysipelas.—Erysipelas is a type of œdematous dermatitis of bacterial origin, which greatly resembles the preceding. The local symptoms, which are observed in the skin, realise the four essential characters of inflammation; namely, redness, heat, pain and tumefaction. Erysipelas commences by a bright, shining and projecting red patch, generally starting from the edge of a mucous orifice such as the eyelid, the nose, the ear, or near to an excoriation. The patch extends more or less rapidly. The inflammation may remain localised to the region where it originated, or it may extend by successive exacerbations, so that starting from the cheek, it may invade the scalp, ear, neck, chest &c. The erysipelatous redness disappears on pressure and leaves a yellow tint in the finger prints. The limit of the patch where the inflammation ends abruptly is distinctly marked by a ridge. The researches on erysipelas at the commencement of this century led to the opinion that it was either a kind of phlebitis (Ribes, Copland, Cruveilhier), or a lymphangitis (Blandin). It is only about fifteen years ago that the precise pathology of this affection was made out. Vulpian[1] first remarked that there was an accumulation of lymph cells in the meshes of the derma. Volkmann and Steüdner[2] demonstrated that the presence of these lymph cells in the meshes of the derma was due to diapedesis. Renaut[3] gave an excellent histological description of the disease. Nepveu[4] showed that bacteria were present in the serum of erysipelas and even in the blood, and Fehleisen proved that erysipelas was caused by bacteria, and he cultivated them and inoculated man with them. In sections examined under the microscope, the infiltrated migratory cells are seen in the fasciculi, particularly around the blood vessels and lymphatics, and in the subcutaneous tissue at the periphery of the adipose lobules and the lymph vessels. These cells are more abundant in the derma than in the papillæ. The fixed cells are tumefied and their nuclei may be seen dividing. Serofibrinous exudation into

[1] *Archives de Physiologie*, March 1868.
[2] *Centralblatt für med. Wissensch.*, August 15, 1868.
[3] *Dict. Encyclop. des Sc. Méd.*
[4] *Comptes Rendus de la Soc. de Biologie*, vol. xxii. p. 164, 1870.

the derma and subcutaneous cellular tissue is also added to diapedesis and cellular proliferation. The endothelium of some of

FIG. 249.—SECTION OF THE SKIN OF THE LOBULE OF THE EAR IN ERYSIPELAS.

e, epidermis; *m*, Malpighian layer; *d*, capillary lymphatics full of leucocytes; *l*, subcutaneous lymphatic distended by the same cells; *g*, sebaceous gland; *h*, fibrous tissue of the derma infiltrated with leucocytes; *n*, arterioles; *o*, adipose vesicles; *p*, leucocytes between them.

the lymphatic fissures is tumefied, and some of the subcutaneous lymph vessels are filled with migratory cells. The micrococci, which are easily seen in sections stained with methyl violet, have a diameter of ·0003 mm. They are united two and two together, or in chains which often have a wavy form. In preparations of erysipelatous skin, the bacteria are seen in groups in the interfascicular spaces (*m*, fig. 250), in the lymphatics (*v*, *v*, fig. 251) and in the subcutaneous adipose tissue. In the latter, it may be seen, that the bacteria are in the cells themselves, and are located in the protoplasm which surrounds the drop of fat. The bacteria are very numerous in figs. 250 and 251, though the inflammation

of the derma was not acute. These preparations were made from a recent patch of erysipelas of the scalp, consecutive to erysipelas

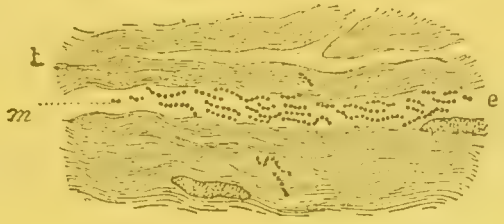

FIG. 250.—SECTION OF THE DERMA IN ERYSIPELAS.

e, interfascicu ar space filled with diplococci and chains; *t*, *t*, connective tissue. Magnified 600 diameters.

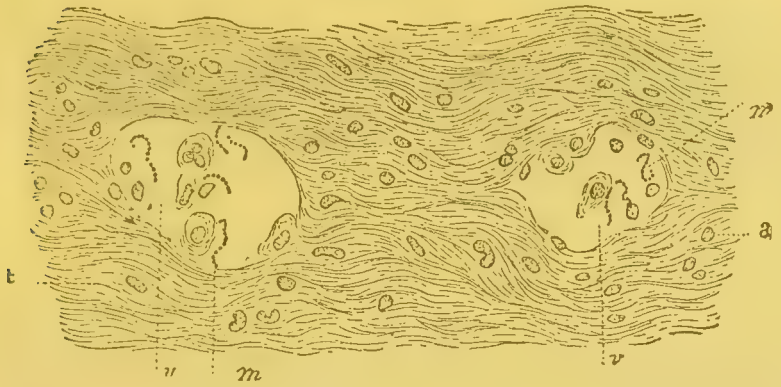

FIG. 251.—SECTION OF THE DERMA IN ERYSIPELAS.

v, *v*, section of two lymph vessels containing leucocytes and chains of micrococci, *m*, *m*; *t*, connective tissue; *a*, connective-tissue cells and migratory cells. Magnified 600 diameters.

of the face.[1] The micro-organisms are also found at the periphery of the hair follicles, a fact which enables us to understand the cause of the fall of the hair, which is almost constant when the scalp is affected by this lesion. When the erysipelatous inflammation is acute, the epidermis is raised by vesicles, phlyctenæ and bullæ similar to those produced by the application of a blister. The fluid of these bullæ contains a rather marked quantity of fibrin and round cells. On searching the fluid for the microbes of erysipelas, by the usual process—drying a drop of the fluid on a slide and staining—bacteria are not always found, though it was by this method that Nepveu observed them. In sections of hardened skin in acute erysipelas, a large number of migratory cells are found in the derma and the cellulo-adipose tissue. In the bullæ or phlyctenæ, the skin is raised at the level of the stratum granulosum, so that the effused fluid is limited on

[1] One of us related the facts of the case in a communication made with Babes to the Société Médicale des Hôpitaux, August 1883.

one side by the horny layer and on the other by the Malpighian layer. The cells of the latter are generally separated from one another by a serous exudation and by migratory cells which escape from the vessels of the derma by diapedesis, and which penetrate

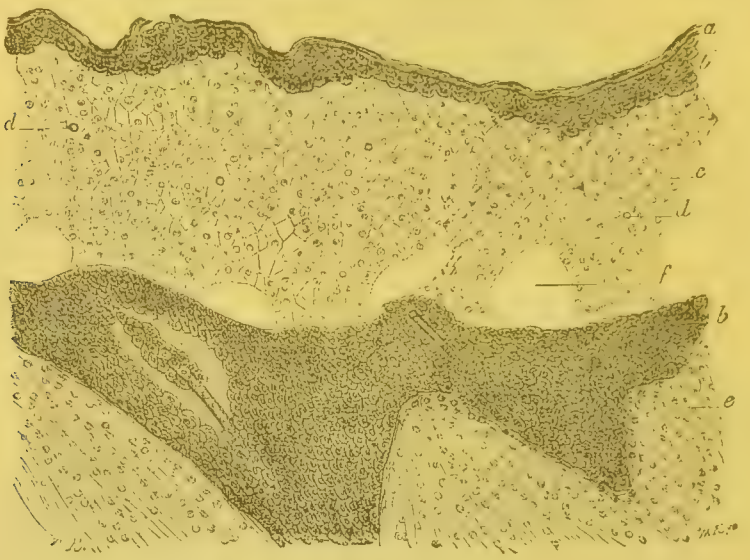

FIG. 252.—SECTION OF A PHLYCTENA IN ERYSIPELAS.

a, horny layer; *b*, raised granular layer; *c*, migratory cells englobed in a fibrinous reticulum; *d*, red blood corpuscles; *f*, arc-like arrangement of the fibrinous network; *b'*, Malpighian layer; *e*, papillæ infiltrated with migratory cells. Magnified 120 diameters.

between the epidermic cells and the distended intercellular canaliculi. The epidermic cells undergo important changes at the same time. The nuclei of some of them show vesicular degeneration; their nucleolus is distended and changed into a vesicle, and distends the nucleus; when the nucleus has become completely vesicular, its substance is reduced to a small semilunar mass attached to one of the poles of the nucleolus (see vol i. p. 65). In some cells not only the nucleus but the protoplasm itself becomes vesicular; the cell then loses its vitality, and allows two or three migratory cells to enter it and they are found inside its nucleus. Epidermic evolution no longer takes place; the cells of the stratum granulosum are no longer charged with eleidin; the epidermic cells fall before passing through all the phases of their normal evolution, before the complete disappearance of their nucleus and before their horny change has taken place. The irregular fall of these cells produces, when mixed with white corpuscles, scales or crusts on the surface of the epidermis. This change in the epidermic evolution is, however, not peculiar to erysipelas, and is generally met with in cutaneous affections with

migration of leucocytes into the Malpighian layer, and vesicular degeneration of the cells of this layer. We shall often have occasion to refer to the formation of eleidin and the horny changes in cells, which have been described by one of us and by Suchard.[1] Erysipelas sometimes terminates by extensive phlegmon, or by localised suppuration of the subdermic connective tissue.

Phlegmonous dermatitis.—Phlegmon, or suppurative inflammation of the cellular tissue, has been already studied from the general point of view (vol. i. p. 415). The connective tissue of the derma may be primarily affected with suppurative inflammation, but the skin is more generally affected consecutively by a phlegmon which has commenced in the subcutaneous cellular tissue. The causes of phlegmon are various: contusions, wounds, surgical traumatism, purulent infection, subcutaneous injections of morphia, ether, quinine, &c. The pus of these phlegmons, even when the inflammation has commenced without any solution of continuity of the skin, always contains micro-organisms. According to the experiments of Straus, if irritating substances be injected under the skin of animals, and the precaution be taken to superficially cauterise the epidermis, and to make the injection with a fine glass pipette which has been previously sterilised, and if the small wound of the skin be afterwards cauterised, no suppuration is produced. If, however, suppuration should occur, the pus contains micro-organisms (Soc. de Biologie, 1884). If pus be taken from a phlegmon in man, at the moment that the opening is first made by the surgeon, and if it be spread and dried on a slide and coloured with fuchsin or methyl violet, it always contains micro-organisms, as we have proved by personal observation. The microbes are associated in twos (diplococci) or in chains. The chains are generally long, sinuous, convoluted or massed together. In diameter these microbes do not measure more than ·0003 mm.; but we may nevertheless ascertain that they never have the same arrangement or the same diameter. Thus chains are seen composed of round microbes, arranged two and two together at pretty nearly equal distances from one another; in some chains the microbes are from a third to one half larger than in others, and in the same chain the microbes vary greatly in size; at one end, for example, they may be large and at the

[1] Suchard, 'Des Modifications et de la Disparition du Stratum Granulosum de l'Epiderme dans quelques Maladies de la Peau' (*Archives de Physiologie*, 2nd series, vol. x., No. 6, August 18, 1882).

other small. When very close together they are often lenticular in shape, as may be seen in diplococci; they are often seen round lymph cells or in their protoplasm, and they seem to be related

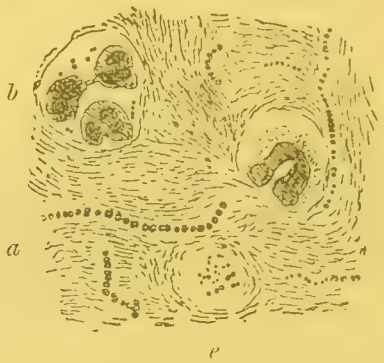

FIG. 253.—PUS OF PHLEGMON SPREAD AND DRIED ON A SLIDE.

a, chain of large micrococci; *b*, smaller micrococci contained in a lymph cell; *c*, group of micrococci. Magnified 1,000 diameters.

to the pyogenic microbe which Pasteur found in the water of Paris. This latter is a short vibrio strangulated in the centre and resembles the bacterium termo; it is both anaerobic and aerobic. Pasteur has succeeded in cultivating it, and on inoculating the animals with the culture fluid suppuration was produced. On injecting it into the jugular vein of a rabbit purulent infection was induced; but we should add that many varieties of bacteria produced suppuration.

Phlegmon generally commences in the deep cellular tissue, and a series of lesions is produced, passing from the base of the derma to the deep subcutaneous connective tissue, increasing as the subcutaneous fat is approached, so that in sections of phlegmon the inflammation is seen to become more and more acute in the deeper layers. Vascular thromboses are also observed; they are probably caused by the presence of microbes in the blood, which by slowing the circulation favour diapedesis and the accumulation of lymph cells in the connective tissue. In sections stained with picrocarminate, the whole of the derma and the subcutaneous tissue is seen to be infiltrated with lymph cells; the interfascicular spaces are also filled, and the exudation contains a large quantity of fibrils of fibrin, which form a reticulum. The fat cells are replaced by nests of small round cells, which accumulation brings about mortification of the connective-tissue fasciculi. Actual molecular gangrene of the extravasated lymph cells may also occur in phlegmon, in consequence of their being crowded together and not receiving a sufficient supply of nourishing juices;

necrosis of the connective tissue follows that of the cells. The mortified elements liquefy, and an abscess is formed, on the wall of which is found the débris of connective-tissue fibres and pus cells. In sections stained with methyl violet and eosine, the micro-organisms are seen stained violet, while the tissue and cells are red. At the edge of the inflamed part, some of the vessels are seen to contain coagulated fibrin, in the meshes of which diplococci are observed or lymph cells containing diplococci. Outside the vessels, the microbes are arranged along the fasciculi of the connective tissue. The fixed cells of the connective tissue are normal or slightly tumefied. The fat cells contain a variable number of bacteria, which are found located in the protoplasm around the fat drops. At the spots there the phlegmonous inflammation is most acute, migratory cells are seen in the interfascicular spaces more or less filled with bacteria, and the large fixed cells of the connective tissue, which are markedly swollen, become either free or partly detached and are seen to be filled with fragments of nuclein and with a large number of microbes which are

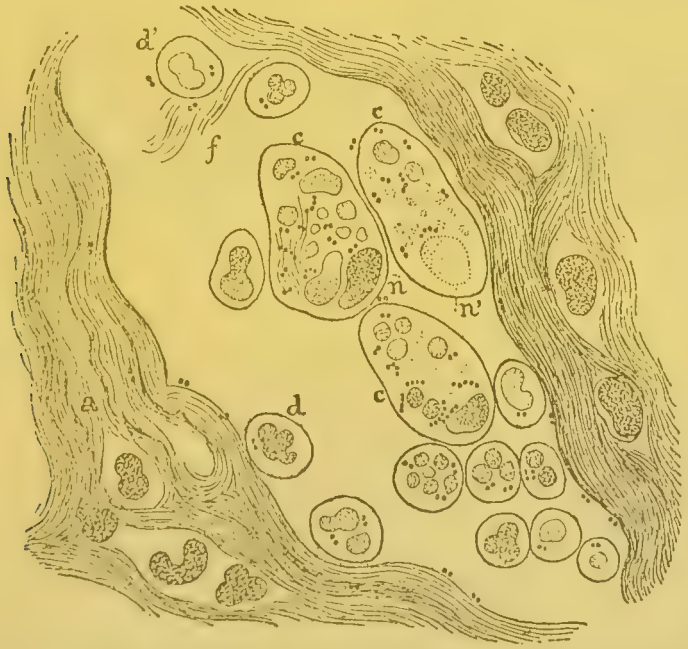

FIG. 254.—SECTION OF THE DEEP CONNECTIVE TISSUE IN PHLEGMON.

d, lymph cells containing microbes; *d'*, lymph cell the nuclei of which are pale; *c, c*, large fixed cells of the connective tissue; they are tumefied and contain several nuclei or fragments of nuclei and microbes; the nuclei, *n'*, in one of these large cells are pale and necrosed. All these elements are contained in an enlarged interfascicular space. Magnified 800 diameters.

either isolated or associated in couples (fig. 254). Among these large cells some are seen with a well-stained nucleus and their

protoplasm contains a relatively small number of microbes; others have no nucleus and their protoplasm is crowded with numerous bacteria; others are seen intermediate between these. In most of the cells the nucleus is fragmented, reduced by granules or entirely destroyed. The latter are mortified and invaded by bacteria. It is probable that the entrance of micro-organisms into the fixed cells of the connective tissue brings about their mortification and the consequent fragmentation and disappearance of their nuclei. Near the wall of the abscess the connective-tissue bundles are pale, altered, broken up and covered with microbes; the lymph cells, accumulated together, are undergoing destructive changes and are filled with bacteria. When a phlegmon, which has commenced in the deep tissue, reaches the derma and the superficial layers of the skin, inflammation and diapedesis are preceded by the invasion of micro-organisms which insinuate themselves between the bundles of connective tissue. In some cases of phlegmon which have commenced in the deep layers, the papillæ are, at a given moment, much hypertrophied and very œdematous. A considerable quantity of fluid containing proteic granules separates the fibrils of the connective tissue of the papillæ; chains and diplococci are also found in this fluid even when there are very few migratory cells present. The epidermis is generally the seat of a migration of lymph cells which also contain microbes. These latter may be met with singly, without there being any migratory cells between the cells of the Malpighian layer. Suppurative dermatitis caused by lymphangitis is often superficial; the derma and papillæ are infiltrated then, as in deep phlegmon, by the same micro-organisms. It is difficult to explain the presence of bacteria in pus when there has been neither purulent infection nor a solution of continuity of the skin, as in a contusion, for example. It is supposed that the bacteria of suppuration exist in the blood in small numbers and in an inoffensive state in healthy subjects, and that when the tissue is inflamed, contused and mortified, they become developed in large numbers in that part which has lost its normal functions, and suppuration is produced. Phlegmon sometimes gives the feel of subcutaneous emphysema; gas may, in fact, be produced in pus, through the action of the large micrococci in chains already described. But there is besides a form of gangrenous septicæmia with the production of a large quantity of gas, traumatic erysipelas, gaseous gangrene, rapid gangrene, &c., resembling phlegmon, which is caused, according to Chauveau and Arloing,[1] by a rod-shaped organism similar to the septic vibrio of Pasteur. This micro-

[1] *Académie de Médecine*, séance du 6 mai 1884.

organism, which is very large, measures from 6μ to 50μ in length and 1·2μ to 1·5μ in diameter; a spore is often seen at one of its extremities which is slightly swollen. It is anaerobic. Chauveau and Arloing succeeded in cultivating it, and have inoculated a number of animals with it. It is destroyed by sulphuric acid and by a temperature of from 212° to 248°. Surgical instruments seem to have been the agent of transmission in some surgical wards where gaseous gangrene has been seen to be endemic.

Boils. Carbuncle.—The boil is a small hard inflammatory nodule, deeply placed in the derma and subcutaneous connective tissue; in the centre the tissues are necrosed, which necrosed part, known under the name of core, is eliminated with the pus. The pus of a boil contains micrococci, diplococci and chains which do not differ in a marked manner, by their physical characters and their mode of staining, from those of phlegmon. **Carbuncle** commences by a deep induration of the subcutaneous cellular tissue; it varies in size from that of a halfcrown to the palm of the hand or even more. Its usual seat is the neck, but it is sometimes seen on the face. The whole of the affected part is infiltrated with pus and fibrin, which distend the connective tissue of the derma and the subcutaneous layer of fat, so that the skin becomes necrosed in places or over a large surface; these losses of substance, which often look as if punched out, leave exposed the subjacent tissue, which is indurated and infiltrated with an exudation of great density. The connective tissue, which is strangled and necrosed by this exudation, is slowly eliminated; the pus is blood-stained and abundant and the patient becomes much exhausted. Carbuncle is a circumscribed phlegmonous inflammation of the same nature as a boil.

Glanders.—Glanders is always produced in man by contagion from an animal affected with the same disease. It commences by a cutaneous or farcinous ulcer or by lymphangitis (see vol. i. p. 211). In acute glanders a pustular eruption similar to that of small-pox finally occurs simultaneously with general pyæmia (see vol. i. p. 213). The etiology of this disease has been elucidated by the researches of Bouchard, Capitan and Charrin of Paris, and Löffler and Schütz of Berlin. It is caused by small bacilli which may be long or short. Bouchard, Capitan and Charrin have succeeded in producing glanders in the guinea-pig and in the donkey with culture fluids.

Cutaneous diphtheria.—Ulcers and wounds of the skin are often found covered, particularly in unhealthy hospital wards, with grey and blood-stained false membranes. This condition of wounds has not been seen in Paris for a long time. In the final period of diphtheria of the pharynx or larynx, more or less extensive patches of diphtheria are found in the moist or excoriated parts of the body, such as around the vulva in little girls, for example. These pseudo-membranous patches on the skin have the naked-eye appearances of the false membranes of the mucous membranes. They may become gangrenous. We have often examined skin in this condition in fragments removed from the living subject. On examining sections of the skin covered with a false membrane, under a low power, it is seen that the diphtheritic membrane is formed by layers of modified epidermic cells. This false membrane is adherent in places to the papillæ, while at others it is detached from them. They have preserved their shape and are only more or less œdematous and infiltrated with migratory cells. In sections stained with safranin or B methyl violet, dehydrated, and mounted in Canada balsam, the stained micro-organisms are seen to form a delicate layer on the surface of the false membrane, and their arrangement is quite characteristic. They are seen in the form of zoogleic collections, which may be round or irregular, and united to one another by a layer of microbes which covers the surface of the false membrane. The microbes are small rods,[1] which are straight or curved, about 1μ in length and from $0{\cdot}1\mu$ to $0{\cdot}2\mu$ in thickness. They are almost always united and wedged together, so that the stained border which they form is from 4μ to 10μ in thickness. The zoogleic masses which are seen from place to place in this layer are from 20μ to 40μ in diameter. They are formed of rods which are so close together that they seem at first sight to be filled with micrococci, but it is easily seen under a high power that they are composed of small bacilli. The false membranes are thicker than the epidermis they replace; their substratum is formed of fibrils of fibrin, in the meshes of which are found mortified, hyaline epidermic cells, migratory cells and a few red blood corpuscles. A few isolated bacilli or micrococci are found in the whole thickness of the false membrane; at its lower part, near the papillæ, a much larger number of

[1] Klebs has described the micro-organisms of diphtheria as rods. Löffler, in a memoir which recently appeared in the *Mittheilungen des Kaiserlichen Gesundheitsamtes*, 1884, also affirms the bacillar form of the micro-organisms of diphtheria, and he has isolated and cultivated them.

bacilli are seen. When the false membrane is attached to the papillæ, a large number of micro-organisms are found at its border. At the points where the false membrane is raised, a large number of bacilli are found on the free surface of the papillæ, some of which are isolated, others united into small masses. A smaller number is found in the connective tissue of the papillæ, and they are still rarer in the derma. We have sometimes found them in the dilated vessels of the papillæ. Inflammation, characterised by migratory cells, is very manifest in the papillæ. In older cutaneous diphtheria, the false membrane is unequal or absent, and the papillary layer is undergoing destruction as well as the surface of the derma. In the false membranes fibrin, migratory cells and bacilli are found; but micrococci which are isolated or attached in couples or chains, are also found. These microbes vary in size, and the chains are often composed of micro-organisms as large as $0{\cdot}5\mu$ to $0{\cdot}6\mu$ in diameter. The rods of putrefaction are also found on the surface, together with the bacilli mentioned above. The derma is inflamed and its surface necrosed.

Gangrene of the skin.—We have already (vol. i. p. 117) described the pathogenic conditions of gangrene and its pathology, and we have shown (vol. ii. p. 655) how this accident may occur in purpura, and have cited the last memoirs on gaseous gangrene. A large number of various bacteria, round, isolated or in chains, or the bacilli of putrefaction, are found at the edge of the gangrene in the case of dry or senile gangrene of the skin, and in the ichorous fluid or pus which is produced by peripheral inflammation, or in the fluid which infiltrates the parts affected with moist gangrene. We have, therefore, only to describe the gangrenous lesion of the skin which results from the introduction and multiplication in the epidermis and derma of the bacteria of anthrax or malignant pustule.

Malignant pustule and anthrax.—Malignant pustule is the primary result in man of the introduction of the poison of anthrax. To comprehend the genesis and evolution of this cutaneous lesion and its sequelæ, it is necessary to know the history of anthrax, which we will relate briefly. Anthrax is a general disease caused by the presence of peculiar bacilli in the blood, and is characterised in animals, in sheep particularly, by a frothy condition of the blood, and by tumefaction and softening of the spleen (*splenic disease*).

The *bacillus anthracis* was discovered by Davaine[1] and Pollender;[2] Davaine ascertained by experiment the part the bacilli play and studied the disease; Pasteur[3] cultivated the bacilli anthracis, and Pasteur and Toussaint succeeded in attenuating them and transforming them into a preservative vaccine. On examining the blood of an animal which has died from anthrax, a large number of motionless rods are seen; they are relatively large in size, measuring from 1μ to $1{\cdot}5\mu$ in thickness and from 3μ to 10μ in length; they are isolated or articulated, and at the joint which unites them the rod is thickened and flattened, so that a characteristic clear line is seen bordered on each side by shaded parts.

FIG. 255.—BACILLI ANTHRACIS.

a, articulated rods; *b*, articulated rods one of which is bent in a hook; *c*, long curved rods. Magnified 1,500 diameters.

Bacilli having the appearances represented in fig. 255 are well observed in preparations stained with methyl violet. The rigid rods, which are sometimes curved like a hook (*b*, fig. 255), take a deep stain with aniline colouring reagents. In the blood of

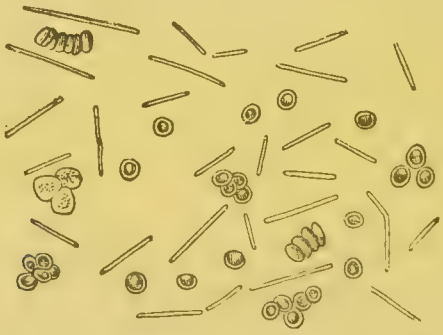

FIG. 256.—BACILLI ANTHRACIS IN THE BLOOD OF A GUINEA PIG.

animals, the guinea pig, for example, the red blood corpuscles are found twenty-four hours after inoculation to be agglutinated to-

[1] *Académie des Sciences*, August 1850.

[2] *Caspar's Vierteljahrsschrift f. g. Medicin*, 1855, vol. viii. p. 103.

[3] *Académie des Sciences*, April and July 1877, July 12, 1880 (jointly with Chamberland and Roux).

gether, deformed and mixed with bacilli, which are often as numerous as the blood corpuscles (fig. 256). If a small drop of blood be conveyed, with all the well-known precautions, to a culture fluid which is kept at the temperature of the human body, the following is observed at the end of twenty-four hours' time: The bacilli undergo rapid development and form long loops entangled in a matted mass; some of these filaments are quite transparent, others are unequally refractive owing to the presence of spores inside them (B, C, fig. 257). These spores, which were discovered by Koch, are small

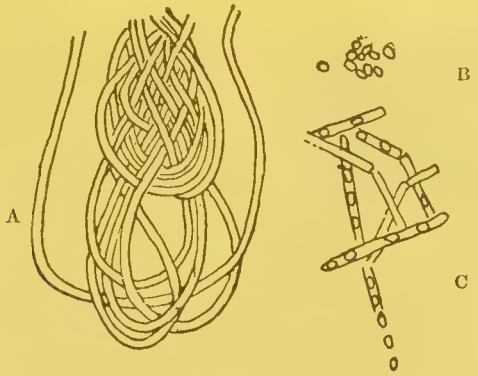

FIG. 257.—BACILLI ANTHRACIS OBTAINED BY CULTURE.

A, long filaments developed as a matted mass; B, free spores; C, rods containing spores inside them.

ovoid refractive bodies, of which the shortest diameter is rather less than that of the rods. The poorer the culture fluid is, the more abundant they become, and they may entirely replace the filaments

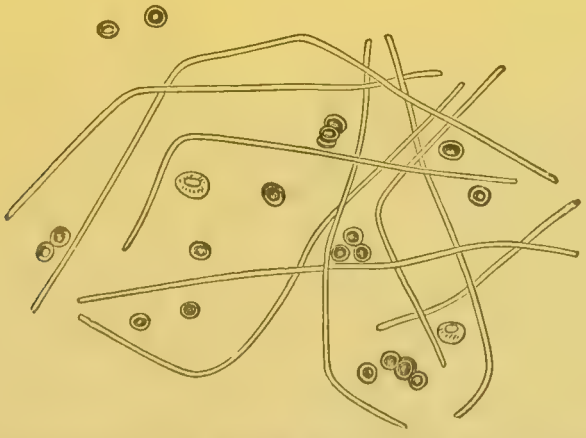

FIG. 258.—BACILLI FROM THE SPLEEN OF A MOUSE, CULTIVATED FOR THREE HOURS IN AQUEOUS HUMOUR.

which disappear. These bacilli are aerobic, that is to say that the oxygen of the air is necessary for their life. They take oxygen

from the medium in which they live, and give out a proportional quantity of carbonic acid. Left to putrefy, they disappear; if the culture fluid is sown simultaneously with bacilli anthracis and with the bacteria of putrefaction, the latter destroy the former, and if animals be inoculated with the fluid they do not get anthrax. This fact was discovered experimentally by Pasteur; its application to malignant pustule we are about to show. The temperature best suited to the development of bacilli anthracis seems to be that of mammalians (98°). The temperature of the blood of birds (105° to 107°) hinders pullulation. By lowering the temperature of fowls by keeping their abdomen and feet in water, Pasteur has succeeded in making them contract anthrax, and by an inverse process Gibier has given anthrax to frogs and fishes which he made live in water at a temperature of 90°. The blood of these animals contained a large number of bacilli, as shown in fig. 259. The

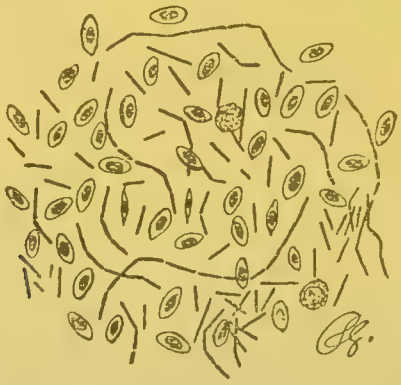

FIG. 259.—BACILLI ANTHRACIS DEVELOPED IN A FROG. Magnified 150 diameters.

vitality of these minute organisms is considerable, as well as their power of resistance to physical agencies, and Davaine has ascertained that the blood of anthrax preserves its poisonous properties for a long time, even after desiccation. The spore of the bacillus which is formed in contact with the air shows a remarkable resistance. When the body of an animal, which has died from anthrax, has been buried in the earth, the spores are brought again to the surface of the earth by earth worms, and Pasteur has proved their presence in the dejecta of lombricales. On examining stained sections of the viscera of a guinea pig, which has died from anthrax, the arteries, veins and capillaries are everywhere found filled with bacilli lying in the same direction as the course of the current. The bacilli are seated only in the vessels, and the cells of the organs, the liver and kidney, for example, do not appear to be at all altered.

Malignant pustule shows itself in man, from the first to the third day after inoculation, by an elevation of the epidermis (first period). This vesicle, containing a brown serum filled with bacteria, is seated in the midst of the Malpighian layer, beneath the horny layer. The bacteria are found in lacunæ surrounded by normal epithelial cells. They form here a thick felting and are prolonged in every direction between the cells (Davaine). Soon the derma is attacked, the papillæ and dermal tissue become filled with bacteria, and under the vesicle a flat lenticular induration appears; it is irregular, sensible to the touch and livid in colour. This is commencing gangrene (second period). The eschar becomes black, and a soft, circular, superficial tumour is formed, which is pale, livid or tinted; it is surrounded by a number of small phlyctenæ which are isolated at first; they then unite together and contain a russet-coloured serum. On making a section of the skin, a black, hard, dry eschar is seen at the centre of the pustule, occupying the whole thickness of the derma. It is of a red colour if examined by transmitted light. Around it, in its deep part, the subdermal connective tissue and the neighbouring skin are œdematous and contain a cloudy serum or a seropuriform fluid. On examining it under the microscope, connective-tissue fasciculi, still recognisable and preserved, are seen in the necrosed part of the skin. Neither cells nor bacilli are visible. It may be said that the bacilli anthracis produce a gangrene of great intensity, probably by abstracting oxygen from the skin in which they are at first located. In the œdematous subcutaneous tissue the débris of the cells and fibres of connective tissue, and various kinds of bacteria are found. The bacilli anthracis exist for a certain time, eight or ten days, at the base of the malignant pustule. In one case we found free, large, oval spores with the bacilli, and they seemed to us to be the spores of the bacilli anthracis. In sections of the œdematous derma, migratory cells and bacilli are seen between the connective-tissue fasciculi. They are also met with in fewer numbers in the lymphatic and blood vessels of the skin. But it is far from being always so, and the characteristic bacilli, replaced by the bacteria of putrefaction, may have completely disappeared from the spot where they were inoculated and first developed. At the base of the malignant pustule, a large number of rods are found, which are smaller than those of anthrax and do not show the characteristic articulations; they are the micro-organisms of putrefaction and micrococci. The absence of bacilli anthracis at the base of certain

old malignant pustules explains the uncertain and often negative results of the inoculations and cultures attempted with the fluid found here. If malignant pustule be not treated at its commencement it is generally fatal. Death results from the general development of the bacilli, which enter the blood and bring about a change in the liquor sanguinis and the blood corpuscles, so that hæmatosis is profoundly disturbed. At the necropsy of patients who have died eight, ten or twelve hours after the commencement of the pustule, a number of bacteria similar to those found in animals which have been inoculated are not always found in the blood: the spleen and the liver almost always contain them, however; at other times the gastro-intestinal mucous membrane is filled with bacilli, which are chiefly localised in the connective tissue and in the tubular glands, where they seem to be eliminated by causing inflammation of the mucous membrane. Meat incompletely cooked from an animal which has suffered from anthrax may cause splenic affection of the stomach and intestine, with ecchymoses and gangrenous ulceration and mycosic inflammation of the mucous membrane.

Eczema.—Eczema, or moist dartre, is a polymorphous superficial inflammation, which is seen sometimes in the form of papules, vesicles and pustules irregularly distributed and pressed close together, or as a diffused redness and swelling of the skin; the surface becomes squamous, moist or covered with crusts. Thus in eczema the following varieties may be considered: *erythematous*, *papular*, *vesicular and squamous*. Pustular eczema, in which the surface is covered with yellow crusts, has received the name of *impetigo* or *impetiginous eczema*. Eczema is acute or chronic. Its polymorphism, the succession of its various stages, varying according to the intensity of its cause, are easily explained when the results are seen of a direct application to the skin of an irritating agent such as heat, turpentine, tincture of arnica, a sulphurous pomade, mercurial ointments, irritating powders &c. If the irritation produced by the contact of these agents is slight, a papular redness is seen on the surface of the skin; if it is more intense, the papules are changed into vesicles crowded together, and containing a clear fluid; these vesicles are opened by scratching the skin and a fluid is exuded which soon forms into scabs. If the irritation is still more acute, the exudation is more constant, and the pustules are followed by a seropurulent flow, which often hardens into yellow crusts. Beneath these crusts, the Malpighian layer is exposed, and the skin is red and punctated (eczema rubrum).

Fissures and ridges are seen on the excoriated surface, particularly in the folds of the skin. Artificial eczema induced thus by a single application of an irritating agent to the skin may last one or more weeks. This is acute eczema; chronic eczema may be induced by successive attacks caused by irritating agents.

Acute eczema.—It may result from irritating agents or from internal causes: among the first we may cite eczema of the hands and arms in cooks, and persons who constantly have their hands in water; eczema of the nipple and breast in women who have the itch, and the intertrigo of children &c.; among the second, eczema of the genital organs due to diabetes, eczema of the scalp and face in young lymphatic and scrofulous subjects, and that which occurs after confinement. Eczema of the face in scrofulous subjects is generally of the impetiginous variety. The anatomical lesions, in acute eczema, consist first in congestion and distension of the capillaries of the papillæ, soon followed by œdema of the superficial part of the derma, and diapedesis of the lymph cells. The papillæ are thickened and elongated. Diapedesis of the cells into the Malpighian layer follow, and a vesicular state of the epithelial cells. If an effusion of fluid and small cells raising the epidermis (vesicles, papules) takes place or not into the superficial layers of the Malpighian body, the granular layer no longer contains granules of eleidin. It is no longer distinctly seen, or does not at least form a continuous layer; whence results an absence of keratinisation of the epidermis. Hence in sections of the horny layer, the cells will be seen to contain nuclei. They are no longer coherent, for they have lost their adhesive property, which is due to their keratinisation; thus they are detached in the form of scales, or crusts. If the eczema is weeping, the cells of the horny layer are carried away, and they are only reformed incompletely, so that the Malpighian layer, which is more or less altered itself, is exposed. If sections of the skin be cut in acute eczema, at its most acute period, that is to say when it exudes a quantity of fluid, and at the spot where the derma appears denuded, advanced lesions of the derma and papillæ are found. In the papillæ, the capillaries are dilated and filled with blood, their walls are altered and softened, and allow both red and white blood corpuscles to pass through, and the tissue of the papillæ and superficial derma is seen in places to be infiltrated with red blood corpuscles. The Malpighian layer is partly destroyed, so that only one or two rows of cells are left, and they are irregular. Above them, in the place of the horny layer, there is a thin amorphous layer of exudation coagu-

lated by the hardening reagents used. This layer contains a small number of round cells and a few flattened epidermal cells. The prolongations of the Malpighian layer around the hairs, and the epithelial sheaths of the hair follicles, are generally preserved. Beside the parts where the epidermis is almost completely absent there are others where the Malpighian layer is intact, but the granular layer, which is incomplete, is deprived of eleidin, or only a few cells here and there contain this substance. Here, in the superficial layer of the epidermis, are seen nuclei stained with carmine and, on its surface, parts which are detached, or which project irregularly, undergoing desquamation. These layers are directly continuous with the epidermis and the normal derma at the periphery of the eczematous inflammation. The derma is generally very superficially attacked. Œdematous and inflammatory infiltration may, however, affect its whole thickness.

Chronic eczema.—Repeated attacks of chronic eczema may give origin to exudations as in acute eczema, but generally the connective tissue of the papillæ and derma undergoes a lasting change, which consists in hypertrophy of the papillæ, and distension with thickening of the walls of their capillaries. This condition is seen with the naked eye from the density and increased thickness of the skin, which is at the same time warty and granular on the surface. The superficial epidermic layers are thickened, and become detached in grey or brown flakes. The chronic eczema of the legs of persons suffering from varicose veins is typical. In sections of the hypertrophied papillæ, the capillaries are dilated, and their walls, which are thicker than usual, blend with the fibrous tissue of the papillæ. This tissue contains a considerable number of flat or swollen cells. In a longitudinal section of a papilla, these vessels are seen cut through both in a transverse and longitudinal direction, and they seem to be varicose like the large veins of the limb. The Malpighian layer is very thick, and it sends out long and large papillæ. The fibrillar arrangement of the protoplasm of its cells is distinctly seen. In the parts near the ulcers, and everywhere where there is no weeping, the granular layer is formed of three or four superimposed layers of cells which are rich in eleidin. The superficial epidermis is also very thick, and shows red lines after staining with carmine. Flakes of this epidermis are raised and detached in places. The derma also contains numerous swollen connective-tissue cells and a few migratory cells. The ulcers of varicose eczema give place to depressed, irregular cicatrices, which are sometimes adherent to the thickened perios-

teum of the tibia. They are often deeply pigmented, which pigmentation may extend to the Malpighian layer without its having been ulcerated.

Exfoliative dermatitis (Wilson[1]).—This polymorphous affection resembles scarlatina at its commencement, and erysipelas, erysipelatous phlegmon, or acute eczema in successive and general attacks; it causes a free desquamation of the epidermis, accompanied with fever and general nervous disturbance, and it ends either in death or recovery. It has been called general (Baxter[2]) or periodic (Bukley[3]) exfoliative dermatitis, scarlatiniform desquamative erythema (Féréol[4]), acute periodic eczema (Fagge), and serious acute dermatitis (Quinquaud[5]). It is nearly related to pityriasis rubra, foliacious pemphigus, and foliacious psoriasis. We have examined fragments of skin brought us by Quinquaud, from two cases of this disease. The inflammation, which is general, varies, however, according to the part examined; but the skin is always infiltrated with a large number of round cells. The capillaries are filled with blood. The epidermic layer is generally thick. The stratum granulosum and the stratum lucidum are generally absent. The cells of the superficial epidermis contain their nuclei more or less, do not become horny, and fall in large flakes (Vidal and Brocq[6]). Much more acute lesions are found in places in the papillæ and derma; there are islets in which the papillæ and the superficial half of the derma are infiltrated with round cells pressed together, filling up all the interfascicular interstices, dissociating and destroying the fibres of connective tissue. In these inflamed islets the blood vessels contain no red blood corpuscles, only white are present. Above, the superficial epidermis is absent, and the Malpighian layer is reduced to a few cells. Around these islets, acute congestion with dilatation of the vessels is observed, and extravasation of the red blood corpuscles into the connective tissue. In one of these cases, Quinquaud and Leloir found lesions of the nerves consisting in fragmentation and degeneration of the myeline of the nerve tubes, and multiplication of the nuclei of the nodes of Ranvier.

[1] Erasmus Wilson, *Diseases of the Skin*, 1867.
[2] Baxter, *British Med. Journal*, 1879.
[3] Bukley, *Archives of Dermatology*, 1878.
[4] Féréol, *Bulletin gén. de Thérapeutique*, February 1876.
[5] Quinquaud, *Société Anatomique*, October 1879.
[6] Vidal, *Société des Hôpitaux*, March 1882. Brocq, *Thèse de Paris*, 1882.

Diffuse chronic dermatitis.—Chronic inflammation of the derma is seen in a number of different diseases, and may affect its whole thickness, or only its superficial or papillary layer. The former comprises *hypertrophic fibrous dermatitis*, which is found around the varicose ulcers of the leg, or in consequence of repeated attacks of varicose eczema, described above; *chronic inflammatory œdema* or the warty elephantiasis of Virchow, *scleroderma*, and *elephantiasis Arabum*. We will describe *ichthyosis* as a chronic inflammation of the papillary network of the skin.

Chronic inflammatory œdema (warty elephantiasis, hypertrophic lichen of Hardy).—This disease occurs sometimes in persons affected with cardiac disease who have suffered from frequent œdema of the lower limb with varicose veins, and more or less acute eczematous inflammation. The skin is then thickened, wrinkled, papillary and warty in places, and covered with a hard horny epidermis. In sections of the skin, the horny layer is first seen, rich in eleidin towards its deeper part, the granular layer is more marked than usual, and the Malpighian layer is enlarged and very solid, but with its fibrillated protoplasmic cells normal; then the papillary network is seen to be hypertrophied, the papillæ elongated, enlarged, fibrous and covered with numerous dilated blood vessels with dense walls; the derma is much thickened and large blood and lymph vessels are seen to gape when divided; vessels more numerous and larger than normally are found in the deep layer of the derma round the sudoriparous glands. The interfascicular spaces in the papillæ and derma, and around the principal vessels, contain numerous round, fusiform or flat cells. J. Renaut has well described and analysed chronic œdema in its relation to changes in the cutaneous lymph vessels.

Scleroderma.—This disease, the sclerema of Alibert, sclerema of adults, is an affection of the skin in which it becomes hard and rigid; it is slow in development and spreads over a more or less extensive surface of the skin. The sclerosed part of the skin is smooth, is slightly prominent or depressed, of a white or waxy colour, pink or brown; it is hard, rigid, cold, adherent to the subjacent parts, and often too much contracted to be wrinkled. As a result the fingers and nails become deformed, the limbs fixed and the face immobile, with contraction of the mouth and flattening of the nose, if the disease is seated in the face. From a pathological point of view, scleroderma is an actual cirrhosis of

the skin. The connective tissue and elastic fibres of the derma increase in size (Rasmussen, Lagrange and Duret); the subcutaneous adipose tissue becomes chronically inflamed, and then changed into dense fibrous tissue in consequence of organisation of the embryonic tissue interposed between the adipose vesicles, and the absorption of the latter. The blood vessels are, according to Lagrange and Duret, contracted and pressed upon by the new fibrous formation. The epidermis is thin and transparent and reduced to two or three layers of cells which are sometimes pigmented; the papillæ are greatly attenuated or even completely effaced on the pulp of the fingers, where they are usually large. The glands also finally atrophy. This atrophy, which subsequently affects the bones, which disappear, and the small nerve trunks, which undergo various changes (perineuritis, interstitial neuritis), is not without analogy in certain conditions called trophic changes of the skin. The scleroderma of new-born children is a progressive and general induration of the subcutaneous connective tissue with œdema and algidity. It generally ends in death. In sections of the skin, œdematous infiltration is observed, but there is no hypertrophy of the connective tissue nor sclerosis similar to that seen in scleroderma of adults.

Elephantiasis Arabum.—By this is understood hypertrophy of the skin and of the subcutaneous cellular tissue, which is limited to certain parts of the body, and which seems to follow chronic inflammation of the blood and lymph vessels, and long-continued œdema. It is generally seated in the lower extremities, or in the skin of the genital organs. Elephantiasis of the lower limbs is preceded by attacks of diffuse erysipelas with phlebitis or lymphangitis; the sequela of each attack is œdema of the skin, which gradually increases. The glands of the groin become tumefied, and at the end of a few months the leg becomes very large and shapeless; the foot is enormous as well as the toes; the skin is generally wrinkled, warty and often pigmented, and is covered by an epidermis which is sometimes thin, and sometimes horny and callous, and often shows ulcers with irregular punched out edges and bleeding base. The scrotum often becomes an enormous size, and may weigh from fifteen to twenty pounds. The skin is the seat of warty growths. On making a section of the skin of a leg affected with elephantiasis, the papillæ are seen with the naked eye to be more apparent than normally, and the derma is seen to constitute the larger part of the hypertrophied skin. It may

measure from one-eighth to a quarter of an inch ; and it is composed of a hard tissue, saturated with a transparent fluid, but it does not collapse as occurs in œdema, neither does any marked quantity of fluid escape on pressing it. Beneath the derma, the cellulo-adipose tissue is often preserved but thickened. The periosteum is always much thickened, and hyperostoses and condensing osteitis are observed in the bones. The arteries and veins, which are visible to the naked eye, are much larger than in the normal condition, and are affected with chronic inflammation, which chiefly attacks the internal coat. The nerves are sometimes also much larger than normally. In sections of skin examined under the microscope, the epidermis seems to be thickened, but it contains the normal series of layers, the horny layer, the stratum lucidum, and the stratum granulosum with many layers of cells very rich in eleidin, and the Malpighian layer; the papillæ are generally hypertrophied, conical or globular; they usually contain leucocytes and red blood corpuscles effused between their fibres. The capillaries of the papillæ are generally very large[1] and remain full of blood after death. Throughout the derma large connective-tissue fibres are seen which lie parallel to one another and to the surface of the skin ; they are very close together and are crossed at right angles by the blood vessels which pass from its base to the papillæ. These vessels are accompanied also by bundles of fibres. The framework of this new fibrous formation contains therefore two kinds of fasciculi, some very numerous and parallel to the surface of the skin, and others less numerous accompanying the blood vessels from the base of the derma to the papillæ. Between these fasciculi a varying number of round cells and connective-tissue cells are found. In sections of the derma, the lymph vessels, very much dilated, look either like irregular slits containing round cells englobed in fibrillar fibrin and bordered by a layer of tumefied endothelial cells, which is raised in places like a membrane, or like circular ducts from 80μ to 100μ in diameter. The peripheral connective tissue limits these ducts and they have a normal endothelium. Their contents are the same as the slits. The glomeruli of the sudoriparous glands are placed very deeply in the thickened skin, at from one-eighth to a quarter of an inch below the surface, for example. The excretory ducts of these glands are then greatly elongated. Their calibre, as well as that of the secretory tubes, has increased, and

[1] See a case reported by Girard and histologically examined by Cornil (*Soc. Anat.*, March 1883).

often contains many layers of cells, the most internal of which are detached and free in their lumen. Fleshy granulations are found at the edge of the ulcers, which are generally deep, having destroyed the papillæ and part of the thickened derma. In a case which we examined, the hypertrophied nerves showed in section marked thickening of the perifascicular connective tissue and of the sheath. The lymphatic glands of the groin, which are much enlarged, show all the anatomical lesions of chronic adenitis; namely, large cortical follicles, surrounded by sinuses containing many lymph cells and tumefied endothelial cells, dilatation of the lymph channels of the medullary substance, and thickening of the fibrous tissue. All these lesions have been well described in Virchow's 'Pathology of Tumours.' According to Wücherer, Lewis, Manson and Crevaux, the presence of *filaria sanguinis hominis* in the blood is the cause of elephantiasis. The germs of this parasite are only seen in the blood during the night (*vide* vol. i. p. 468, note). Instead of taking the warty form, cutaneous elephantiasis may be characterised by smooth hypertrophy of the skin. The papillæ are then normal in size or atrophied. In a section of elephantiasis of the skin of the breast, removed by Tillaux, we observed an entire absence of the papillæ. The derma was bordered by a straight line and was covered by a delicate layer of epidermis, in which the Malpighian layer and the horny layer were nevertheless recognisable.

Ichthyosis.—This disease, which we describe here as a chronic inflammation of the surface of the skin, is, in reality, a peculiar affection dating back from the earliest infancy and persisting throughout life. It is characterised by a peculiar harshness and dryness of the skin, which is covered with fine scales or flakes, or with thick epidermic lamellæ, or horny protuberances. Ichthyosis simplex, serpentina or hystrix, is distinguished according as the skin shows horny, blunt or pointed excrescences. In sections of the skin, hypertrophy of the papillæ is observed, which is more marked as the ichthyosis is more pronounced. The papillæ in ichthyosis are very long and are covered with thick layers of epidermis like so many small papillomata. The papillary vessels are both longer and wider than normally, and the connective tissue surrounding them contains numerous round or fusiform cells; the derma is sometimes slightly thickened, and its elastic fibres are less numerous than in the normal condition. The hair follicles are atrophied, and sometimes elongated, and blocked by

masses of horny epidermis which hinders the development of the hair. The sebaceous glands are partly absent or show cystic dilatations. The sudoriparous glands are present, but they also seem much atrophied. The muscular fasciculi are decreased in number or are absent in places. The blood vessels of the derma only show a certain amount of distension. The horny layer is generally much thickened and the granular layer contains eleidin; the Malpighian layer, which is normal in thickness, often contains a quantity of pigment, particularly the cells of the first layer.

Squamous Dermatoses.

We conclude the description of cutaneous affections by the squamous diseases, pityriasis rubra, scarlatina, erysipelas, eczema and exfoliative dermatitis. There are other forms of dermatoses, which are squamous, and which we shall treat of when studying vegetable parasites, such as trichophytis, pityriasis alba, pityriasis versicolor, &c.; we shall also describe those forms of psoriasis in which squamæ are often primary, but which we include nevertheless among papular affections. There only remains pityriasis rubra for us to describe here.

Pityriasis rubra.—This affection consists in a general superficial inflammation of the derma, over the whole surface of the body; it is characterised by a dull red colour and by an abundant and continuous epidermic exfoliation of the skin; this occurs in the form of large, thin, leaf-like, white scales, without any previous weeping. These scales, which are often imbricated, fall and re-form incessantly and abundantly. The skin is generally thin. This affection, which is rather rare, often ends fatally. According to Hebra, the skin shows under the microscope the characteristics of subacute inflammatory infiltration. In a case in which death occurred at an advanced stage of the disease, the skin was much atrophied and the papillæ had disappeared, the sclerosed connective tissue of the derma contained a number of elastic fibres, and a deposit of pigment, and the sudoriparous and sebaceous glands were destroyed. This frequently fatal affection is related to exfoliative dematitis.

The pityriasis rubra pilaris, described by Devergie, may affect the whole surface of the skin, but is limited chiefly to the hair follicles.

Papular Dermatoses.

We have already described papules which are anatomically characterised by œdematous congestion and rapid evolution, and which are seen in erythematous affections, such as papular erythema, polymorphous erythema, urticaria, pityriasis. There is no occasion to describe them again; but there is another series of dermatoses in which more or less prominent papules are related to congestion and infiltration of the papillæ and the superficial part of the derma by round or oval cells, or by newly-formed connective-tissue cells. These papules develop slowly and project like pimples for weeks, months or even years. The diseases in which these papules are seen are syphilis, psoriasis, lichen and prurigo.

Papular syphilides.—There are two varieties, that with small papules, and that with large papules. The first have often a conical apex, the latter are flatter or project slightly; both are regularly circular and are of a coppery red or yellow colour, which is quite characteristic. Around the papule a white epidermal line may be seen, the epidermal circle of Biett. When recent, they partly disappear under pressure and become much paler after death. In sections of syphilitic papules, examined under a low power, the projection is seen to be partly formed by a regular thickening of the papillary network, which is progressively more marked towards the centre, and partly by the derma. The dermal layers contain a considerable quantity of migratory cells effused between the fibres of the papillæ and the derma; the Malpighian layer is also slightly thickened towards the centre of the papule; the blood vessels are dilated; the horny layer is thinner at the prominent part and it no longer undergoes the normal horny change. This change of the superficial epidermis gives the papule a smooth and shining appearance; it is moist in certain parts of the body, and is so transparent that the red colour of the congested papillary network is seen. In sections also, modified red blood corpuscles are almost always seen extravasated in varying numbers between the fibres of the connective tissue, and in the papillæ and derma. It is partly the red blood corpuscles and the blood pigment which give the papules their characteristic copper colour, and the ecchymotic and pigmented tints observed at their centre or periphery, when they undergo cure. The papules leave a white or pigmented spot behind, which remains for some time. When the small papules are close together, epidermal thickening

and desquamation take place and give them a lichenoid appearance, or, which is much rarer, a small pustule is produced which dries rapidly (syphilitic acne).

Large papules show lesions similar to the preceding; they are identical with mucous plaques of the vulva and mouth; their change into moist papules may be seen in all those parts where the skin is moist, as in the axillæ, the inguinal folds and the umbilicus. They may last for months and are very obstinate; they then become the seat of thickening of the whole of the derma and justify the name of papulo-tubercular syphilide, which Willan has given them. They often become covered with squamæ which make them resemble psoriasis. On examining a section of one of these large squamous papules, under a low power, it is seen to be regularly raised in a semicircular form. All the layers of the skin, the epidermis, the Malpighian layer, the papillary layer and the derma show thickening which commences at the edge of the papule where its layers are continuous with those of the normal skin, and which reaches its maximum at the centre. The horny layer of the epidermis is four or five times thicker than normally; it stains yellow with picrocarminate; in the strata parallel to its horny layer, delicate red transverse striæ are seen, formed by the eleidin. When the superficial epidermis is thus increased and contains eleidin in its deep layers, the granular layer is thick and stains red with carmine. The Malpighian layer is two or three times thicker than normally and it sends prolongations between the papillæ. These latter are hypertrophied both as regards their length and breadth. Between the fibrous tissue of the papillæ are seen numerous round cells which have penetrated between the delicate and close fibres of the papillæ, and even between the larger fasciculi of the derma. This latter is infiltrated throughout its whole extent, and the chronic inflammation may even reach the deep layers, the periphery of the sudoriparous glomeruli, and the cellulo-adipose tissue. The lobules of this tissue are changed, after absorption of the fat, into islets of embryonic connective tissue. Papules in this state constitute actual small neoplasms. The thick horny layer which covers them is sometimes hard and difficult to detach; this is owing to the fact that horny change still takes place, as the granular layer is preserved and forms eleidin. But sometimes, owing to an attack of congestion, the horny layer becomes squamous and white and is thrown off, while new cells are formed in the deep layers of the epidermis. If a section of these papules be examined, the detached superficial

layers are seen to be still adherent to the external epithelial sheaths of the hairs. When the squamæ fall accidentally, the papule is seen with its red copper colour and its smooth shining surface. In such a case, the granular layer of the epidermis does not any longer elaborate eleidin. These large papules are sometimes moist at the beginning, in their acute period, or during the period of inflammatory recrudescence. The horny layer then entirely disappears and does not form again. The Malpighian layer is only present at the surface of the derma. This layer is thick and traversed by numerous migratory cells. The deep red colour of the papules is often in a great measure due to extravasation of red blood corpuscles into the papillæ and the superficial layer of the derma, and sometimes, as one of us has noticed,[1] between the papillæ and the Malpighian layer, which are then separated by red blood corpuscles. The lesions of the hair follicles, and of the sweat and sebaceous glands, have nothing special in syphilitic papules, and have not the same importance as those of the epidermis, papillæ and derma.

Syphilitic onychia, which appears simultaneously with the papules, is a disease of the matrix and bed of the nail. A papular eruption occurs around the nail and in the derma which constitutes its bed ; the nail splits, cracks, and breaks easily ; it is hard and is detached in the form of superficial scales, and soon loses its adhesion to the subjacent derma. Syphilitic onychia may also be characterised by whitlow, that is to say by suppuration of the matrix of the nail and of the supra-ungueal fold. In the forms of onychia which accompany syphilitic papules, the essential lesion is congestion and infiltration of the derma by migratory cells, hypertrophy of the papillæ, and the new formation of papillæ on the surface of the bed of the nail. At the same time the changes which have been described by Suchard are observed. Normally the nail is produced by a process similar to that of the horny change of the epidermis ; the formation of the nail is due to the presence, in the matrix of the bed of the nail, of a substance which one of us has called onychogen, and which plays the same part in the formation of the nail, as eleidin does in the formation of the horny layer of the epidermis. If the matrix or bed of the nail be inflamed, onychogen disappears from the cells of the Malpighian layer, and in its place eleidin is found. The epidermic cells, formed in great abundance, accumulate on the surface of the Malpighian layer of the matrix and of the bed of the nail, and they become horny,

[1] *Leçons sur la Syphilis*, p. 182.

non-nucleated cells. The process of unequal keratinisation is replaced by epidermic keratinisation.

Psoriasis.—Psoriasis is characterised by dry, shining, white, silvery, imbricated scales, taking either the form of elevations or patches. According to the diameter and form of the growths the disease is divided into psoriasis punctata, psoriasis guttata or nummular, in which the scales measure about a quarter of an inch across; if these small patches unite into large, round or irregular groups, the psoriasis is called figurate, diffused, generalised, and if they extend, annular psoriasis, lepra &c. This disease, which

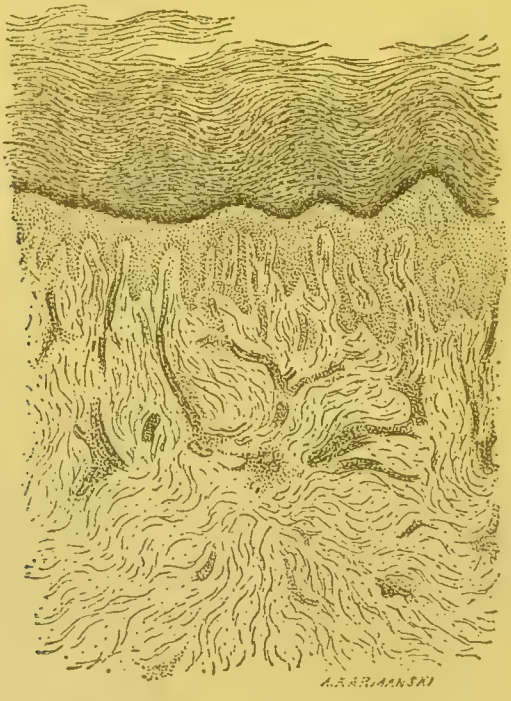

FIG. 260.—SECTION PASSING THROUGH A PAPULE OF PSORIASIS.

a, hypertrophied papillæ; *b*, Malpighian layer; *c*, much thickened horny epidermis. Magnified 40 diameters (after a drawing of Vidal and Leloir).

is essentially chronic, may be ameliorated or cured temporarily, but it always returns. It is seated in the knees, elbows and scalp; but it may invade all parts of the body. It is, however, very rarely found on the palms of the hands or the soles of the feet, which are, on the contrary, very frequently affected with syphilitic papules. The lesions of subacute or chronic inflammation of the papillary layer are seen in sections of the papules of psoriasis. The papillæ are hypertrophied and much elongated, and between their fibres a small number of round and fusiform

cells are seen; the blood vessels are distended and their walls thickened. The hypertrophied Malpighian layer sends processes deeply between the papillæ. In old patches, the papillæ are so much hypertrophied that the papule has a warty appearance. During the acute stage and that of growth, numerous migratory cells are to be found in the Malpighian layer of the papules, and some of them are vesicular. Nucleated cells are also found in the epidermal scales (Vidal and Leloir). According to Suchard, the granular layer and eleidin are absent, and the epidermis does not any longer undergo horny change. The presence of nuclei in the desquamated epidermic cells is also explained. But in some patches of chronic psoriasis, the horny layer is abundant and coherent, and the cells of the granular layer contain eleidin. The horny layer also contains streaks of eleidin in its deep layers, as occurs, as we have shown, in some forms of chronic eczema with thickening of the derma and the horny layer.

Lichen.—There are various forms of lichen, lichen pilaris, lichen planus, lichen ruber and lichen scrofulosorum. It is characterised by small papules, with pointed or depressed centres, and covered with scales; they show no tendency to develop either into vesicles or pustules, and they remain for a long time. The lichen of scrofulous disease, described by Hebra, seems to be much more frequent in Austria than in France, where it is almost unknown (Besnier). According to the description given by Hebra, Neumann and Besiadecki, the papules of the various forms of lichen are chiefly seated around the hair follicles. The lesions consist in infiltration of the papillæ with small cells and distension of their blood vessels; these small cells are particularly seen around the edge of the hair follicle near to its radicle, and around the sebaceous and sweat glands. According to Besiadecki, the elevator muscle of the hair follicle is in a condition of permanent contraction, which causes the prominence of the hair follicle. **Lichen planus** is characterised by small papules, which are generally polygonal in shape, with their centre slightly depressed; they are violet in colour, with a shiny and slightly scaly surface. The pathology of this disease has been studied by Hebra, Kaposi, Neumann, Balzer and Bernard Lavergne. The horny layer of the epidermis is thickened, and the granular layer is rich in eleidin. The Malpighian layer often contains vesicular cells. The papillæ as well as the superficial part of the derma are hypertrophied, infiltrated with cells in which the connective-tissue

fasciculi are often atrophied. The blood vessels are surrounded with cells. The lesions of the hair follicles are very important, and give this disease its anatomical character. They consist in inflammation of the follicle in which the epithelial cells of the external sheath become hyperplastic. At the base of the follicle, these cells accumulate so as to distend it, and to cause the formation of many diverticula. The centre of the follicle is changed into a cone with the point downwards, owing to the great abundance of the epidermis found here, which results in the formation of obvious scales at its orifice. The hair alters and falls. The ducts of the sweat glands as well as their glomeruli are surrounded by small round cells (Balzer) and their proper membrane is thickened. In lichen Planus corneum, the superficial epidermal layer is greatly increased, its lower edge is rich in diffused eleidin and contains many nucleated cells. The granular layer is also much thickened and charged with eleidin (Vidal and Leloir, 'Soc. de Biologie,' April 1883).

Prurigo.—The elementary lesions of prurigo are papules measuring in size from that of a millet seed to a pin's head. They are white and acuminated, and are so irritable that the most prominent part becomes excoriated from scratching; the erosion becomes covered with a black crust, which is due to dried blood. This disease, which may last a very long time when it is spontaneous, is liable to repeated relapses. Papules of prurigo are seen in old persons, or as the result of vermin. It has not been discovered what causes the pruritus of the papules of prurigo; infiltration of the papillæ and derma by round cells when recent, and thickening of the Malpighian layer and the derma with pigment when older, are found here as in all other papules.

Vesicular Eruptions.

Eruptions purely vesicular include miliary vesicles, varicella and herpes; but many pustules commence by being papules or vesicles. Such are impetiginous eczema, varioloid, variola and varicella. We do not intend to describe vesicles separately, nor the miliary vesiculo-pustules which are caused by poultices, sweating &c., nor those caused by local irritating applications, such as castor oil, for example, for they resemble artificial eczema, of which we have already spoken.

Varicella or chickenpock.—Varicella, which is distinguished from variola by most observers, is regarded by Hebra as a lesser form of variola, and as belonging to the same disease. It must

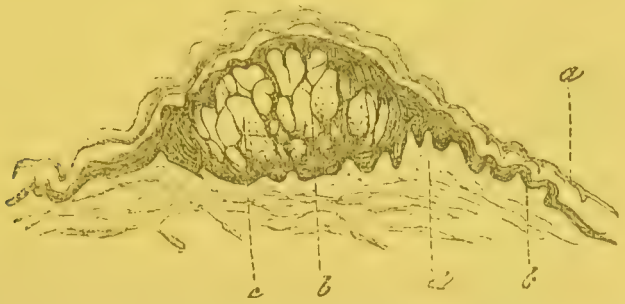

FIG. 261.—A VESICLE OF VARIOLA.

a, epidermis; *b*, granular layer; *b'*, septa, and *c*, cavities formed in the Malpighian layer.

therefore be asserted anew that varicella is a distinct eruptive fever, in which the eruption is purely vesicular, and which lasts at most a fortnight. The eruption, which is at first papular, soon becomes vesicular. The vesicles, which contain fluid and are transparent, are seated in the Malpighian layer. This layer is changed into a series of cavities which are generally oval, anfractuous, irregular, and limited by trabeculæ. These trabeculæ, which anastomose together, are formed of epithelial cells which remain attached and are pressed upon by the fluid contained in the cavities. This fluid contains a small number of migratory cells and red blood corpuscles. The septate and hollowed condition of the Malpighian layer is preceded by congestion and œdema of the papillæ, migration of the lymph cells and fluid across the Malpighian layer, and vesicular change in its cells and nuclei. The contents of the vesicle soon become cloudy, which is caused by the effusion of a larger number of lymph cells. These cells undergo more or less fatty degeneration. They are soon eliminated with the horny layer, which becomes softened and disintegrated after having proved a resisting barrier for some days. A crust is then formed. The lesion undergoes cure without the formation of a cicatrix.

Herpes.—Herpes is characterised by groups of vesicles of rapid evolution with transparent, serous or blood-stained contents; they dry and become covered with a crust. The vesicles are seated along the course of the cutaneous terminations of a nerve, and they are often accompanied with neuralgia of this nerve. The

principal varieties are herpes zoster or zona, genital herpes, and labial or facial herpes. Bärensprung has carefully described all the sites of herpes, referring them to the course of nerves in the branches on which herpes is observed. Thus in herpes he distinguishes the occipito-cervical, the cervico-subclavicular, the cervico-tracheal, the dorso-pectoral, the dorso-abdominal, the sacro-ischiatic and the genital. All the nerves along which herpes is observed are spinal, with the exception of the trigeminal. According to Bärensprung, the eruption is caused by a lesion of the intervertebral ganglia for the spinal nerves, and of the Gasserian ganglion for the trigeminal nerve. Sattler and Kaposi found hæmorrhage in a case of frontal zoster followed by destruction of the Gasserian ganglion, and Kaposi has seen hæmorrhagic foci and inflammatory infiltration into the spinal ganglia, with extravasation of the red blood corpuscles into the capsule of the ganglionic cells, in a subject affected with lumbo-inguinal zoster. Chandelux has ('Arch. de Phys.,' 1879) published a case of zona in a tubercular subject, in which the intervetebral ganglia were pigmented and sclerosed, with disappearance in places of the nerve cells and tubes. A certain number of the nerve tubes of the intercostal nerves had degenerated. Dubler ('Virchow's Arch.,' 1884, vol. xcvi. p. 195) has been able, in two cases of zona, to follow the lesions of the nerves throughout their whole course, from the point where they traverse periosteal caseous foci. He observed all the degenerative lesions as far as the skin, namely, fragmentation of the myeline, multiplication of the nuclei of the nerve tubes, collapse of the sheaths of Schwann &c.; but he was unable to trace their terminations by the chloride of gold method. In spite of this, it must not, however, be concluded that a material morbid condition of the ganglion is always the cause of herpes. It may also depend on the nervous centres, on the brain, spinal cord and sensory nerves. Whatever it may be, herpes generally takes a track which is that of one of the cutaneous nerves. The eruptive patches are each composed of vesicles rather close together, with clear contents, and which project like small beads; the fluid, after remaining clear for two or three days, becomes cloudy and puriform, and the vesicle becomes flatter and covered with a crust. This evolution takes from a week to a fortnight, according to its intensity and diffusion. Vesicles with hæmorrhagic contents often cause erosions of the superficial layer of the derma, and subsequent cicatrices. Zona then lasts much longer. It, like the eruptive fevers, hardly ever

recurs. The lesions observed in the vesicles of zona resemble those in the vesicles of varicella. Septate cavities are formed in the Malpighian layer and are filled with fluid; there are few cells in this fluid at first, but they afterwards become more numerous; the horny layer, which is at first intact, opposes a barrier to the escape of the fluid; the papillæ become infiltrated with small round cells; and in the case of hæmorrhagic herpes blood is extravasated into the tissue of the papillæ and the fluid of the vesicle; the papillæ are then destroyed and their elements mortify. The nerves which are distributed to the groups of vesicles only show the lesions of neuritis. Haight has observed infiltration of embryonic cells around the nerve fibres.

Eruption of Bullæ.

The cutaneous diseases which are characterised by bullæ are pemphigus and rupia. We have also seen erysipelas become phlyctenoid.

Anatomy and histology of bullæ.—Bullæ are nothing else than large vesicles, in which the patch of affected skin is more extensive, and the fluid effused into the epidermis more abundant. A blister furnishes us with the most simple example of the artificial formation of bullæ and phlyctenæ in the skin. A burn of the second degree by hot sealing wax, for example, causes almost immediately the appearance of a bulla filled with serum. The parts of the skin which are superficially affected with gangrene become also covered with bullæ or large phlyctenæ. In all of these cases the process is the same. The papillary network being congested and its blood vessels dilated by a neuro-paralytic action, the fluid part of the blood serum passes between the cells of the Malpighian layer, carrying with it both red and white blood corpuscles. Effusion takes place easily into the Malpighian layer, for its cells are only held together by filaments, whence it acts like a filter. But these same uniting filaments are too strong to be ruptured by the fluid, which at first accumulates in the Malpighian layer. It is on its surface in the granular layer, which has less resistance, where the fluid finally accumulates. Here the fluid is arrested by the horny layer of the epidermis, which is homogeneous and formed of cells solidly united together without there being any spaces between. The horny layer thus offers an effectual barrier to the escape of the fluid, so that it becomes raised for a certain distance,

and may remain extended for two or three days without breaking. On examining bullæ with the naked eye in their ripe condition, in various artificial, spontaneous and morbid lesions, they are seen to have various aspects according to the parts of the skin where they are located. If the epidermis is thin the contents of the bulla seem limpid, for the epidermic layer which borders it is transparent. On looking at it close with a magnifying glass, small opaque spots are seen, which are nothing else than the open-

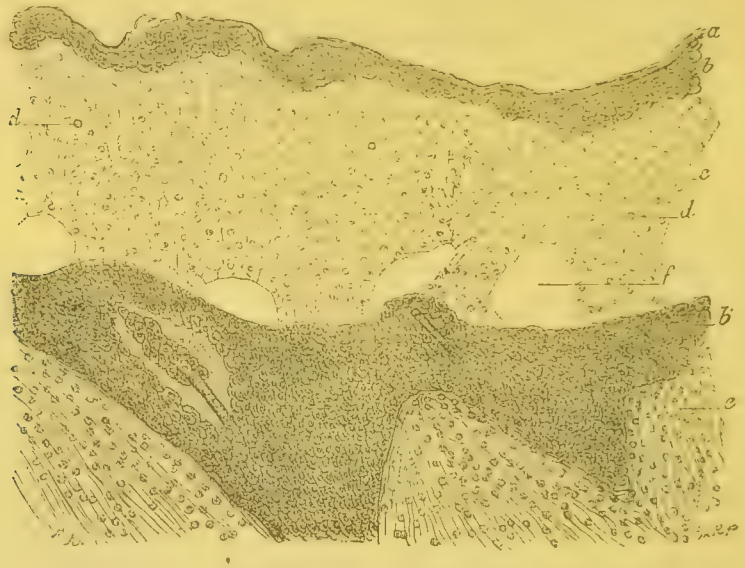

FIG. 262.—SECTION OF A PHLYCTENA IN ERYSIPELAS.

a, horny layer; *b*, raised external granular layer; *c*, migratory cells contained in the fibrinous reticulum; *d*, red blood corpuscles; *f*, arc-like arrangement of the fibrinous network; *b'*, Malpighian layer; *e*, papillæ infiltrated with migratory cells. Magnified 120 diameters.

ings of the sweat glands. Where the horny layer is thick, as on the palms of the hands and the soles of the feet, the contents of the bladder seem more cloudy. When the effusion of fluid occurs rapidly, it is sufficient to prick the cuticle of the bulla to let the fluid escape. On examining the contents of one of the large bullæ which are formed by the splitting up of the epidermis and which only contain one cavity, the opaque parts are seen to be formed by the pus which is deposited in the dependent parts, while the serous transparent fluid is found in the upper part; this cannot take place in multilocular pustules (Leloir). When the fluid is seated partly under the horny layer and partly in the Malpighian layer, and in areolar cavities similar to those already described in vesicles, puncture of the epidermis does not give issue to the fluid contained in the bulla. It is the same in the large phlyctenæ formed by the application of a blister; the raised and infiltrated

epidermis must be cut in different places before the fluid escapes from the meshes which contain it.

On examining a section of a bulla at its commencement, an arc is seen formed of the raised horny epidermis. This arc is extended over the derma. The fluid contained between the raised epidermic layer and the papillæ occupies spaces divided by the cells of the Malpighian layer, which is pushed back. If a section of a well-formed and distended bulla be made after desiccation, all the fluid escapes and only the solid parts are visible. In some bullæ the upper arch is formed of a delicate layer of epidermic cells with conglomerations of horny cells from place to place, which from their concentric arrangement seem to border the orifice of the sweat glands. At the base of the bulla, the Malpighian layer still adheres in places to the papillæ; whilst it is almost entire at the edges of the bulla, at the centre it is partly disintegrated, where only a few changed granular or refractive epithelial cells remain, the nuclei of which do not stain. These cells still adhere to the papillæ, where they are mixed with round cells. In other bullæ, the epidermal arc is seen in sections to be rather thick and to be formed not only by the horny layer but in a measure by the Malpighian layer. One of us has described this arrangement in a case of hæmorrhagic pemphigus following patches of purpura.[1] In sections of the bullæ of pemphigus in newborn or stillborn children, we have often seen two distinct elevations caused by the fluid, one between the papillæ and the Malpighian layer and the other between the Malpighian layer and the superficial epidermis. It is probable that the maceration of the epidermis after death played some part in this separation of the Malpighian layer from the papillæ.

Pemphigus.—Pemphigus is sometimes acute and sometimes chronic. Acute pemphigus may be compared to one of the exanthematous fevers; it is characterised by an eruption of bullæ which undergo spontaneous cure and do not recur. Chronic pemphigus is divided into two principal varieties. In one, the different bullæ, after having run their typical course, terminate by the reproduction of the epidermis: this is *common pemphigus*. On examining the serum of a bulla of this form of pemphigus, which has been collected with care, micrococci are found in chains. The urine also contains them. In the other variety, the epidermis

[1] Rigal and Cornil, *Société Médicale des Hôpitaux*, meeting on February 28 and March 28, 1879, with a plate.

is not reformed after the bullæ; it becomes detached, and the denuded derma is red and weeping. This is *foliaceous pemphigus*.

FIG. 263.—THE BACTERIA OF PEMPHIGUS. (After Gibier.)

If it last some months or years, almost the whole of the skin becomes affected, but no bullæ are then found, for the epidermis has lost its cohesion, and is thrown off in scales, and cannot therefore be raised in blisters. The surface of the skin is denuded, red, excoriated, cracked, moist and weeping in places, and more or less covered with crusts. Bullæ are found in the mucous membrane of the lips, cheeks, and even in the pharynx. The general condition is very bad; hectic fever is usually present, and the disease generally ends fatally. Déjerine[1] has found parenchymatous neuritis in a case of acute pemphigus in a patient affected with general paralysis. Leloir[2] has observed a similar lesion of the nerves in a patient affected with myelitis and acute pemphigus, and also in chronic pemphigus. Schwimmer has recognised the same lesions, and P. Meyer[3] has observed them in a case of fatal pemphigoid dermatitis. The *pemphigus of newborn children* is seated, when it is syphilitic, in the palms of the hands and the soles of the feet. It corresponds to papular syphilide, which is so often seen in the same regions in adults, and which has been improperly called psoriasis (Ollivier and Ranvier).

Rupia.—This syphilitic affection commences by the formation of bullæ filled with colourless or blood-stained serum, which soon becomes cloudy and purulent. On bursting some of the fluid escapes and dries, the surface soon becoming covered with a crust. These dried crusts remain where they are while new crusts are

[1] *Archives de Physiologie*, 1876.

[2] Note read at the Société de Biologie, 1881, in common with Brocq, and article 'Trophonévrose' in *Nouveau Dict. de Médecine*.

[3] *Virchow's Archiv*, vol. xciv. p. 185.

formed in the same way underneath them, and grey or black imbricated crusts are formed which have been compared to oyster shells. Rupia is the syphilitic disease in which the crusts are the thickest, largest, blackest and most characteristic. Under the crusts, the papillæ and derma are suppurating and ulcerated. Rupia, which commences by the formation of bullæ, belongs to the type of pustulo-crustaceous ulcerative syphilides, and terminates after a considerable time in the formation of depressed cicatrices.

Pustular Eruptions.

The type of pustular eruptions is seen in variola. Thus by describing fully the pustule of small-pox, we shall have no occasion to describe that of ecthyma, which has the same structure. We have already described the pustules of eczema (impetigo), and the pustules of acne will be described separately, with inflammation of the hair follicles and glands, for from their mode of formation they are related to lesions of the pilo-sebaceous apparatus.

The difference between a pustule and a vesicle is only one of degree of inflammation, a pustule being nothing more than a vesicle in which the fluid is richer in lymph cells, thicker, and purulent, while at the same time the inflammation of the papillæ and derma is deeper and more acute.

Variola.—Variola is a febrile, contagious, and inoculable affection characterised by a pustular eruption distributed more or less over the skin, the buccal, pharyngeal, and respiratory mucous membrane. It is a general disease of precise evolution, and which, after a varying period of incubation, passes through the four stages of invasion, eruption, suppuration, and desiccation. *The period of invasion* lasts from two to four days. A rash appears on the skin which is composed of red spots, which may vary in size and be general or circumscribed ; sometimes they disappear on pressure (hyperæmic rash), and sometimes they do not (hæmorrhagic rash). The *period of eruption* commences when, first on the face and then on the body and limbs, spots appear which change rapidly into papules and then into vesicles. The papules are small and pointed, and disappear on pressure during the first few days ; they are sometimes surrounded by a red circle due to an effusion of blood. The papules are either separated from one another by intervals of healthy skin (the discrete form), or touch one another at their circumference (the coherent form), or impinge closely on one

another (the confluent form). The eruption on the face decides if the small-pox is of the discrete, coherent, or confluent form.

Suppuration, the third period, commences on the eighth or ninth day. The vesicles are changed into pustules which are generally depressed in the centre. This suppuration is accompanied with subcutaneous œdema. In confluent variola, the lips are thickened, the eyelids œdematous, and the features absolutely unrecognisable. The pus of the pustules hardens on the surface of the skin in the form of crusts. Pustules often appear also on the mucous membrane of the mouth, tongue, pharynx, larynx, and trachea. They are the cause of the laryngitis and tracheitis so often seen in the course of small-pox.

The papules begin by congestion of the papillary blood vessels, elongation of the papillæ, and œdematous inflammation of the Malpighian layer. On examining a section of a papule, pale

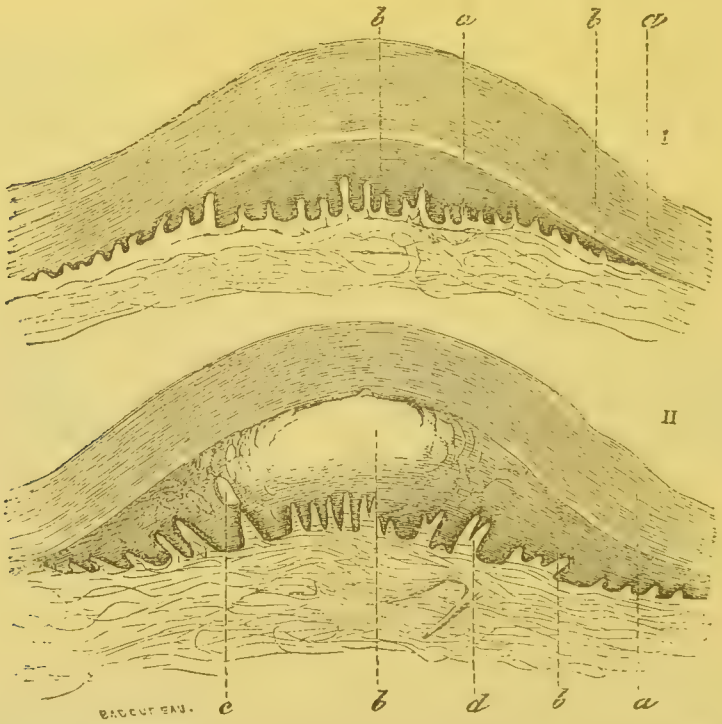

Fig. 264.—I. Section of a Small-pox Vesicle at its Commencement.
a, horny layer; *b*, Malpighian layer, thickened as the pustule is approached; *d*, papillæ.

II. Older Small-pox Vesicle. The letters have the same signification.

granular cells are seen at the lower part of the Malpighian layer, near the derma, at the edge of the papillæ; it is impossible to discover a nucleus in these cells by the aid of staining reagents;

they have long processes, and resemble to a certain extent the cells which Wagner has described in the false membranes of diphtheria, and which have undergone a vitreous change. They are necrosed cells, and these cell changes, the knowledge of which is due to Wagner, constitute according to him what he calls the initial necrosis of the cells of the Malpighian layer. According to Weigert, this change is due to the presence of bacteria, which are first contained in the blood vessels and papillæ. Weigert thinks that this is the initial change in variola, and that all the subsequent changes are secondary and inflammatory. This opinion of Weigert was accepted with much reserve at first by pathologists, but it is now generally admitted in Germany. This layer of mortified cells forms a hard disc at the centre of the pustule, interposed between the papillæ and the horny layer of the epidermis, and hinders the passage of fluids from the papillæ, thus causing the umbilical depression at the centre of the pustules. Rayer and G. Simon had previously described this pseudo-membranous disc, which they had demonstrated by scraping the surface of the pustules. In sections of the vesicles, no change is

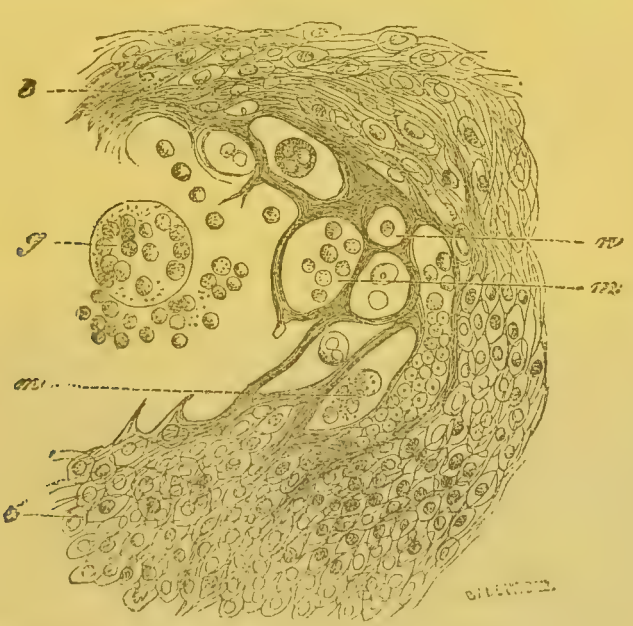

FIG. 265.—CAVITIES HOLLOWED IN THE MALPIGHIAN LAYER AT THE LEVEL OF THE VARIOLAR PUSTULE.

b, b', cells of the Malpighian layer; *m, m*, cavities limited by septa, and containing leucocytes and vesicular cells; *n*, vesicular cell containing a leucocyte; *g*, large vesicular cell free in the central cavity of the pustule; it contains several leucocytes, and is surrounded by the same free elements.

at first seen in the epidermic layer. The Malpighian layer, above the papillæ, contains a series of anfractuous cavities divided by

anastomotic filaments, and containing a fluid in which there are migratory cells and filaments of fibrin. In hæmorrhagic small-pox, these cavities contain a number of red blood corpuscles. Leucocytes are scarce in the vesicle, but become more abundant in the pustule. The trabeculæ which form the reticulum of the cavities of the Malpighian layer are formed of altered cells, which are sometimes, however, recognised by their nuclei. Large multinucleated cells in a state of colloid degeneration are also found in the fluid of the pustule. In the vesico-pustules, which are in course of formation, the mode of development of the septate cavity, which we have just described, may be observed. Multiplication of the nuclei of the epidermic cells situated above the disc of necrosed cells first takes place. The cells and nuclei of the Malpighian layer undergo vesicular degeneration. These cells

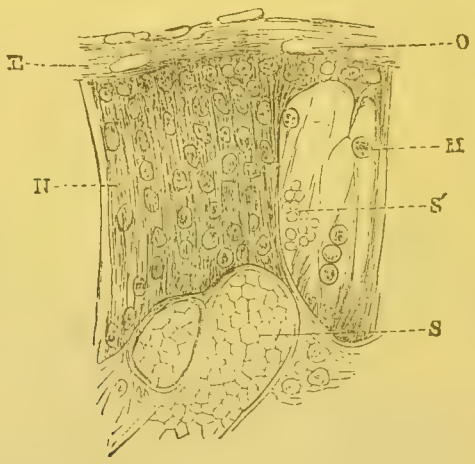

FIG. 266.—SECTION OF SKIN AFFECTED WITH PUSTULES OF CONFLUENT VARIOLA.

S, dilated vessel of a papilla; S', red blood corpuscles, and M, lymph cells, situated in the reticulum which replaces the Malpighian layer; N, modified Malpighian layer; E, horny layer containing vesicular cells, O.

may be compared to vegetable cells; their walls touch and are destroyed in places; the cavities then intercommunicate and allow the entrance of red and white blood corpuscles derived from the papillary blood vessels by diapedesis. Epidermic evolution is arrested; the granular layer is changed or destroyed, and eleidin has entirely disappeared from the part contiguous to the centre of the pustule. The most superficial epidermic cells, those which correspond to the horny layer, have not undergone horny change. On the other hand, an opposite phenomenon occurs in the epidermis around the pustules; this is an exaggeration of the formation of eleidin, and around the pustule in the cells of the granular layer there is a kind of rampart of eleidin (Ranvier).

The papillæ of the derma under the pustule are much larger than normally; their blood vessels are distended, and the meshes formed of connective-tissue fasciculi are filled with embryonic cells. The microbes of variola are seated in the cavities of the

FIG. 267.—SECTION OF THE MALPIGHIAN LAYER IN VARIOLA.

a, horny epidermis; *d*, Malpighian layer; *b*, cavity hollowed in the Malpighian layer; *m*, *m*, the micro-organisms of variola stained with B, methyl violet. Magnified 850 diameters.

Malpighian layer and along the filaments which divide it. They are in the form of slightly ovoid granules isolated or associated together. They are also present in the peripheral parts of the pustule and on the surface of the papillæ; in the latter the microbes are found in the lymph spaces. To stain these microbes, Weigert has used hæmatoxylin after having previously washed the sections for a few minutes in a solution of potash. Methyl violet is, however, a better staining reagent than hæmatoxylin,

and the microbes, in fact, staining easily with it, while the albuminous granules remain colourless or stained only a very pale violet. The débris of nuclei and altered cells, which are found in the areolæ of the pustule, stain also violet, it is true; but their unequal size and larger diameter than the microbes are sufficient to distinguish them. The epidermis of the pustule is profoundly altered throughout its whole depth, either by the initial necrosis of Weigert, or by vesicular degeneration. It is then invaded and destroyed by suppuration. The papillæ themselves are infiltrated with pus, and disappear in the most serious cases, from ulceration. If recovery takes place, an indelible depressed cicatrix remains in the place of each pustule. The papillæ are not reproduced.

It is useful from the histo-pathological point of view to compare **vaccinia** with variola. The histological formation of the vaccinal pustule is exactly similar to that of variola. The anfractuous cavity of the pustule contains red blood corpuscles, leucocytes, the débris of nuclei, and microbes united into masses without any apparent order. There is, either as regards the structure of the pustule or the form of the microbes, no element which distinguishes vaccinia from variola. After filtering the vaccinal fluid, Chauveau obtained a fluid, and a cloudy solid residuum. He found that only inoculation with the solid part gave vaccinia. Chauveau also showed that the virulent element was in the solid granular elements, but the actual nature of this element is still unknown. The microbes of variola were first demonstrated by Weigert ten years ago.

Ecthyma.—The pustules of ecthyma, both as regards their form and their histological characters, are exactly similar to those of small-pox. It is not necessary, therefore, to describe them. The pustules of ecthyma are chiefly seen in debilitated subjects, in typhoid fever, for example, where the skin is congested and inflamed by lying in bed; they generally terminate in ulceration of the skin, which may be more or less deep. They are found also in scrofulous subjects, in old persons, and in syphilis. In the latter disease, the pustule succeeds an inflamed papule, or it occurs spontaneously in certain serious forms of which it is an initial accident. The pustules of syphilitic ecthyma are accompanied with extensive and deep infiltration of the derma. In sections, lacunæ of the Malpighian layer are seen similar to those of the pustules of variola, in the part where ulceration has not commenced; these lacunæ vary in size and contain free cells, and

their walls are formed of modified and generally flattened epithelial cells. The papillæ are swollen, enlarged, and changed into embryonic tissue, in the midst of which the capillaries are seen to be much dilated. This inflammation extends deeply into the derma. Under the crusts, in the ulcerated parts, the papillæ are generally preserved, but they may be also destroyed by ulcerative inflammation. After the pustule, which is covered by a crust, has suppurated for a variable time, it undergoes cure, and a smooth, regularly circular cicatrice is formed, which is white or pigmented, and depressed at the centre. If a person be inoculated with the pus of non-syphilitic ecthyma, the pustule of ecthyma is produced (Vidal, Tanturri).

Lesions of the Sweat Glands, the Sebaceous Glands, and the Hair Follicles.

We do not propose to describe here anomalies of secretion of the glands of the skin, which affections belong more to physiological chemistry and pathology than to histology; such are seborrhœa, sebaceous acne, &c.; but circumscribed periglandular inflammation is within our subject; such inflammation frequently results from accumulation of the products of secretion in the secretory ducts. It is thus that sudamina and most of the pimples of acne are formed.

Sudamina.—When the sweat is secreted in excessive amount, as in acute articular rheumatism, or in certain fevers, small phlyctenoid elevations are seen to appear on the surface of the skin; their contents are at first transparent, and they resemble small dewdrops on the skin. The fluid contained in these small phlyctenæ is distinctly acid (Lallier), which fact distinguishes it from all other morbid secretions. The sudamina contain leucocytes, similar to those present in the blood, and they are so numerous that in a drop of fluid recently taken from a phlyctena they seem to be in contact. At the end of from twenty-four to forty-eight hours, the sudamina which are not emptied by spontaneous rupture are opalescent or yellow. Their contents are alkaline like any other purulent fluid, and their white corpuscles have become granulo-fatty. In transverse sections of recent sudamina, it is seen that they are developed at the orifices of the sweat glands, where epidermic cells have accumulated and slightly raised the horny layer (*vide* I. fig. 268). In sections of completely developed sudamina, it is seen that at the orifice of

the glandular duct, in the Malpighian layer, a very small phlyctena is produced, in which white corpuscles are found

FIG. 268.—I. ACCUMULATION OF EPIDERMAL CELLS IN THE DUCT OF A SWEAT GLAND AT THE LEVEL OF THE EPIDERMAL LAYER, IN A DRIED AND COLLAPSED SUDAMEN.

II. SECTION OF A SUDAMEN THE CAVITY AND CONTENTS OF WHICH ARE PLACED IN THE COURSE OF A SWEAT GLAND THROUGH THE EPIDERMIS.

pressed closely together. Above, the epidermal layers form a roof or vault. It is probable that the fluid in which these white corpuscles float is sweat, for it almost always gives an acid reaction.

Acne punctata. Comedones.—Comedones are seen as small black spots, chiefly in the skin of the forehead, nose, temples, &c. They are found at the orifice of the sebaceous duct of a hair follicle. On pressing their base, a long greyish plug can be squeezed out, which has the shape of a small white worm terminating by an external black spot, resembling a head. This plug is solely formed of horny epidermic cells, agglomerated together, and of sebaceous cells. After the removal of the plug, the orifice and course of the pilo-sebaceous duct can be seen empty. In sections of skin passing through a comedone, this epidermal growth may be observed in the hair follicles. Sometimes one or two hairs which have been hindered in their development may be found in the follicles or at their base; their upper extremity is often turned in. Sometimes also the **acarus or demodex folliculorum** is found with this epidermal hyperformation. This parasite is described later with parasites of the skin.

Milium.—This affection of the skin occurs in the form of small round, slightly projecting granules, the size of a millet-seed or pin's head; they are found particularly near the eyelids, and on the skin of the cheeks and temples. They may be incised and

extracted, when they are seen to be composed of an envelope containing dry epidermic cells, arranged like the scales of an onion; they resemble the epidermal nests of cancroid in which evolution has been arrested. They are seated in the hair follicles or in the sebaceous glands.

Horny acne.—In this lesion the prominent hair follicles are surmounted by a hard horny point, without peripheral inflammation. These conical projections form a patch set with numerous points.[1] In sections of the skin, the hair follicles, and particularly their dilated necks, are seen to contain a large quantity of horny epidermic cells. In the deeper layers of this horny epidermis, soft cells are present, the nuclei of which stain with carmine. The hairs are in some way smothered by this growth of epidermis. The papillæ of the derma are greatly elongated and slightly enlarged. Their vessels are dilated and surrounded here and there by round cells (*vide* fig. 269).

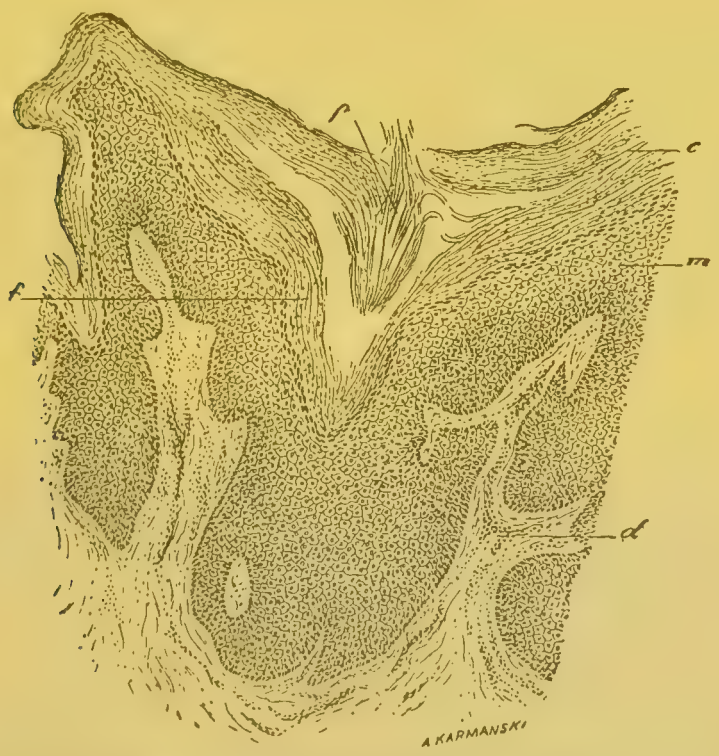

FIG. 269.—HORNY ACNE. (Figure borrowed from the *Traité de Pathologie Cutanée*, now in course of preparation by Vidal and Leloir.)

p, orifice of the hair follicle; *f*, follicle filled with cells; *m*, Malpighian layer near to the neck of the hair follicle; *d*, elongated papillæ of the derma. Magnified 100 diameters.

Pustular acne.—In the centre of pustules of *acne pilaris* a downy hair is generally present. On removing the hair or hairs

[1] Vidal and Leloir, *Société de Biologie*, April 1, 1882.

from the centre of the pustule, and pressing the red and inflamed base of the pustule, a small drop of pus may be squeezed out. Around the hair are a large number of epidermic cells, and some pus cells, and in the expressed fluid a large number of pus cells

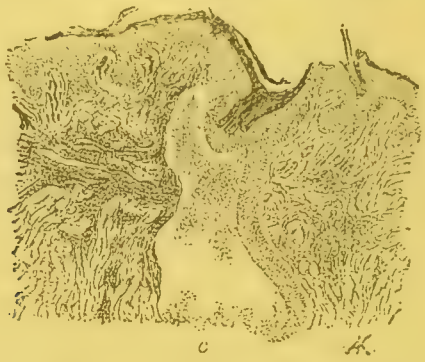

FIG. 270.—SECTION OF AN INFLAMED PUSTULE OF ACNE.
The cavity, *c*, of the follicle is dilated and filled with pus. The epithelial layers of the follicle are partly destroyed. Magnified 15 diameters.

may be found; they have undergone fatty change if the pustule is some days old. They are mixed with masses of epidermic cells. In vertical sections passing through the centre of pustules, the distended cavity of the hair follicle may be seen to contain one or more downy hairs and an accumulation of horny cells and pus cells (fig. 271). The enlarged orifice of the follicle is crowded with

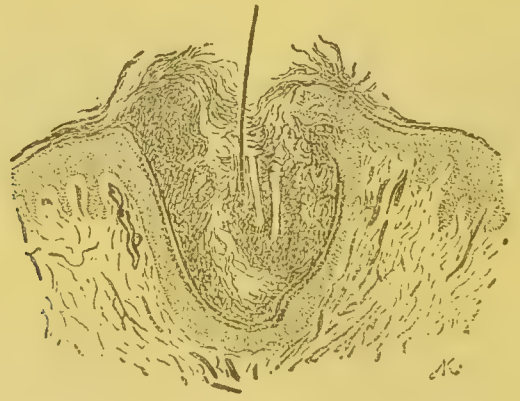

FIG. 271.—PUSTULE OF ACNE PILARIS AT ITS COMMENCEMENT.
The hair follicle has in its centre a hair with a full bulb, and accumulated horny cells. Magnified 15 diameters.

the same elements. Its epithelial sheath is thickened and contains migratory cells. At the beginning the sebaceous glands take no part in the inflammatory process. The papillæ near the orifice of the hair follicle show their capillaries full of blood, and a few migratory cells in their connective tissue. If the pustules are

large and more inflamed, the cavity in the centre of the follicle is larger and full of pus, and the epidermal layers are more or less destroyed (*vide* fig. 270). In the preserved parts, the epidermic cells are vesicular and separated by lymph cells which are more or less numerous and agglomerated; the papillæ near the orifice of the follicle, as well as the derma around the follicle, contain a large number of small round cells. The sebaceous glands are destroyed by inflammation. If these lesions of the follicles are deep and are accompanied with partial destruction of the derma, a small depressed cicatrix is the result.

In *acne rosacea*, which is generally seated on the nose and cheeks, there is a succession of pustules like those described above, and which are accompanied after some time with permanent congestion of the papillary network and varicose dilatation of the small superficial veins. Chronic œdema also often results, with

FIG. 272.—SECTION OF A PUSTULE OF OLD INDURATED ACNE.

o, cavity of the follicle which opens at *s* on to the surface of the skin; *m*, horny layer; *n*, granular layer; *d*, mucous layer lining the cavity of the follicle; *k*, *k*, section of the hair; *b*, superficial horny epidermis; *c*, Malpighian layer; *q*, normal hair follicle; *p*, *p'*, newly-formed papillæ surrounding the dilated follicle. Magnified 15 diameters.

hypertrophy of the skin and new formation of connective tissue and infiltration of the various layers of the skin with small cells.

The pimples of old *acne indurata* are sometimes found the size of a small pea or bean, in which the hair follicle, chronically inflamed, is changed into a cavity containing a mass of horny epidermis which is sebaceous in appearance. These small tumours constitute an intermediate form between the pustules of acne and sebaceous cysts. In sections, the more or less disintegrated contents consist solely of horny cells. The rather narrow neck of the follicle is crowded with them. This neck communicates with the central cavity by a more or less irregular tract. In the epidermic sheath of the follicle sections of one or more hairs are seen. This sheath is formed of a superficial layer of horny cells and a very thick mucosa. Between the horny epidermis and the mucosa, the granular layer is thick and rich in eleidin. In the connective tissue which forms the wall of the follicle, papillæ covered by the Malpighian layer are seen from place to place. Sometimes the sebaceous glands belonging to the distended follicle are found outside of it. Around the cutaneous orifice of the follicle the papillæ are large and inflamed, with round cells interposed between their fibres.

Hypertrophic acne.—This lesion is characterised by thickening of the skin, the surface of which is raised and pierced by punctiform depressions like the skin of a Seville orange. It is accompanied with inveterate acne and congestion, and its seat is usually the nose. It often causes the formation of round lobular tumours, the size of a pea or larger, whence it has been called *Acne elephantiasis.* The nose is then enormously increased in size, lobulated and nodular. Sections of the skin show thickening of the derma due to chronic inflammation, and considerable hypertrophy of the sebaceous glands. These appear as large lobules formed of saccules distended by an accumulation of transparent reticulated sebaceous cells, with brilliant fat granules. Beyond these normal cells the walls of the saccules are lined with one or more layers of pavement cells. These large glands open very rarely into the hair follicles; they generally open on to the surface of the skin. Secondary ducts meet in a common duct which is lined with a very thick epidermal lining continuous with the neighbouring epidermis. These hypertrophied sebaceous glands form the projections seen on the surface of the skin, and their orifices are the depressed points seen with the naked eye. There is in the derma marked thickening of the small arteries and veins, an abnormal development of the capillaries of the papillæ, infiltration with round cells, and swelling of the fixed connective-tissue cells.

Acne varioliformis (Bazin), (*Molluscum contagiosum* of Bateman, *Molluscum sebaceum* of Hebra).—This lesion is seen in the form of small, flat, irregular tumours with a hard and horny surface. This affection shows a curious deviation from the evolution of the cells of the sebaceous glands. If a vertical section of the centre of the tumour be examined under a low power, it will be seen to be composed of a series of lobules which correspond to so many saccules of a sebaceous gland spread out, the duct and opening on to the skin being laid open. In fig. 273 the relief of the tumour

FIG. 273.—SECTION OF A SMALL TUMOUR OF VARIOLIFORM ACNE.

c, horny layer of epidermis, and *m*, Malpighian layer of normal skin at the edge of the lesion; *d*, connective tissue; at the edge of the new growth are seen numerous saccules, *m'*, of the sebaceous glands, the cells of which are altered; *g*, globular cells; *c'*, horny and globular cells; *f*, septa between the glandular saccules. Magnified 40 diameters. (Taken from the *Traité de Pathologie Cutanée* of Vidal and Leloir.)

is seen to be formed by an elevation of the skin covered at its edges by normal epidermis, *c*, *m*, which is directly continuous with the epidermal layers of the glandular lobules. Each of these lobules is separated from neighbouring lobules by connective-tissue septa continuous with the derma. The centre of each lobule is filled with globular cells, which are derived from the altered glandular saccules. In these, a quite peculiar epidermal evolution is observed. To perfectly understand it, it must be remembered that the glandular or sebaceous cells, properly so called, are derived from the walls of the saccules, and that they become globular as they become charged with fat in their progress towards the centre of the acinus. There are, moreover, in man in the large sebaceous glands, cells which become flattened and which join together to form trabeculæ which divide the glandular cavity and limit spaces containing sebaceous glands. If the lobules of varioliform acne be examined under a high power, it will be seen that the sebaceous process of the glandular cells is entirely suppressed, and at the edge of the saccules cylindrical cells will be

seen similar to those of the deep layers of the Malpighian layer (*p*, fig. 274), and then a series of rows of polygonal cells, *m*. In the middle of the lobules round cells appear, having the form of homogeneous globes, and which progressively increase in size. Other cells, which are polygonal and granular at first, then flattened (*g*) as they near the centre of the acinus (*e*), contain

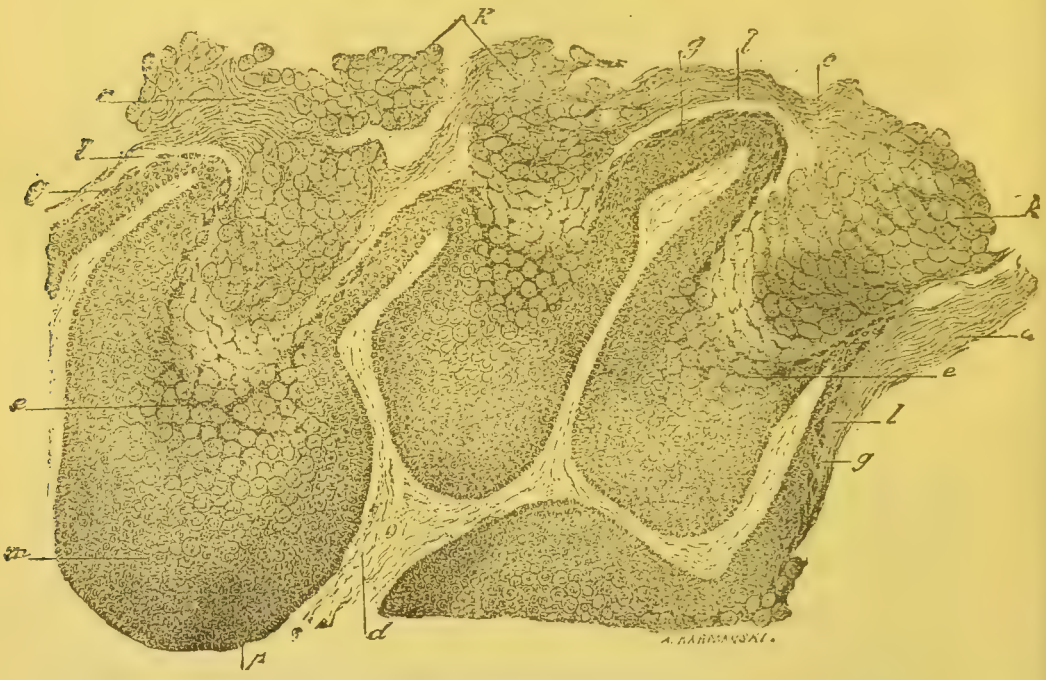

FIG. 274.—VARIOLIFORM ACNE. (From the *Traité Pratique de Pathologie Cutanée*, by Vidal and Leloir.)

Three degenerated saccules of a sebaceous gland; *k*, superficial globular cells; *c*, horny cells; *g, g*, polygonal and flattened cells containing eleidin; *e, e*, eleidin interposed between the globular cells; *l, l*, septa between the cells of the granular layer and the horny epidermis; *t*, connective tissue; *d*, papillary connective tissue between the saccules; *p*, layer of cylindrical cells. Magnified 200 diameters.

eleidin. They resemble those of the granular layer. The eleidin afterwards disappears, and the cells which contained it undergo horny change and form horny trabeculæ (*c*), between which the globular cells are lodged. Eleidin takes so little part in the formation of globular cells, that the latter are found at the base of the lobules beneath the zone where this substance is present. The whole of the upper part of varioliform acne, the large opening towards which the different lobules converge, is formed of horny and globular cells, which stain an orange red with picro-carminate, while the granules of eleidin take a deep red stain. In sections first stained with hæmatoxylin, then with eosin, the globular cells take a violet stain, while the horny trabeculæ which separate

them stain red, as well as the horny layer of adjacent epidermis belonging to normal skin. It is not known exactly what is the substance which infiltrates the globular cells, but from the action of these reagents it is obviously neither colloid nor horny substance.

Pilo-sebaceous perifolliculitis.—Inflammation of the skin surrounding the hair follicles is either acute or chronic, diffused or localised. *Isolated perifolliculitis* sometimes follows a lesion of the hairs, or what is more frequently the case lesions of the hair follicles (hyperkeratinisation and accumulation of epidermic cells in the follicle, cystic change in the latter &c.) The altered follicle becomes a kind of irritating thorn to the surrounding vascular tissues, and provokes inflammation. The sebaceous glands only play a secondary part. At the commencement of perifolliculitis, redness and slight swelling of the skin is observed, then a small pustule around the hair. In the adjoining derma the vessels are dilated and surrounded with migratory cells; these pass into the follicle, mix with the epidermic cells, and pus soon after makes its appearance at the point of emergence of the hair. At the end of a certain time the epidermic sheaths of the hair are softened, and the hair falls. The epidermis of the skin near the follicle undergoes various changes; sometimes horny plates are formed, sometimes nests of pus cells in the midst of a more or less solid reticulum of epithelium. In the latter case, the perifolliculitis often resembles a pustule of impetigo. The hair follicles are then greatly dilated, filled with epidermic masses, degenerated pus cells, and often contain several downy hairs. The erector muscle cell of the hair has disappeared, and inflammation often so alters the follicles that cavities varying in size are the result. Sometimes the base of the pustules undergoes induration, and on it spreading to the surrounding tissues tubercles are formed; a sycosic condition is then induced. At other times the inflammation extends and invades the deeper parts of the derma, when sycosis takes on a phlegmonous character. This form of suppurative perifolliculitis, which is found in hairy parts of the body, causes the formation of very small cicatrices.

Confluent perifolliculitis, in the form of pustules, tubercles, and dermic abscesses, constitutes non-parasitic sycosis or **kerion,** when it is located in hairy parts of the skin, such as the upper lip, the chin &c. Leloir has described ('Soc. Anat.,' May 1884) a peculiar form of perifolliculitis in patches seated on the glabrous parts of

the skin, such as the back of the hand, the arm &c. In its acute stage, this affection is characterised by a circular elevation of the skin, with sharply defined borders. It is of a livid colour, and its surface is riddled with a number of small holes about the size of a pin's point. No hair is found in these orifices. On pressure, a dew of small drops of pus may be emitted, or caseous masses resembling fine vermicelli. On examining the patch histologically, Leloir has ascertained that the lesion is seated in the pilo-sebaceous follicles, and not around the sweat glands, as was previously thought, for this affection was looked upon by the physicians of St. Louis as a conglomerate hydro-adenitis. The epidermis is preserved on the surface of the whole patch, though its layers show the changes which lead to desquamation and the formation of pustules. The horny layer is thin and contains a large number of protoplasmic cells with nuclei which stain with carmine. The granular layer is thick and charged with eleidin. The Malpighian layer contains vesicular nuclei and migratory cells which sometimes accumulate around the orifices of the hair follicles. The hair follicles themselves are filled with epidermic cells and granulo-fatty pus cells. Sometimes a few hairs are met with more or less altered and in irregular positions. The erector muscle-cells have disappeared. The follicles are sometimes cystic, when they appear to the naked eye as yellow points; but they are more generally dilated and open on to the surface by the characteristic orifices described above. These patches of perifolliculitis are not consequent on eczema and are not trichophytic in character. Their pus contains microbes similar to those of phlegmon. In the blood of subjects affected with this disease, Leloir and Duclaux twice found a microbe, which on being cultivated resembled that which Duclaux discovered in Biskra's pustule. It was dumb-bell-shaped and in zooglia. This disease runs its course in about six weeks, and undergoes cure by simple compression without leaving a cicatrix.

Tubercles of the Skin.

The elementary lesion of the skin called a tubercle is characterised by swelling with deep induration of the derma and even of the subcutaneous cellular tissue. The skin becomes red or livid in colour, though sometimes it is scarcely pink or is not changed at all. The anatomical lesion of tubercle consists essentially in a diffuse inflammatory infiltration, which is generally

subacute or chronic, of all the layers of the derma as well as of the cellulo-adipose tissue. The diseases which give origin to tubercle are lupus, lepra and syphilis. The two first will be described later, and here we will only indicate the pathological histology of syphilitic tubercle.

Syphilitic tubercles[1] are intermediate between papules and gummata. They form large and deep papules and are isolated or in groups. They are seated on the face, forehead, neck and legs, or at the juncture of the mucous membrane and skin. There are two varieties, dry tubercular syphilide and ulcerative tubercular syphilide. The first, characterised by a copper colour, are grouped in circles or segments of circles, and are covered with thick scales, almost crusts, though there has been no ulceration, and they may undergo cure leaving white or pigmented cicatrices. The cellular infiltration of the connective tissue and its partial destruction when undergoing cicatricial change may take place under an epithelium which is either intact or only slightly irritated. Ulcerating tubercles may be discrete, or grouped, which is more frequent. They may cover a considerable surface of the skin of the scalp, face, forehead, nose, cheeks, shoulders and limbs, and the back of the body. Extensive losses of substance result from the ulcers, and the depressions, which unite in a circinate form, correspond to destroyed tubercles. The ulcers are deep and punched out of a thickened and hard skin, which is infiltrated with small cells; the edges are red and inflamed and sometimes much hypertrophied. Under the microscope inflammatory lesions are discovered similar to those found in phlegmon, and the connective tissue, crowded with round cells, mortifies in blocks varying in size.

Between syphilitic tubercles and **cutaneous gummata**[2] there is only a difference of degree, so that Fournier described them together. A gumma consists in inflammation of the subdermic tissue which is propagated to the derma; it finally opens externally and a deep crater-like pit is produced, with its base larger than its orifice, and through this opening the inflamed and mortified tissue is slowly eliminated like the core of a boil. During their crude period, gummata are characterised by a deep indolent swelling which often passes unobserved. At the time, the superficial layers, the epidermis, the dermo-papillary layer and the middle layer of the derma, are seen, in microscopic sec-

[1] For a description of indurated chancre see vol. i. p. 187.

[2] For a general description of gummata see vol. i. p. 191.

tions, to be intact.[1] Slowly the tumour grows, and may attain, exceptionally, it is true, the size of a hen's egg. When fully developed, the adipose tissue and the lower half of the derma are crowded with small cells, which having replaced the fat, strangle the connective-tissue fasciculi; the vessels, the walls of which are thickened and infiltrated, are often obliterated and filled with fibrin and lymph cells. In consequence of this process, mortification and caseation of the exudation and of the tissue of the derma are the result. The deep layers of the derma, and particularly

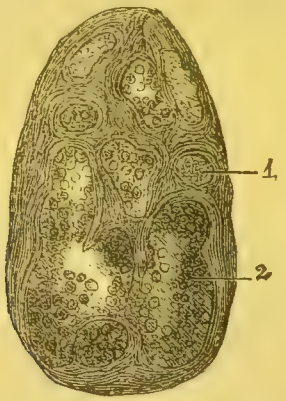

FIG. 275.—SWEAT GLAND IN A GUMMA OF THE SKIN.
1, excretory duct; 2, secreting tube filled with small cells. Magnified 80 diameters.

the sweat glands, are inflamed (fig. 275). Soon ulcerative inflammation occurs, and from this moment there is a slow elimination of the mortified products which may last one or two months, and which is followed by a depressed cicatrix. Gummata may often reach the periosteum when the skin affected, like that of the leg for example, is near the bone.

Ulcers of the Skin.

We will only describe here soft chancre and perforating ulcer of the foot.

Soft chancre commences by a small papule, which rapidly develops into a pustule; it then bursts and gives place to an ulcer which extends both in depth and surface. In a week, soft chancre is at its fullest development, and consists of a loss of substance which is deep and crater-shaped, with cut everted edges, and with a granulating and anfractuous base secreting blood-stained pus. The swollen inguinal glands frequently suppurate and open, giving place to chancrous ulcer. In sections of soft chancre, it is seen

[1] Cornil, *Leçons sur la Syphilis*, p. 219.

that the epidermis, the papillæ and the superficial layer of the derma are destroyed at the level of the ulceration, and that the base of the latter is lined with fleshy granulations. After this description, the anatomical differences between soft and hard chancre are recognised. The latter is in fact papular at the commencement, the epidermic layers are long preserved though altered, and the papillæ are never destroyed. Hard chancre is a new growth which indurates the derma, while soft chancre is a destructive and ulcerative inflammation. In the serum of soft chancre, isolated micrococci or diplococci are found which have proved capable of cultivation. Inoculation of a subject who has already had soft chancre gives no positive results (Julien), while the pus of soft chancre, inoculated under the same conditions, always produces soft chancre.

Perforating ulcer of the foot.—Perforating ulcer is a deep ulcerative and progressive lesion of the sole of the foot. It commences by a corn which gives place to a round ulcer, limited by a sharp epidermic ridge and with a reddish, villous base which secretes a seropurulent fluid. It extends in depth till it reaches the bones and joints. When cured it does not show the least tendency to return. The derma looks as if a piece had been punched out; a stylet generally demonstrates a fistulous track which leads to a bone affected with ostitis.

In a section, passing through the ulcer and the neighbouring skin, the horny layer of the epidermic ridge of the opening is seen to be almost a centimetre in thickness; it is thicker on the ulcerated side and is stratified; on the other side it is thinner and continuous with the normal epidermis. The papillæ are greatly hypertrophied and elongated around the ulcer. The derma is thickened and chronically inflamed; its blood vessels are embryonic, and the tissue lardaceous, similar to that of fleshy granulations which constitute the ulcer as far as the altered bone, which may itself be affected with rarefying ostitis. This curious affection, which has been looked upon as the result of an atheromatous lesion (Péan, Delsol, Dolbeau), or of simple pressure (Leplat, Larrey, Sédillot, Després, Gosselin, Pitha and Billroth), or of ostitis, seems to be now referred to neuritis. Poncet (of Cluny)[1] was the first to discover, in the nerves distributed to the ulcer, anatomical lesions similar to those observed in the peripheral

[1] *Mémoires de Médecine Militaire*, vol. xii.

segment of a divided nerve. Duplay and Morat[1] have verified the accuracy of Poncet's observations.

Tumours of the Skin.

It is difficult in the skin to say exactly where chronic inflammation ceases and a tumour commences. There is, in fact, a series of inflammatory new growths of long duration, and which behave like actual tumours; some of these may, however, undergo spontaneous cure, while others persist indefinitely, so that there are all intermediate forms between chronic inflammation and tumours. Some new growths may be equally well looked upon as inflammatory or as tumours. Condylomata, for example, which are due to urethritis, syphilis, vaginitis, or even to a vaginal discharge induced by pregnancy, are caused by hypertrophy of the papillæ and an exuberant formation of epidermic cells, and they belong to papillomata. When, however, these papillomata are small and the cause which produced them has disappeared, they shrink and undergo spontaneous cure, which is against their being looked upon as tumours.

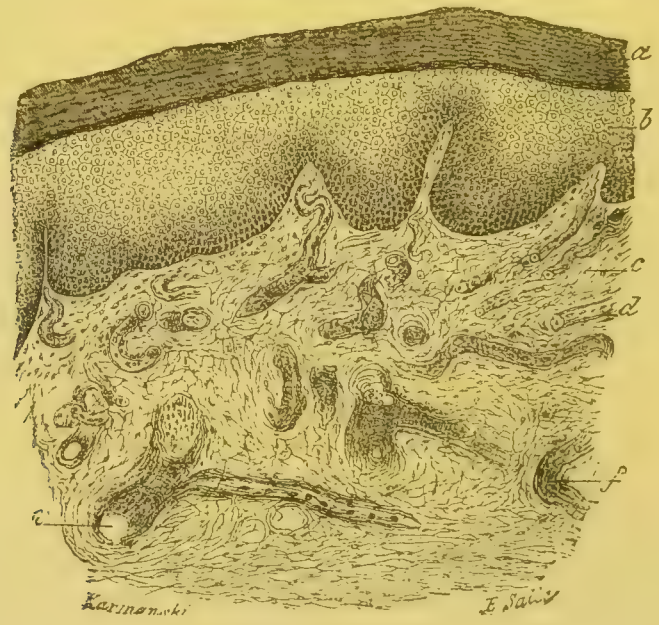

FIG. 276.—PAPILLOMA DEVELOPED AT THE ORIFICE OF THE URETHRA.

a, horny layer; *b*, Malpighian layer; *c*, connective tissue in which ramify numerous vessels *v*, and capillaries *d*; these vessels take a peculiarly sinuous course in the papillæ and at their base. Magnified 60 diameters.

We will proceed now to describe the cutaneous tumours which are related to micro-organisms.

[1] *Arch. de Méd.*, 1873, vol. i.

Warts.—Warts are chiefly seen on the hands, fingers, fore-arm, both on the dorsal and palmar surface, but more often on the dorsal. They are generally small and multiple, and they are sown by scratching around a pre-existing wart. A description of them has been given in vol. i. p. 279, and we will only add here that in sections of warts stained with aniline reagents, the presence of bacteria may be ascertained. Majocci (quoted by Thomasi Crudeli, 'Anatomia Pathologica,' vol. i. 1882) has discovered a very small long bacillus which he has called the *bacterium porri*. In a small wart which one of us removed and placed immediately in alcohol, Babes saw, in the tissue of the papillæ, a large number of microbes which stained with aniline dyes; these micrococci measured from 0·4 μ to 0·5 μ and were united as diplococci, sarcinæ, or in strings of three, four or five together, or in round or square

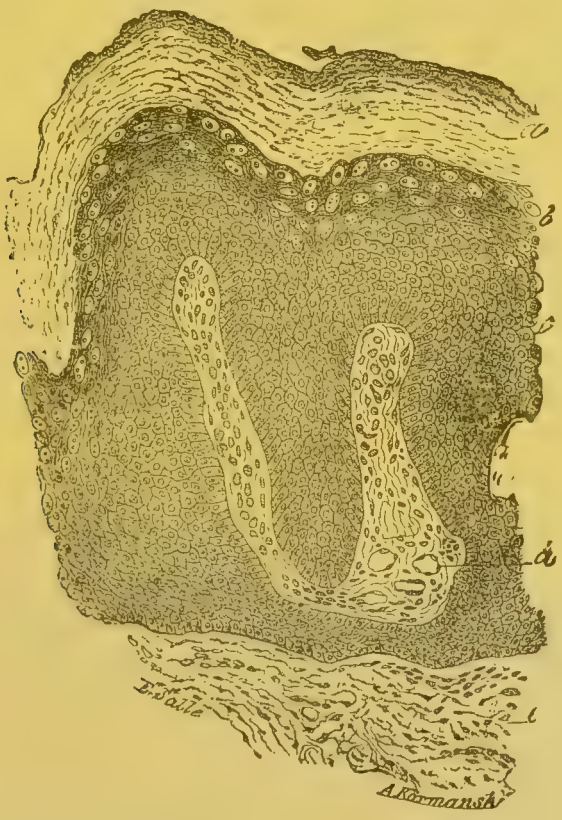

FIG. 277.—HORNY PAPILLOMA OF THE LOWER LIP.

, horny investment; *b*, granular layer; *c*, Malpighian layer; *d*, vessels of the papillæ; *e*, connective tissue. Magnified 100 diameters.

masses. Warts certainly develop by contact. Thus it is not rare in children, who have warts on the hands or fingers, to have them developed on the face, or at the corners of the lips, at the spots where they are accustomed to rub or scratch the skin.

Lepra or elephantiasis Græca (Lepra Arabum, Spedalsked, Aussatz, Morphea).—Lepra or leprosy is a serious affection of the skin which was perhaps formerly the most universal and destructive of diseases. Owing to rigorous measures, and the isolation of leprous patients, Europe has been almost entirely freed of the disease, with the exception of Spain, Greece and Norway.

There are three varieties of leprosy, the tubercular, the macular and the anæsthetic.

Tubercular lepra is characterised at its commencement by round ecchymotic irregular spots, of a brown or sepia colour, at which the skin gradually thickens so as to form spread-out tubercles, which are sharply defined and separated from one another, or extended into patches which often cover the whole of the surface of a limb. The face is chiefly affected; the forehead is seamed with ridges and furrows, separated by irregular edges, due to tubercular development of the skin between the transverse folds; the eyelids are swollen and the lips thickened; the upper lip is pendant (leontiasis). The face is of an earthy colour and wears a torpid expression. The sensibility of the skin over the tubercles is sometimes preserved, sometimes diminished, at others completely absent. Projecting patches or tubercles soon appear on the mucous membrane of the mouth, tongue, soft palate and pharynx; and the conjunctiva is also the seat of small flat tubercles. Later, fissures, bleeding erosions and actual ulcers, appear on some of the tubercles; the laryngeal mucous membrane is also affected as well as the epiglottis, and the voice is lost, as in tubercular laryngitis. Ulcers on the face, losses of substance of the nostrils, and flattening of the bones of the nose are also sometimes observed. The fingers are also changed, there is a thickening of the skin, tubercles are formed, and deep fissures cause hæmorrhage. Presently inflammatory grooves appear around a digital extremity, and one or more phalanges are separated from the living parts, and fall off after being mortified or mummified.

Macular lepra consists in brilliant red or brown spots, with or without infiltration of the derma. This spotted appearance of the skin may be more or less deep in colour; the spots resemble vitiligo; sometimes their centre is white, hard and lardaceous, while their periphery is red, yellow or brown. Macular lepra often becomes complicated with tubercles and this becomes turned into tubercular lepra. The patches of macular lepra are often anæsthetic.

Anæsthetic lepra owes its name to the fact that it commences by patches in which the skin is completely anæsthetic without there being at first any appreciable change in structure. Sometimes, however, bullæ of pemphigus or various eruptions occur on the anæsthetic parts; later, the skin atrophies and becomes wrinkled. The face has a quite peculiar expression of precocious decrepitude and of stupor. Deep ulcers, due to trophic changes, occur at the articular folds of the fingers and are the cause of the fall of a joint or part of a finger; the hands and feet are often deformed, and many fingers and toes may be replaced by stumps. From these lesions the form of leprosy is often called *mutilating lepra*.

Anæsthetic lepra may be observed as an isolated condition, and may terminate in mutilation of the extremities and without the formation of leprous tubercles.

The pathology of lepra has been described by Daniellsen and Boeck,[1] Simon, Virchow,[2] Bergmann,[3] A. Hansen,[4] Neisser[5] &c. We have studied the lesions of the tubercles, skin, mucous membranes, organs, nerves, bones &c. In the infiltration of the derma, mucous membrane, lymph glands, testicles &c., a considerable quantity of the lepra bacilli was discovered by Armauer Hansen. The nerves are altered in all those cases of tubercular, macular and anæsthetic lepra in which the skin is anæsthetic. Bacilli are not usually found in simple anæsthetic lepra, while on the contrary all the products of tubercular lepra are crowded with them in a manner which cannot be imagined.

In sections of the skin of recent leprous tubercles, the layers of epidermis are seen to be normal and perfectly well preserved; the papillæ are slightly hypertrophied and filled with round cells; the derma is infiltrated with round or oval cells which are often arranged in ill-defined islets; they are found in the whole thickness of the derma, from the base of the papillæ to its lower limit and as far as the cellulo-adipose tissue. The adventitious coat of the blood vessels is thickened, and generally also the internal coat, which causes a narrowing of their calibre. The sweat and sebaceous glands and the hair follicles are affected almost from the commencement with leprous tubercles and

[1] *Traité de la Spedalsked*, with an Atlas. Paris, 1848.
[2] *Path. of Tumours*, vol. ii.
[3] *Die Lepra in Livland.* Petersburg, 1870.
[4] *Archives de Phys. Belges*, 1877.
[5] *Breslauer ärztl. Zeitschr.*, 1879; *Virchow's Arch.*, vol. lxxxiv.

strangled by the production of small cells around them. They finally atrophy and disappear entirely. Sometimes, however, large multinucleated and actual giant cells are found accumulated in old tubercles; these cells seem to us to result from the multiplication of nuclei and hypertrophy of the cells of the sweat glands. On staining sections of newly developed tubercles with 5B violet, and on decolourising them with alcohol after allowing them to be acted upon by a solution of carbonate of soda, preparations are obtained in which the bacteria are stained blue violet, while the cells are hardly stained at all (Cornil and Suchard, 'Soc. Méd. des Hôp.,' June 10, 1881). In these sections, almost all the round or fusiform cells which infiltrate the derma are seen to be filled with a varying number of rods which are straight or slightly curved, rigid, deeply stained a blue violet, sometimes isolated, crossing one another like brushwood in the same cell, sometimes attached together as an elongated bundle at the extremities of which are seen the isolated points of the bacilli. Sometimes the rods are found outside the cells in the lymph spaces of the derma, and they may be found in the flat and concentric cells of the adventitious coat of the blood vessels, as well as in the cells of their internal coat. Very good preparations may be obtained by staining with Ehrlich's fluid and decolourising with nitric acid, a process which is used to demonstrate the bacilli of tuberculosis. It can then be ascertained that the bacilli are often seated in the sebaceous glands and hair follicles (Babes, 'Arch. de Phys.,' July 1, 1883, No. 5). In older tubercles, large multinucleated cells, which have been called leprous cells by Virchow, are found in the leprous islets of the derma. These large oval, spherical or irregular cells, contain oval nuclei and are sometimes as large as the giant cells of tuberculosis, with which they might be confounded. They also contain an enormous quantity of rods. In old tubercles no trace of glands or hair follicles is any longer met with. The epidermis is thinned and the papillary network is effaced. In blood obtained by pricking a leprous tubercle with a needle, rods are found either free or contained in the lymph cells. These bacilli seem to us to be endowed with movement.[1] The most marked distinction between tubercular and leprous tissue is shown, in stained sections, by almost every cell of the leprous

[1] The bacilli of lepra resemble those of tuberculosis; they stain, however, more easily; thus, for example, fuchsine and 5B violet stain them in simple solution, while they do not affect the bacilli of tuberculosis. They resist longer, for an hour, decolourisation by nitric acid (Babes, *Ac. des Sc.*, April 1883).

nodules always containing a large number of bacilli, while the cells of tubercles often contain only a very small number; they

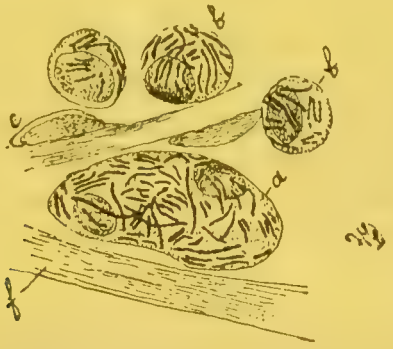

FIG. 278.—THE CELLS AND BACCILLI OF LEPRA.

a, large oval cell containing a large number of bacilli; *b*, *b*, smaller round cells the diameter of lymph cells and containing an oval nucleus; *f*, fibres of the connective tissue. Magnified 800 diameters.

may be even entirely absent in fibrous tubercle and in old sclerosis of tubercular origin, while there are always myriads in every leprous growth. It seems as if all the bacilli of lepra remained for an indefinite time in the tissues where they are developed and showed no tendency to be eliminated or destroyed. Their power of resistance is most remarkable. Thus thousands of bacilli were found in a small fragment of a leprous nodule, which had been dried in an envelope of paper where it had been left forgotten for ten years. Bacilli have been stained in histological preparations which had been previously stained with picro-carminate and preserved for years in glycerine between two glass slides. The bacilli are found in the fragments which are inserted under the skin of inoculated animals, as we shall see further on. By the extreme abundance of bacilli infiltrating equally everywhere the pathological growths of lepra, and by their persistence at all stages, this disease is the most characteristic type of affections of bacillar origin. When leprous tubercles ulcerate, the blood and the transparent or slightly opaque fluid, which is secreted on the surface of the fissures and ulcers, are found to contain a large number of bacilli. The tubercles, infiltrations, erosions and ulcerations of the buccal, lingual, pharyngeal, and laryngeal mucous membrane show exactly the same lesions as the skin, namely, infiltration of the derma with small cells, and an enormous quantity of bacilli both inside and outside the cells. The lymph glands of the neck near to the diseased parts are hypertrophied and infiltrated with micro-organisms. We have examined a gland sent from Grenada by

Hernando, which showed marked sclerosis with new formation of fibrous tissue, with caseous points as well. In sections of the gland, the adenoid tissue was found to have disappeared and to be replaced by thick fasciculi of connective tissue. The lumen of the vessels was often obliterated by round masses which stained with aniline dyes. Under a high power, groups of very short bacilli were seen. They were about 1 μ in length and were conglomerated together in the midst of a homogeneous substance which stained feebly. The vascular walls still contained recognisable epithelial cells, but it is probable that the islets of bacilli did not have a vascular origin, and were simply small cysts containing destroyed cells full of bacilli. Similar lesions may be met with in very old cutaneous tubercles. The function of the testicles is sometimes compromised from the first or second year of the eruption of cutaneous tubercles. The connective tissue of the gland, which is thickened, and the contents of the seminiferous tubes are chiefly affected. The connective tissue is filled, as in tubercles of the skin and mucous membrane, with round or plasmatic cells which contain a large number of bacilli; in old lesions masses are found formed of confluent and broken-up cells, which are necrosed and filled with the same micro-organisms. The parenchymatous organs are also degenerated when the disease has lasted a long time, particularly after ulceration of the skin and mucous membrane; they are in a condition of fatty and amyloid degeneration and of chronic pyæmia, resulting from suppuration. Thus amyloid degeneration of the liver and albuminuria may be co-existent. Most of the tissues may be affected by lepra. The lesions of the bones have been well described by Dr. Hernando, but the more important lesions of the nerves were discovered by Virchow. The nerves distributed to the diseased parts are changed into fibrous cords. This change is accompanied and preceded by degeneration of the nerve tubes, which lesion has been investigated by Tschiryeff, Leloir, and by Drs. George and Frances Hoggan.[1]

It is thus seen that the lesions of lepra differ entirely from those of tuberculosis, though the bacilli which cause both these diseases resemble one another in shape and their behaviour towards staining reagents. Lepra chiefly affects the skin and the nerves, while it generally spares the lungs and the serous membranes; tuberculosis is, on the contrary, seated in the lungs, and the serous membranes, and rarely affects the skin. Lepra is essentially caused by parasites, and it is hence concluded that it

[1] *Arch. de Phys.*, 1882.

is contagious and inoculable from one human being to another. Armauer Hansen has proved this by inoculating with tubercular lepra the conjunctiva of a man affected with anæsthetic lepra. This proof is not absolute, for anæsthetic lepra may terminate in tubercular lepra. Attempts have been made to inoculate animals with lepra, but the kind of animal susceptible to the disease has not yet been discovered. Hillairet and Gaucher [1] inoculated a pig, but the result was not conclusive. Neisser has inoculated dogs, and Kobner [2] has inoculated frogs, fish, and eels. He found in these animals, as well as in dogs, fragments of tubercles which had been introduced, and which always contained a number of bacilli; but his conclusion is that the bacilli are not reproduced and that the inoculations have not proved anything. Otto Damsch [3] has not been more fortunate. Vidal gave us the skin of a pig to examine into which a fragment of leprous tubercle had been inserted, more than a year previously. Babes made the sections which passed through the skin in which the fragment had been inserted, and the surrounding skin. He found a quantity of characteristic bacilli in the first, but none in the latter. Thus we are justified in saying that hitherto the inoculation of animals with this disease has given no positive results.

Lupus.—This disease has received its name from its tendency to devour the surrounding flesh like a wolf (Latin, *lupus*), '*quasi lupus famelicus proximas sibi carnes exedit*' (Manardus). It is a tubercular affection of the skin, and is characterised by deep miliary nodules, which develop slowly and terminate by a cicatrix with thinning of the skin, or by ulceration and destruction of the deep parts. We will describe in order the different varieties of lupus, which are, 1st, tubercular or common lupus, ulcerative or non-ulcerative (exedens or non-exedens); 2nd, sclerous lupus; 3rd, erythematous lupus; 4th acneic lupus.

1. **Tubercular lupus.**—Lupus commences by small deep nodules, which are hard to the touch and of a pink, red or brownish colour; they are due to infiltration of the derma, and are confluent or isolated in small groups which take from one to two months to develop; they flatten at the same time that the epidermis wrinkles and is exfoliated (exfoliative lupus). A small white depressed cicatrix is left in their place, without any ulceration having occurred. Other tubercles ulcerate at their centre, and by confluence

[1] *Soc. de Biol.*, 1881.

[2] *Virch. Arch.*, 1882.

[3] *Virch. Arch.*, vol. 92, 1st book.

of many tubercles large ulcers are produced (ulcerative lupus). The continuous evolution of these tubercles, with successive exacerbations, may be observed during the duration of the disease, with periods of rest and recrudescence. In certain varieties of lupus, the disease extends in depth, and causes serious ravages, such as, perforation of the septum of the nose, destruction of the alæ of the nose, perforation of the soft palate, ostitis &c. The face, cheeks and nose are generally the seat of lupus, but it may also affect the limbs and the trunk. Originating in the nose, it may reach the palatine and pharyngeal mucous membrane; in fact it being often seated near the mucous membranes it affects them; then, for example, it may pass from the eyelids to the conjunctiva, and from the labia majora to the vulva. The pathology of this disease has been carefully studied by Virchow, Wedel, Auspitz, Kaposi and Neumann in Germany, and by Malassez, Grancher, Renault, Chandelux, Vidal and Leloir in France.

In sections, stained either with picrocarminate or safranin, and examined under the microscope, it is seen that the epidermal layers are thicker than they are normally. The papillary layer is generally much developed, so that the papillæ, which are prominent, elongated and irregular, are separated from one another by interpapillary processes or columns of the Malpighian layer, which penetrate deeply. The derma is infiltrated with small cells as well as the papillæ; but beneath the papillæ, small round or irregular islets are seen; they vary in extent, and are confluent in places and are formed by the agglomeration of small cells. In the middle or at the periphery of these cells very characteristic giant cells are seen, even under a power magnifying from forty to fifty diameters. These islets of small and large cells are generally seated at the edge of the hair follicles and the sebaceous glands. They have been likened to tubercular follicles, and they are, in fact, identical with tubercular follicles. It is even difficult to find more typical tubercles, and those containing so many giant cells. These islets of small round cells with giant cells are never absent in tubercular lupus. This pathological infiltration generally extends to the cellulo-adipose tissue, when the lupus becomes rodent, and causes necrosis of the periosteum and bones, which are, like the derma, destroyed by encroaching ulceration. On examining sections of lupus under a very high power, and the lesions in detail from the surface downwards, it is seen that the epidermis is generally thickened, and in the horny layer streaks stained red by carmine are observed. The stratum lucidum and stratum

granulosum are thickened as well as the Malpighian layer. In the latter a large number of migratory cells are interposed between

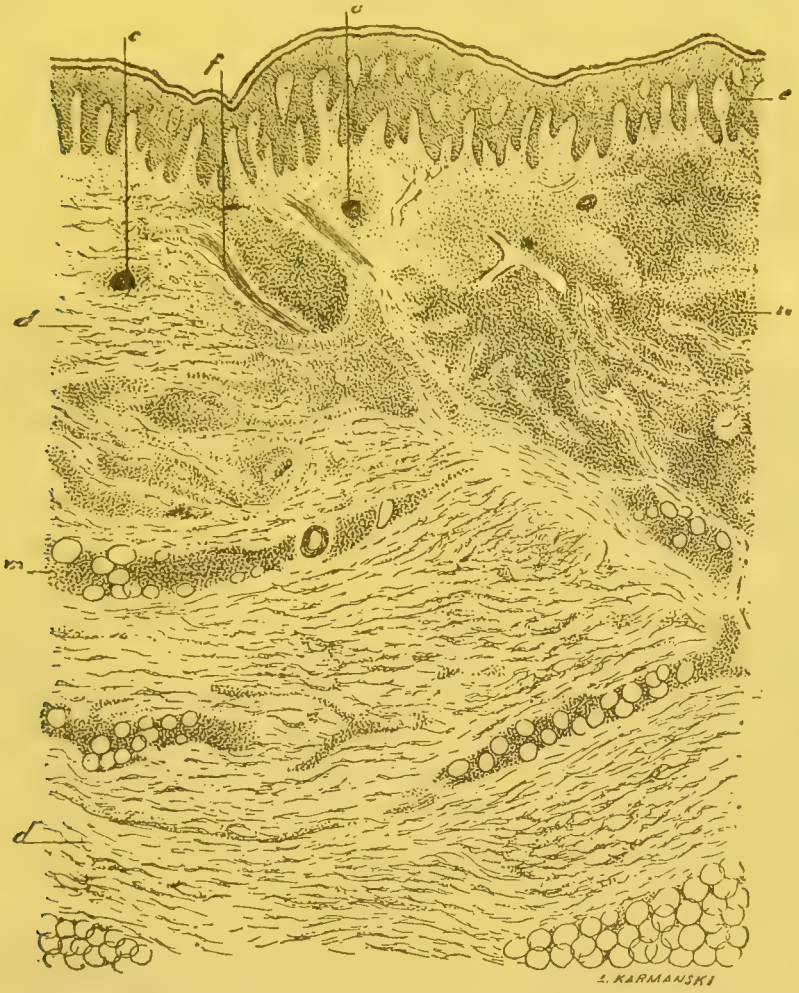

FIG. 279.—TUBERCULAR LUPUS. (Figure taken from the *Traité de Pathologie Cutanée* of Vidal and Leloir.)

e, thickened Malpighian layer covering hypertrophied papillæ; *f*, muscular fasciculi; *d*, connective tissue; *n*, derma infiltrated with small cells; *c*, giant cells; *m*, tracts of inflammation around the adipose cells at the base of the derma. Magnified 30 diameters.

the epithelial cells, and in its interpapillary processes, balls of horny cells are sometimes found. In the irregular papillæ, which are frequently pointed and much elongated and generally hypertrophied in every direction, many migratory and swollen fixed cells are present. Sometimes the development of the papillæ is so marked, and the interpapillary processes of the Malpighian layer are so long and broad, that on examining oblique or transverse sections, lupus might be mistaken for pavement-celled tubular epithelioma; but the examination of accurately cut

vertical sections removes all doubt. This form of lupus might be called papillomatous. Giant cells are not found either in the papillæ or on the surface of the derma. In the follicles of the derma the giant cells vary greatly in size; sometimes they are so close together that they form actual foci. The large giant cells are surrounded by epitheloid cells; at other times they are isolated and only surrounded by small round cells. Their protoplasm is granular and stains yellow with picrocarmine, and their nuclei are oval, globular, or flat; according to Thin, the giant cells of lupus are always vascular in origin. In the follicles, the connective tissue is formed of small fasciculi reticulate in appearance; around them fasciculi of thick fibrous tissue are found. We have searched for the bacilli of tuberculosis in twelve cases of lupus removed from the living subject, and though we examined many sections of the fragment removed, we only once found a bacillus. Malassez has searched in vain for the bacilli of tuberculosis in many cases of lupus. Pfeiffer, Doutrelepont and Demme have been more fortunate and have found them frequently.

Ulcerative tubercular lupus, *lupus exedens*, is caused by a more acute inflammation of the superficial layers of the papillæ and derma. These parts are infiltrated with a large number of migratory cells, which, in their passage across the epidermic layers, cause softening and destruction of the filaments which unite the elements of the Malpighian layer, and hinder the formation of eleidin in the granular layer and consequently keratic changes in the cells. At a given moment, the entire epidermis is exfoliated and the papillæ suppurate and are destroyed as well as the lupous follicles. Before ulcerating, small purulent phlyctenæ are often formed in the epidermis, which hasten its destruction and the ulceration of the derma. Sometimes ulceration is preceded by slow atrophy of the epidermic cells (Larroque). The ulcer once formed, it granulates, becomes covered with a black crust, and after the elimination of a certain amount of lupous tissue, the derma undergoes actual cicatricial sclerosis. The progress of ulceration is then arrested.

2. **Sclerous lupus** has, according to Vidal and Leloir,[1] the appearance of papillomata or warts. It is either primary or secondary to tubercular lupus. It is characterised by rough, unequal, mammillated nodules, covered with warty growths which are frequently horny and separated by fissures or grooves. These tumours finally wither and leave a depressed cicatrix. In sections,

[1] *Soc. de Biol.*, 1882, p. 705.

these nodules of lupus are seen to be composed of fasciculi of connective tissue, arranged in concentric layers. They are separated by a few round cells. Sclerosis commences at the periphery of the islet, and progresses till no embryonic tissue is left in the centre. In this variety of lupus, the vessels are sclerosed. In certain parts of the tumour, chiefly in the deep layers, the tissue of tubercular lupus with its giant cells may be found.

3. **Erythematous lupus** is characterised by diffuse infiltration of the derma. The inflammation is generally superficial and subacute, and shows a great tendency to become localised around the glands, as Hebra, Kaposi, Vidal and Leloir have remarked. The blood vessels are often much dilated, and hæmorrhage frequently results. The sebaceous glands, surrounded by embryonic tissue, are inflamed and secrete more profusely, which gives this form of lupus a peculiar appearance. The glands often become obstructed, globular and cystic, and form an elevation on the surface of the skin. The epidermis desquamates, and when cure takes place, a depressed cicatrix is found without erosion.

4. **Acneic lupus** is a variety similar to the preceding. In it the sebaceous glands, greatly hypertrophied and frequently cystic, project on the surface of the skin, or, inflamed and filled with a purulent fluid, they ulcerate and cause loss of substance and a depressed cicatrix like those of acne. The derma is much infiltrated and thickened. When Friedlander, Köster and others had described the tubercular follicle with its giant cells, and it had been shown, moreover, that in lupus was seen its most perfect type, the identity of lupus and tuberculosis was asserted, the former being considered by some as a local tuberculosis of the skin. Such was the opinion formulated by Besnier. In 1882[1] Leloir commenced to inoculate lupus. In these experiments, undertaken with one of us, Leloir obtained[2] positive results in half the cases, that is to say a general tuberculosis, in which the tubercles contained bacilli, was reproduced by a series of inoculations. We always remarked that the result was obtained much more slowly when pulmonary tubercles were employed as the material of inoculation. The most recent researches of Koch[3] have proved completely the similarity of

[1] *Société de Biologie*, December 1882.

[2] Cornil and Leloir, *Société de Biologie*, June 1883.

[3] *Mittheilungen aus dem Kaiserlichen Gesundheitsamte von Dr. Struck*, vol. ii. Berlin, 1884.

tubercle and lupus. It is true that Koch has only four times found the bacilli of tuberculosis in lupus, and in very small numbers. In one case, for example, he examined twenty-seven sections and in another forty-three before finding a single bacillus.

FIG. 280.—ACNEIC LUPUS. (Figure taken from the *Traité de Pathologie Cutanée* of Vidal and Leloir.)

c, horny epidermi ; *m*, Malpighian layer; *t*, connective tissue ; *v*, vessel ; *e*, hair follicle into which open the different hypertrophied lobules, *s*, of a sebaceous gland. Almost the whole of the derma is infiltrated with round cells. Magnified 80 diameters.

But in a series of successive sections he found at a certain spot from one to three in every section. He has never found more than one bacillus in a giant cell. Koch has, moreover, succeeded in cultivating bacilli derived from hypertrophic lupus. It may therefore be now affirmed that ordinary or tubercular lupus and sclerous lupus belong to tuberculosis. There is nothing to prove that the same is the case with exanthematous and acneic lupus.

Cutaneous tuberculosis.—Lupus is not the only tubercular lesion of the skin. Tubercular nodules covered by epidermis have been described as well as tubercular ulcerations. We have

frequently seen them, chiefly on the under lip and around the anus. Hanot has recently published ('Soc. Méd. des Hôp.,' Feb. 22, 1884) a case of serpiginous tubercular ulcerations of the forearm, which looked as if punched or gouged out; they were bordered by healthy skin and resembled ulcerative and progressive lymphangitis. The pus contained a large number of bacilli. The patient had died of pulmonary tuberculosis, and in the preparations of the edges and base of the cutaneous ulcers a large number of bacilli were found in the diseased tissue.

Anatomical tubercles.—Contact with cadaveric fluids sometimes induces on the back of the fingers and hands of physicians and students prominent papillary tubercles which resemble papillomata; their surface is irregular, and they are covered by a horny or weeping epidermis. The superficial part of the derma is generally only affected; but small foci of suppuration are often more deeply placed. In sections of these growths, the epidermal layers are seen to be much thickened, and the papillæ much enlarged with infiltration of their tissue by round cells; their blood vessels are also dilated if the lesion is of long standing. The budding of the papillæ is often irregular and some of them project singly under the epidermis; between the largest of the papillæ there are grooves and depressions, and the epidermis dips down between those least hypertrophied. The derma is infiltrated, and micrococci, diplococci and chains are found in recent tubercles during the period of inflammation. Later, when they become wart-like in appearance and shrink, micro-organisms are no longer found. We have searched in vain for the bacilli of tuberculosis. We have, however, rather often seen dissecting-room attendants become phthisical who had their fingers covered with these warts. Besnier believes that anatomical tubercles belong to true tuberculosis.

Rhinoscleroma.—This tumour, which commences in the nose, the septum and the nostrils, and which spreads to the neighbouring parts, the upper lip in particular, is seen in the form of patches, ridges and nodules of the skin and mucous membrane. These growths are smooth or prominent, sharply limited, hard, elastic, brilliant, of a light red or grey colour, and painful on pressure. They are continuous with the derma, which is deeply infiltrated. They resemble cheloids and have neither hairs nor superficial glands. The neighbouring parts are tumefied, the

nose flattens and enlarges at its lower extremity, the alæ of the nose are stiff and immobile, the nostrils are obstructed, and the upper lip is in its turn indurated and invaded by the neoplasm, which may even attack the gums and the buccal mucous membrane at the same time that it is propagated by the nasal fossæ to the mucous membrane of the soft palate, pharynx and even the larynx; stenosis of the glottis may even result. This affection, which was formerly confounded with syphilis and lupus, differs from them entirely histologically and anatomically. It is also quite uninfluenced by antisyphilitic treatment. Its histological characters assign it a place apart in the classification of morbid tissues; and it is thus that we describe it. It has been observed in Vienna, Hungary and Italy, and it seems to be rather common in South America. Hebra and Kaposi [1] described it in 1870, and since then it has been the subject of a considerable number of monographs, by Mikulicz,[2] Frisch,[3] Chiari,[4] Klebs and Eppinger, Celso, Pellizari [5] &c. It has never been seen at the St. Louis Hospital for Skin Diseases. One of us [6] had the opportunity of microscopically examining two cases, one that of a young American under the care of M. Verneuil, and the other from San Salvador, a town where this disease is not rare.[7] On removing a fragment of rhinoscleroma the bistouri passes easily through the lardaceous tissue, though it appears very hard. In the sections cut from pieces taken from the two cases mentioned above and simply hardened in alcohol, we observed the following lesions. In vertical sections, the epidermic layers are seen to be well preserved, the horny and granular layers are thickened and eleidin is normally distributed. In the Malpighian layer, the cells with fibrillated protoplasm are as characteristic as possible. In parts there is a more or less considerable number of migratory cells interposed between the cells of the Malpighian layer. The papillæ are developed and vascular, and their connective tissue infiltrated with small migratory cells. The sebaceous and sweat glands show, at least at the

[1] Sydenham Society's translation.

[2] 'Ueber das Rhinosclerom' (*Langenbeck Archiv*, vol. xx. 1876).

[3] 'Aetiologie des Rhinosclerom' (*Wiener medicinische Wochenschrift*, August 12, 1882).

[4] 'Stenose des Kehlkopfs und der Luftröhre bei Rhinosclerom' (*Medicin. Jahrbücher von der K.K. Gesellschaft der Aertze*, vol. ii. Vienna, 1882).

[5] *Il Rhinoscleroma*, with 5 plates. Florence, 1883.

[6] Cornil, *Société Anatomique*, 1883, p. 319.

[7] Quevara, *Sur le Lupus Scrofuleux des Fosses Nasales*. Thèse. San Salvador, 1883.

commencement, no evident lesion. It is in the derma that are seen the characteristic lesions of the tumour. Here the blood vessels have thickened walls, infiltrated and surrounded by small round cells disseminated between the fibrils of connective tissue. A zone of these cells is seen pressed one against the other, encircling every section of the small vessels and capillaries. Connective tissue is formed between the vessels, either as a network of fibrils or as thick fasciculi. In the midst of this tissue, between the small round cells, large spheroidal cells are seen of a diameter of 20 μ or more. They contain one or more nuclei. These large cells, which are disseminated without order amidst the fibrous tissue of the derma and surrounded by small round cells, are the characteristic elements of rhinoscleroma. The protoplasm of these cells is reticulated, which fact can be clearly demonstrated in sections acted upon by osmic acid. These nuclei vary in size and are often very small, so that there may be two or three in one cell. Refractive hyaline masses are often found in the protoplasm of these cells; these masses are round or irregular in shape, and are in some cells very large; when this is the case only one may be present in a cell and fill it entirely. The nucleus is then pushed to the side as in adipose cells filled with fat. In other cells the refractive granules are smaller and found in the midst of the cellular reticulum, the trabeculæ of which surround them. What is the nature of these refractive masses? Their examination is simplified by the fact that they are sometimes found outside the cells which gave them origin. All reagents stain them; osmic acid a light yellow; picrocarminate an orange yellow; methyl violet a blue violet; and safranin a deep red. Solutions of iodine stain them yellow, but neither iodine, safranin, nor Paris violet gives the peculiar reactions of an amyloid substance. They are simply composed of a hyaline substance. This neoplasm, which is characterised by infiltration of the thickened derma with small cells, by sclerosis of the small vessels surrounded by circles of round cells, and by the presence of large cells with a reticulated protoplasm which often contains hyaline masses, belongs properly to rhinoscleroma and is not found in any other tumour. The description given above agrees entirely with that given by all other observers. It is quite a peculiar tissue. Some pathologists, Frisch and Chiari, have observed bacteria in the cells of rhinoscleroma and between the surrounding fibres of connective tissue. They have been also described by Pellizari, as small oval rods. We have searched for them, but without success,

though we used the whole series of aniline stains. We only found granules which stained with B methyl violet, and which were accumulated in the cells or isolated between the connective-tissue fibres, and which we referred to the large granular cells (*Mastzellen*) described by Ehrlich. The morbid tissue penetrates deeply, and alters the muscles of the lips, the fasciculi of which are atrophied, the cartilage and the bones. It very rarely causes losses of substance. It returns after removal.

Xanthelasma or xanthoma.—By this name are called small patches of tubercles formed of connective tissue and in which the cells have undergone fatty degeneration; they are characterised by a chamois-leather colour. On the eyelids they sometimes project and are sometimes level with the surrounding skin. Small hard, yellow tubercles are sometimes found on the skin of the face, nose, cheeks, chin, hands, prepuce or at the base of the penis. They are opaque, hard, projecting slightly and have no pathological secretion; they are grouped or isolated and are painless. This is tuberous or tubercular xanthelasma. Chambard has given an excellent pathological description of them in the 'Archives de Physiologie,' 1879. He examined both patches and tubercles of xanthelasma. Their tissue is essentially characterised by granular degeneration of the connective-tissue cells. In the tuberous and tubercular forms, there is moreover a new formation of connective tissue, and new tissue formed around the sweat glands, nerves and vessels, from which may result actual obliterating endarteritis and chronic inflammation of the nerves. Balzer first described, in xanthelasma, the round granules which appeared to him to be bacteria. In recent cases he observed that the patches and nodules contained a considerable quantity of elastic fibres which were often thickened, broken up, split and reduced into small cubes or fine granules. This disaggregated elastic substance often forms masses appended like a cauliflower to the hypertrophied elastic fibres. The disaggregation of the elastic substance also affects the fibres of the vascular walls, and even the elastic apparatus of the hairs and sweat glands. The granules of elastic substance are found in the more or less hypertrophied cells of the connective tissue, and they are the small granules which Balzer mistook at first for micro-organisms. To examine the elastic fibres and the changes they undergo, Balzer stains the sections with eosine dissolved in alcohol, and then treats them with a forty per cent. solution of potash. The elastic fibres and granules are

stained a deep red, while the other elements are but slightly stained.

Sarcoma.—Primary sarcoma of the skin is seen in the encephaloid, fasciculated and melanotic varieties. We have frequently seen small cutaneous or subcutaneos tumours removed by surgeons, about the size of a pea or almond, seated on the fingers, wrist and other parts. Some were small-celled sarcoma, others fasciculated sarcoma. In the latter there is a very large number of giant cells with numerous ovoid nuclei. Their prognosis is not serious if they are removed early when still of small size. Melanotic sarcoma of the skin is, on the contrary, of extreme gravity. It may commence on the feet or hands, on the eyelids or face. In the feet and hands it begins by small nodules about the size of a shot or pea, which are often seated on a nævus. The round, hard, prominent nodules, of a brown or bluish colour, and which may be discrete or confluent, unite into patches varying in size from that of a halfcrown piece to the palm of the hand. The fingers and nails become turgid and fusiform. The nodules soften and shrink and leave in their centre a deeply pigmented cicatrix. After lasting from one to three years, similar nodules appear on the eyelids, the face, and then on other parts of the body. They sometimes ulcerate and expose pigmented tissue gorged with blood. Cachexia and fever supervene, and the subject dies from secondary growths in all the tissues and organs. In sections of these tumours it is seen that the derma (see histological details, vol. i. p. 126), as well as the papillæ, are infiltrated with round or fusiform pigmented cells, interposed between the fibres. Cutaneous sarcoma originates at the expense of cellular granulations springing from the blood vessels. An indirect division of the cells of the endothelium may be seen, and of the circumepithelial cells of the blood vessels which are the point of departure (Babes, 'Centralblatt,' 1884). In melanotic sarcoma there may be seen, according to Babes, an atypical process of the formation of red blood corpuscles; at the beginning large cells are seen with vacuoles, containing pigmented white corpuscles, and large pigmented cells undergoing indirect division.

Myxoma. Fibroma.—Tumours of the skin composed of myxomatous and fibrous tissue are very common. Elephantiasis Arabum may be justly looked upon as a diffused and greatly extended fibrous neoplasm. This affection need not be redescribed here.

Molluscum elephantiasis is one of the large tumours of the skin which may attain a considerable size; the derma and subcutaneous cellular tissue are œdematous and greatly thickened, and let a quantity of transparent serum escape on division. In sections of the tumour it is seen to be composed of fibrous tissue, the meshes of which contain fluid and round cells; the fixed cells of the tissue are swollen and the blood vessels encircled by a zone of round cells. Smaller, sessile or pediculated tumours, which are solitary or multiple and polypoid, are called by the name of **molluscum pendulum.** They are sometimes tense and at others withered; they are elastic and soft to the touch and are covered by a thin skin; their tissue is fibrous and directly continuous with the derma and papillæ of the skin covering them. One or more arteries and veins are found in the centre of the pedicle. These tumours may be formed of mucous tissue, and they sometimes contain adipose lobules.

Cheloids.—Cheloids, which generally follow wounds, burns, cauterisations and ulcers of the skin in young and often scrofulous subjects, may be looked upon as vicious and exuberant cicatrices (*vide* vol. i. p. 115). They are characterised by projecting bands and round or radiating tuberosities, and by their hardness, their smooth surface covered by a thin epidermis without hairs or glands, and by their white colour marbled by the small blood vessels which ramify on their surface. They are continuous with the derma which moves with them. They are seated on the neck, where the contraction they occasion often causes permanent torticollis, or on the sternum, the breast, the face &c. They behave like actual tumours, in the sense that they do not undergo retrogressive changes, and they often return in situ after being removed. Besides cheloids which result from wounds, there are some which develop spontaneously in the form of prominent radiating bands, which may be simple or multiple. They are generally seated on the sternum. On examining sections of a cicatricial cheloid, a delicate normal epidermis is first seen, but beneath it there are no papillæ. This epidermis rests on a fibrous tissue composed chiefly of fasciculi parallel to the surface. If the cheloid is recently developed, it is composed of round or fusiform cells and of fine connective-tissue fibres; it does not then differ in structure from fasciculated sarcoma. Later, thick transverse or oblique bundles of fibrous tissue are found, separated by a few flat cells. In the deep parts of the tumour there are bundles intersecting the preceding at right angles. These bundles form

thick sheaths to the vessels. In spontaneous cheloids the papillæ are often hypertrophied, and between them the Malpighian layer sends processes which penetrate the derma. The fibrous tissue of the thickened derma has the same appearance as in elephantiasis.

Lipoma is rarely found in the skin; it is always primarily developed in the subcutaneous cellular tissue before extending to the base of the derma and the skin. Lipoma of the skin is often angiomatous.

Carcinoma.—Primary carcinoma is very rare in the derma. It is generally secondary to cancer of the breast. It commences by small round or flattened projections, which may be pink, livid or the same colour as the skin; they are continuous with the derma and dip into the cellulo-adipose tissue. In sections of these growths at their commencement, the papillæ and derma are seen to be thickened, and are infiltrated with small round cells. The epidermis is normal. Already at the centre of the new growth, rows of large cells with large nuclei are seen, interposed between the fasciculi of connective tissue and limiting the alveoli of carcinoma.

Chondroma. Osteoma.—Chondroma of the skin is very rare. Osteomata are sometimes developed in old persons as small sand-like granules in the thickness of the derma, or more generally in its superficial layers; sometimes they are found in the subcutaneous cellular tissue. They are probably derived from the connective tissue. Wilckens has, however, seen in some of them points of cartilaginous tissue. According to the description given by Virchow, their cortical ossified layer, which is perfectly eburnated and scarcely stratified, contains bone corpuscles arranged parallel to the surface.

Myoma.—Certain myomata, having excrescences and the form of polypi, have been described under the name of *molluscum* by Virchow, Verneuil, Malassez [1] and Besnier.[2] They are more often fibro-myomata in which smooth muscle fibres are mixed with fasciculi of fibrous tissue; the smooth muscular tissue may pre-

[1] *Etude sur le Molluscum*, with plates, 1872, and *Soc. Anat.*, 1871.
[2] *Annales de Dermatologie*, 2nd series, vol. i. 1880.

dominate, and the cutaneous tumours may become very numerous in the same subject, as in a case published by Besnier.

Neuroma.—True neuroma of the skin is very rare. Two cases have been reported by Dühring.[1] In one of them there were small hard flat tubercles, about the size of a pea, seated on the elbow and the right arm along the course of the nerves. At this spot the skin was pink or violet and scaly. Under the microscope, the tumours were seen to be formed of fibrous tissue, and bundles of non-medullated nerve fibres derived from the papillary layer of the derma. In a second case under the care of Kosinski, the tumours were seated on the thigh and had the same structure. These were non-medullated neuromata (*vide* vol. i. p. 236). Painful subcutaneous tubercles, which may be looked upon as neuromata, are more generally fibromata in which a more or less considerable number of nerve tubes are compressed by the fibrous tissue. Recklinghausen [2] has remarked that these tumours often commence in the glomeruli of the sweat glands. The structure, however, of small painful tumours varies. Thus Legros and Labbé[3] have described three cases of painful subcutaneous tumours, which contained a considerable quantity of medullated and non-medullated tubes. One of these tumours contained large tact-corpuscles. They called them papillary neuroma. Trélat and Monod have described painful subcutaneous tumours which were angiomata.[4] In one of these cases, Monod found nervous filaments in the subjacent connective tissue. Other small painful tumours contain hypertrophied sebaceous glands, sweat glands (Poncet and Chandelux[5]) and cartilaginous tissue. Some of them are nothing else than pavement-celled tubular epithelioma. In one case, Chandelux found a corpuscle of Pacini. He concludes, after the histological examination of a number of these painful tumours, that their structure varies, but that medullated or non-medullated nerve fibres may always be found at the base of the tumour, and that it is pressure on them which causes the pain. Malherbe showed at the Congress at Copenhagen (August 1884) five cases of painful tumour of the skin caused by myomata. **Plexiform**

[1] *Diseases of the Skin.* Philadelphia.
[2] *Ueber multiple Fibrome der Haut.* Berlin, 1882.
[3] *Journal de l'Anatomie*, 1870–71.
[4] *Bulletin de la Société de Chirurgie*, vol. v., 1879.
[5] 'Recherches sur les Tubercules Sous-cutanés Douloureux' (*Archives de Physiologie*, 2nd series, 1882, vol. ix. p. 639).

neuroma [1] of the skin of the neck and of the prepuce have been described by Verneuil; they are composed of a close plexus of serpentine cords, and under the microscope it is seen that the nerve tubes are surrounded by a fibrous envelope.

Angiomata of the skin are very frequently seen in the form of *nævi materni* during the early years of life (*vide* vol. i. p. 239). They very often develop later into vascular patches, telangiectasic or prominent vascular tumours, prominent angiomata, tubercular nævi, venous telangiectasiæ (Schuh) and vascular erectile tumours (Dupuytren), which are seated on the head, orbit, face, body, extremities, or genital organs. They sometimes form immense projecting tumours spread over the surface, varying in depth, and covering the whole of an upper extremity, the back or thigh; they are soft, compressible and turgescent, and may invade the muscles and compress and erode the bones. On opening them a large number of chambers are seen intercommunicating with one another, with the large vessels of the tumours and with surrounding vessels. These tumours are generally developed in the subcutaneous adipose tissue, and they then consecutively invade the derma and papillæ, the pre-existing blood vessels of which are changed into large lacunæ. But sometimes their initial seat is in the derma and the papillæ. The vascular dilatations are then often surrounded in the derma by cellulo-adipose tissue (lipomatous angioma) or by embryonic connective tissue. Thus we have seen cutaneous angiomata, about the size of a cherry, seated at the same time in the derma and the subcutaneous cellulo-adipose tissue, in which the dilated vessels were regularly surrounded by a zone of round or flat cells. When the tumour attacks the superficial layers of the skin, either primarily or by extension, the same changes are seen in the papillary network which we have described in angioma of the mucous membranes (*vide* vol. i. p. 242). Here, as in angioma of the mucous membrane, the cavities primarily filled with blood may be changed into small serous cysts. We have examined an angioma of the labium majorum in which a rather large collection of pus simulated an abscess of the vulvo-vaginal gland. Puncture of the abscess gave issue to a fœtid pus streaked with blood. The patient dying a few days afterwards from chronic tuberculosis, we had the opportunity of seeing that the posterior wall of the abscess was formed of a cavernous

[1] 'Observations pour servir à l'Histoire des Altérations Locales des Nerfs' (*Archives Gén. de Méd.*, November 1861).

angioma about two centimetres in width and one in thickness. This tumour, which projected into the cavity of the abscess, was composed of lacunæ filled with blood; they were round or polygonal, rather regular in size, separated by thin septa of fibrous tissue containing a small number of oval cells and lined by an endothelium. The tumour had all the appearance of cavernous angioma of the liver. At its periphery the connective tissue was denser, the septa thicker and the lacunæ larger and longer.

Cutaneous lymphangioma has been described in vol. i. p. 243. Kaposi has described [1] cutaneous lymphangioma under the name of multiple tuberous lymphangioma.

Cutaneous lymphadenia (fungoid mycosis of Alibert).—This skin disease has been described clinically by Alibert, Bazin, Hillairet, and Besnier, and its histological character was determined by one of us,[2] and has since been studied by Debove, Landouzy, Malassez, Demange,[3] and recently by Galliard.[4] Its duration is long and its termination generally fatal. It commences in various ways, by an eruption similar to urticaria, or by spots of congestion, at which the skin slowly and progressively thickens, with periods of rest and even of retrogression. At a given moment tumours appear on the face, scalp, neck, body and limbs in the form of hard projecting nodules, about the size of a pea or nut, white, pink, reddish or livid in colour, and around which the skin may be infiltrated. They occupy the whole thickness of the derma. These tumours may appear in crops and attain in a few days the size of a grape stone or small nut; some form larger masses and may by uniting become as large as an orange. The face, with the infiltrated skin containing many of these tumours, is sometimes deformed in the strangest manner. They frequently ulcerate, the general health is affected, at the same time there is tumefaction of the spleen and lymphadenic growths in the viscera. At the autopsy, the organs may be either healthy or diseased, and lymphadenomata of the spleen, lymph glands, Peyer's patches and tonsils may be found.

On dividing these tumours of the skin and examining them with the naked eye, the surface is seen to be grey and uniform; sometimes the vessels are congested and there is infiltration of blood.

[1] Kaposi, *loc. cit.*, vol. ii. p. 229. [2] Ranvier, in *Thèse de Gillot*, Paris, 1868.
[3] Demange, Thèse de Paris, 1874. [4] *Annales de Dermatologie*, 1882.

In vertical sections, stained with picrocarminate, the epidermic layers are seen to be normal, the papillæ generally hypertrophied,

FIG. 281.—SECTION OF SKIN AFFECTED WITH CUTANEOUS LYMPHADENIA. (Magnified 20 diameters).

l, *m*, the epidermic layers beneath which are seen the swollen papillæ. In the cellulo-adipose tissue adenoid tissue is present in which the elements of the skin, the sweat glands, *s*, and the vessels, *v*, can still be recognised. The thickness of the derma is considerable.

and the much thickened derma, as well as the papillæ, infiltrated with round cells. In preparations in which the cells have not been brushed away, they are seen to be in contact with one another

and with the bundles of connective tissue ; but if the section is very delicate or the cells have been brushed away, the fibrillar reticu-

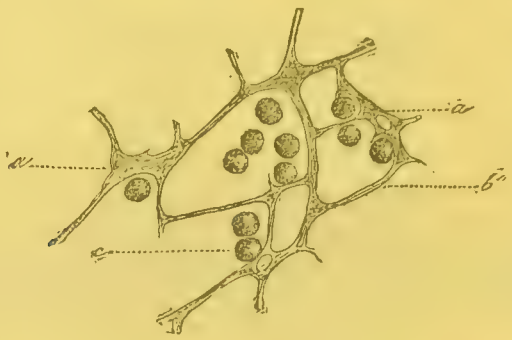

FIG. 282.—ADENOID TISSUE DEVELOPED IN THE ILIUM.

a, flat cells attached to the trabeculæ ; *b*, fibrils of new stroma ; *c*, some of the cells contained in the meshes of the reticulum. Magnified 500 diameters.

lum will be seen which contained the cells. This reticulum is absolutely identical with that of the lymph glands and of lymphadenic new growths. Its delicate fibrils are attached to the adventitious coat of the blood vessels and to the surface of the fasciculi of pre-existing connective tissue. The new growth being chiefly composed of migratory cells and the fibres of the retiform tissue occupying but a small space, it is easily understood that these tumours may contract and partly or completely shrink without leaving cicatrices when the lymph cells which they contained are absorbed. The infarctuses formed in the blood vessels are the point of departure of the ulceration which sometimes occurs.

Epithelioma.—Tumours of this kind are frequently seen at the mucous orifices, and also occasionally on the skin of the cheeks, nose, forehead, back of the hand, and dorsum of the foot. They are rare on the body. Cutaneous epithelioma belongs to the pavement-celled variety, lobulated, tubular or with cell nests. The latter is characterised by the presence of epidermic cell nests in the centre of the epithelial lobules. The cells at the periphery of each lobule resemble those of the Malpighian layer. Near the nests, the cells are full of granules of eleidin and form a layer similar to the *stratum granulosum* of normal epidermis. In some lobulated pavement-celled epitheliomata, the nests do not undergo horny change, and the cells become colloid (*vide* vol. i. p. 259); these epitheliomata do not generally contain eleidin. Tubular epithelioma of the face often takes the macroscopic

characters of partial sebaceous acne. A dirty grey desquamation and black crusts appear on the surface, and the edge of the tumour is limited by a ridge. It extends superficially, but does not generally affect the deep parts. Thus at the edge of the vulva, for example, a tumour may be seen to attain the size of the palm of the hand, and to have at its edges irregular festoons limited by ridges, while the centre is thinned in places, cicatricial, white and cured. The solid epithelial tubes of pavement cells, of which these tumours are composed, and which show no tendency to undergo horny change, are present in large numbers in the peripheral ridges, but are found only exceptionally in the centre of the tumour. There are sometimes small painful nodules in the skin formed of tubular epithelioma. Tubular epithelioma rarely affects the subcutaneous tissue, while lobulated epithelioma, on the contrary, frequently does so. The naked-eye appearances of these various species of epithelioma, their structure, mode of development at the expense of the Malpighian layer and the glands, have been already described (vol. i. p. 255, vol. ii. p. 192).

Independently of the preceding varieties of epithelioma, tumours have been described by Malherbe and Chenantais under the name of **calcified epithelioma**[1] as sometimes present in the skin and subcutaneous cellular tissue. This calcification of cutaneous tumours, which had been already pointed out by Wilckens,[2] had passed unobserved. Malherbe and Chenantais described a series of twenty tumours, varying in size from that of a haricot bean to that of a closed fist, and seated in the skin and subcutaneous connective tissue. They are hard, ossiform, superficially lobulated, and generally surrounded by a capsule of loose connective tissue, like a serous sac. They are easily enucleated and are absolutely benign. In sections of these tumours, obtained after decalcification with picric acid, it is seen that they belong to the tubular variety of epithelioma, or less frequently to the lobulated form. They have a stroma and islets or tubes filled with epithelium. The stroma is formed of dense hyaline connective tissue, or by osseous tissue with irregular lamellæ and bone cells. The cavities, limited by their fibrous or osseous tissue, are filled

[1] Malherbe and Chenantais, *Société Anatomique*, 1880. Malherbe, *Recherches sur l'Epithéliome Calcifié des Glandes Sébacées*, Paris, Doin, 1882. Chenantais, *De l'Epithéliome Calcifié des Glandes Sébacées*, Paris, Doin, 1881.

[2] *Ueber die Verknocherung und Verkalkung der Haut.* Inaug. Thesis. Göttingen, 1858.

with calcified epithelial cells. Their protoplasm is compact, solid, and grey or greenish yellow, in the midst of which the oval nucleus, which is often vesicular, is perfectly recognisable, though it is impossible to stain it with picrocarminate or other staining reagents. These polyhedrical, tesselated epithelial cells, which are thus mortified and calcified, are in contact with one another and, by their accumulation in the meshes of the stroma, form lobules or tubes, resembling in their arrangement the islets and tubes of epithelioma. In the former, even epidermic cell nests are found. At the edge of the epithelial masses, giant cells or myeloplates are sometimes found which have often undergone partial calcareous degeneration. Malherbe and Chenantais were of the opinion that these calcified epitheliomata were developed at the expense of the sebaceous glands. Ossification being complete, they remain in the connective tissue as foreign bodies, and never recur if removed.

We connect here with epithelioma a disease of the skin which terminates in epithelioma, namely **xeroderma pigmentosum**, which Vidal[1] proposes to call the *dermatosis* of *Kaposi*. It is a rare and curious disease which commences during the first two years of life by an eruption of red spots on the uncovered parts of the body; the skin becomes dry and thin, and has a cicatricial shining appearance and is veined by dilated vessels. In a few years' time, papillary, fungoid and ulcerating epithelioma developes. Most of the subjects die at from ten to twenty years of age from the ravages of the epithelioma, or from marasmus caused by suppuration. This disease is observed in children of the same sex in the same family. The pathology of these lesions has been described by Kaposi[2] (1870), Neisser[3] and Vidal and Leloir. Under the thinned skin the papillæ have in places entirely disappeared, while they are hypertrophied in others. The horny layer of the epidermis is thickened, and the stratum lucidum and stratum granulosum are absent. The deep parts of the Malpighian layer are pigmented like the skin of the negro. The derma is atrophied and contains pigment granules. The vessels of the papillæ are sometimes atrophied, sometimes dilated and atelectasic in places. The elastic fibres are very numerous in the atrophied parts of the derma.

[1] Vidal and Leloir, 'Anatomie Pathologique du Xeroderma pigmentosum' (*Soc. de Biol.*, July 1883). Vidal, 'De la Dermatose de Kaposi' (*Annales de Dermatologie et de Syphiliographie*, 1883, p. 621).

[2] Kaposi, *loc. cit.*, vol. i. p. 224; vol. ii. p. 186.

[3] *Vierteljahrs. f. Dermatologie und Syphilis*, 1875, vol. ii. p. 114, and *All. med. Zeitung*, No. 35, 1874.

The smooth muscle fibres and the glands also show a tendency to atrophy. This form of epithelioma sometimes belongs to the lobulated variety with epidermic nests, and sometimes to the tubular variety.

Sebaceous cysts.—We have already described the structure of small cysts of indurated acne. They are sebaceous cysts in miniature and are developed from the pilo-sebaceous follicles. In vol. i. p. 293 the structure of wens and sebaceous cysts is fully described.

III. Parasitic Affections of the Skin and Cutaneous Parasites.

The parasites of the skin in man are of two kinds, animal and vegetable or fungoid. They will be described in order.

A. The animal parasites of the skin in man.—The actual parasites of the skin are those which originate, grow, live and die on the surface of the skin or in its substance. The principal of them are the acarus of scabies and the acarus of the sebaceous follicles. We do not consider here fleas and lice, which are only found temporarily on the skin.

a. **The acarus of scabies** (*Sarcoptes hominis*) causes an eczematous eruption on the skin, and hollows characteristic tunnels in the epidermis. The female acarus, which is that most frequently met with, is visible to the naked eye, for its long diameter measures 0·33 mm. Its integument appears under the microscope to be striated by numerous parallel lines, and the abdomen is covered by conical projections each of which ends in a long fine hair. On each side of the head are two pairs of legs furnished with suckers; posteriorly there are two more pairs of legs without suckers and which end in long hairs. The legs spring from the ventral surface. The head consists of two sharp mandibles in the form of a pair of scissors, behind which are two palpi ending in hairs. Behind the head is the alimentary canal, opening posteriorly. The ovary is distinct and generally swollen by eggs. Respiratory organs seem absent or rudimentary; the acarus can live for a long time deprived of air either in the substance of the skin or immersed in naphtha oil (Burchard). According to Bourguignon it only breathes by swallowing air, which spreads from the œsophagus through a mass of sinuses. The male acarus is smaller and ten times rarer than the female. It has an appendage or penis between

the two posterior pairs of legs. The fecundated female acarus scabiei being deposited on the skin, uses its mandibles to eat through the superficial layers of the epidermis, and reaches the

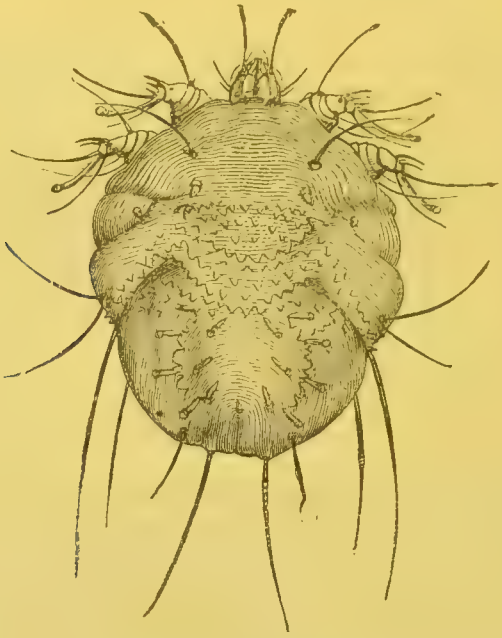

FIG. 283.—FEMALE ACARUS SCABIEI VULGARIS (DORSAL SURFACE).

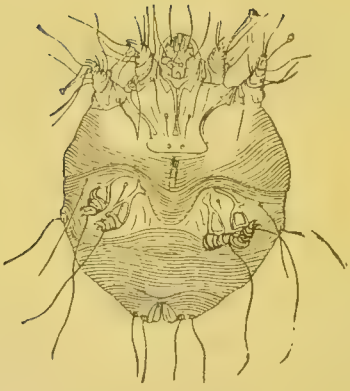

FIG. 284.—MALE ACARUS SCABIEI VULGARIS (VENTRAL SURFACE).

FIG. 285.—ACARUS SCABIEI VULGARIS (DORSAL SURFACE).

Malpighian layer, leaving an oblique sinus behind it. From place to place it deposits an egg, so that it cannot retrace its steps, the egg blocking the passage. It lays in this way from forty to

fifty eggs, after which it dies. A certain number of these eggs are destroyed, for generally but ten or fifteen are found in each sinus. A fortnight after the eggs are laid the young parasites, having passed through the first phases of development, break through the wall of the epidermic sinus and appear on the surface of the skin. They have then only six legs, two pairs anterior and one pair posterior, and they are asexual. They attain their final form after three successive changes.

Vesicles and pustules are formed in the Malpighian layer in consequence of irritation of the papillæ caused by the presence of the acarus at the end of the sinus. Migratory cells collect below and around the end of the sinus and a vesico-pustule is formed. This cutaneous inflammation, increased by scratching and kept up by the presence of the parasites, and successive crops of them, causes the polymorphous eruption so characteristic of scabies.

b. **The Acarus folliculorum** (*Entozoon, Steatozoon, Demodex folliculorum*).—This parasite, discovered in 1842 by G. Simon, is

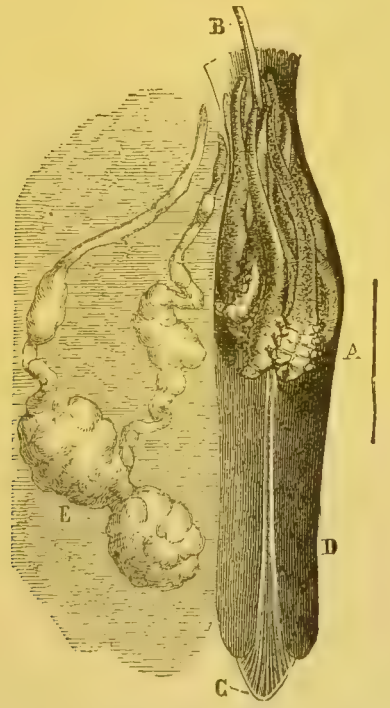

FIG. 286.—GROUP OF DEMODEX FOLLICULORUM.

A, demodex; B, hair; C, root of the hair; D, follicle; E, sebaceous gland.

found in normal or cystic hair follicles. Its body is long and measures nearly 0·30 mm. On each side of its head is a pad formed of three joints, and it has a proboscis or swelling sur-

mounted by a peculiar trifurcated organ the points of which end in fine hairs. The head blends with the thorax, which together forms a quarter of the whole length of the parasite. To the thorax are attached four pairs of very short legs, composed of three joints, the last ending in three small hook-like claws. The posterior or abdominal part of the body is elongated and contains, according to some observers, an intestinal tract and hepatic gland. According to Neumann, there is another variety of demodex which has only three pairs of legs. The acarus folliculorum exists in comedones and acneic glands. Its presence in the gland does not cause any cutaneous local lesion. To examine it, it is only necessary to squeeze out a few comedones from the skin of the nose or face, to tease out the contents in glycerine, and the parasite can be studied under a low power. They are also frequently found in the sebaceous glands of the external meatus, or in the skin of the concha of the ear which has become acneic.

B. **Fungoid parasites of the skin in man.**—If a section of unstained normal skin be treated carefully with ether, and mounted in Canada balsam or Damar resin, a certain number of fungus spores will be found in the horny layers at the spots where the epidermis is thick. These spores vary in size and shape. They do not correspond to any cutaneous disease, and the probably multiple botanical species to which they belong have not been yet exactly defined. If inflammation occurs in the skin, and particularly when it has been covered with poultices, these microscopic vegetable parasites increase in number. But actual parasites of the skin, that is to say those which accompany and cause the cutaneous affections clinically known under the name of tinea, are never found, like the preceding, in the epidermis of normal skin, but they produce characteristic lesions in diseased skin. It is only the latter we propose to describe.

a. The *fungoid parasite of favus* (*Achorion Schönleinii; oïdeum*) was discovered in 1839 by Schönlein in the crusts of the cups of favus, afterwards described by Gruby and Wedl, and inoculated successfully for the first time by Remak in the skin of the arm. We will consider consecutively the characteristics of the parasite and its mode of growth in the skin and hair. If a minute portion of the yellow substance of the cups be removed with a lancet, and dissociated in ammonia, it becomes disaggregated in a few minutes and the isolated parasite can be observed. If iodine dissolved in an aqueous solution of iodide of

potassium be introduced under the cover glass after removing the ammonia, the parasite takes a reddish brown stain and details

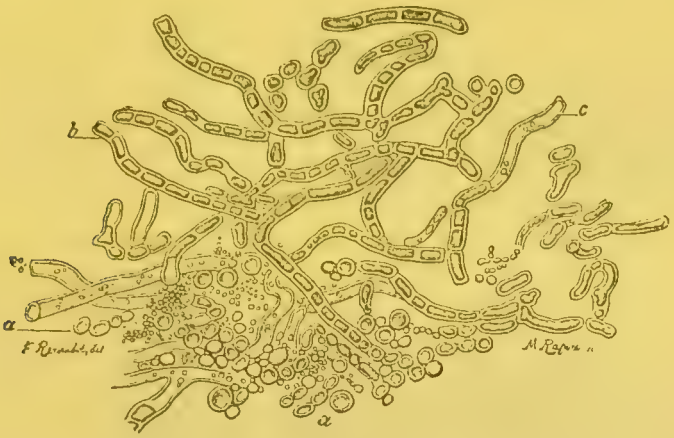

FIG. 287.—ACHORION SCHÖNLEINII PREPARED BY DISSOCIATION AFTER THE ACTION OF A 40 PER CENT. SOLUTION OF POTASH.

a, spores; *b*, chains of spores ending in filaments of the thallus, which are then composed of short joints; *c*, actual filaments of the thallus composed of long and clear joints. Magnified 400 diameters.

can be observed. It is seen to be composed of round spores, isolated or united so as to form chains. These chains of spores generally end in filaments of mycelium or a thallus. At their free extremity they are round; they then become slightly elongated, so that the filaments are composed of a number of short joints. The actual filaments of mycelium are finally composed of long, clear, punctated and solidly united joints; they ramify by dichotomous division. The spores at their termination fall easily, on the contrary, and are looked upon as the germinal portion.

In a transverse section of skin passing through a cup, the following details are observed: at the projection formed by the cup, the epidermic layers are filled with spores, which are found between the horny cells. Micrococci, bacteria and drops of fat are constantly met with beside these spores. It is the accumulation of all these foreign elements which causes the projecting ridge of the cup. In the depressed centre one or more diseased hairs are generally found. This is the spot where the favus has commenced, and where cure has a tendency to show itself. The disease, like other forms of tinea, undergoes cure in the centre and is propagated at the circumference, extending in a circle. In cups of a certain diameter, the extension of the parasite is not limited by the epidermic layers. The mycelium penetrates deeply into the derma and ramifies there. In such circumstances the

tissues are not pushed back, but they are actually attacked (Malassez); in sections, in fact, the tubes of mycelium springing from the bottom of the cup may be seen to insinuate themselves in a straight line into the connective tissue and between its fasciculi like tap roots. The derma offers little resistance to this invasion, but continual weeping or even suppuration takes place near the cups. In every case in which the connective tissue is invaded by the thallus of Achorion Schönleinii it is slowly absorbed, and it is probably owing to this absorption that the cicatrices beneath the cups are often deep after the tinea is cured. The hairs in the centre or around the cups are affected by the parasite;

FIG. 288.—TRANSVERSE SECTION OF THE SKIN PASSING THROUGH A CUP OF FAVUS.

a, epidermis; *b*, superficial layer of the irritated derma; *c*, deep layer of the derma; *d*, *d'*, filaments of mycelium dipping into the derma and ending in chains of spores.

it grows principally in the sheath of the hair, and the filaments are chiefly formed of chains of spores; but mycelium is met with in the coats of the hair bulb and near the root. After the hair is shed, the follicle suppurates and a small pustule is formed at its orifice. The cups of favus are sometimes developed elsewhere than in the scalp, in the skin of the face, hands, arms &c. Lailler has shown us beautiful specimens of favus of the nails, in which

the filaments of mycelium were in the substance of the nail. Instead of having its characteristic appearance of isolated or nummular cups with sulphur-yellow crusts, favus is sometimes seen in the form of thick grey and imbricated crusts (squamous favus).

b. **The fungoid parasite of Tinea tonsurans** (*Trichophyton tonsurans; oïdeum*).—This parasite causes *ringworm* in the scalp; *parasitic sycosis* in the skin of the face where there is no hair; and *herpes circinatus* in the glabrous parts of the skin. An identical parasite produces different conditions in the skin, owing to differences of structure in various parts. Tricophyton causes circinate herpes on the hairless skin of a child, and if a patch of ringworm be scratched with the back of the hand, parasitic herpes may be produced by transplantation of the parasite, which may be transmitted to a cat, dog or even horse, which then becomes an agent of contagion. **Tinea tonsurans** or **ringworm** is characterised by nummular patches at which the hairs are broken and the surface looks as if shaven. For the distance of nearly a millimeter from their base of implantation they are covered by white or grey epidermic squamæ. On trying to pull out one of these hairs with a pair of tweezers, it breaks across, and on examining the line of fracture with a magnifying glass or under a low power, filaments like brushwood are observed. **Erythema** and **circinate herpes** are seen in the form of small spots or vesicles arranged in circles; they are covered by a superficial furfuraceous desquamation; the centre undergoes cure while the disease extends at the periphery and progressively invades the healthy skin. **Sycosis**, which is seen on the chin and cheeks in men, particularly where there is a beard, is characterised by pustules varying in size and similar to those of acne, and by deep inflammation of the skin. A hair follicle is always at the centre of the pustules, and a hair which is easily eradicated. The anatomical lesion of the skin produced by sycosis is the same as that already described in folliculitis and perifolliculitis (*vide* p. 711). The sole difference is in the invasion of the hair and follicles by the fungi of trichophyton. These three last diseases constitute trichophytia.

Trichophyton tonsurans was discovered by Malmsten in 1843. It is a fungus formed of round spores measuring at least 5 μ in diameter. These spores are isolated or grouped between the lamellæ of epidermis. A certain number of them are cylindrical, placed end to end. Neumann has demonstrated the presence of

a ramifying mycelium. The fungus is generally shown by treating flakes of epidermis detached from the surface of a patch of herpes

FIG. 289.—TRICHOPHYTON TONSURANS, DISSOCIATED FROM EPIDERMIC FLAKES DERIVED FROM A PATCH OF HERPES CIRCINATUS.

a, a, spores; *b, b*, filaments of mycelium composed of short joints; *c, c*, filaments of mycelium composed of long and transparent joints; *d*, epidermic cells. Magnified 400 diameters.

circinatus by a forty per cent. solution of potash, or by ammonia. The growth of the parasite in the hairs differs little from that of favus. The spores are generally abundant near the root of the hair, and increase from below upwards between the

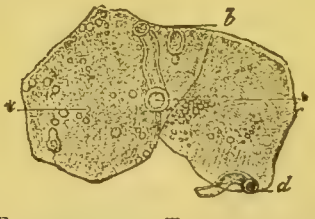

FIG. 290.—SPORES AND FILAMENTS OF TRICHOPHYTON IN CONNECTION WITH CELLS OF THE HORNY LAYER OF THE EPIDERMIS IN HERPES CIRCINATUS.

longitudinal fibres of its sheath. The hair in which the cells are dissociated in this manner, becomes friable and breaks. Around it in the internal epidermic sheath, the spores accumulate, and there is an abundant production of epidermic lamellæ separated from one another by rows of spores. This ensheathing of the hairs

has a certain diagnostic importance, but it is also observed in affections other than parasitic, in eczema of the beard and scalp. In doubtful cases, the diagnosis can only be determined by histological examination. Some dermatologists, Hebra among others, look upon *Trichophyton tonsurans* simply as a variety of *Achorion Schönleinii*. But Köbner has, in cultivating the parasite, seen it reproduce itself indefinitely with its specific characters. On the other hand, Hallier looks upon it as identical with *Penicillum*, and Neumann is of the same opinion.

c. **The fungoid parasite of Tinea versicolor** (*Pityriasis versicolor*). **Microsporon furfur** is generally found only in the epidermic layers. It causes yellow, brown, or dirty superficial patches; they vary in size and are found in the skin of the back, chest, abdomen, limbs and face; they are generally slightly elevated, and epidermic flakes are detached by scratching. The sowing and growth of the *Microsporon furfur*, and the grouping of its elements, are quite characteristic. The spores are round and form from place to place round groups in the horny layer of the epidermis. From the periphery of these groups spring ramifying filaments of mycelium, the joints of which are extremely long (fig. 291). This mucedinea develops extremely slowly; it is easily cultivated, for it will germinate even in neutral glycerine (Neumann). The spores divide by scission and some of them by elongating constitute the filaments of mycelium; others originate new spores by endogenous generation. This fungus was discovered by Eichstedt in 1846; in 1864 Köbner succeeded in inoculating it in the skin of a man. The contagiousness of *Tinea versicolor* had been previously proved by the physicians of the Hospital of St. Louis.

d. **Alopecia areata** (*Area Celsi*).—*Alopecia areata* is characterised by decolourised patches of the scalp at which the hairs are replaced by down. These patches, which are quite circular, show a slight desquamation at their circumference; the derma appears thin and atrophied; the downy hairs are shed in their turn, and the patches become as smooth as ivory. In 1843 Gruby ('Compt. Rend. de l'Acad. des Sc.,' vol. xvii. p. 301) described a parasite in alopecia called the *Microsporon Audouini*, and Bazin classified it among parasitic affections; but many dermatologists deny the mycosic nature of alopecia (Hebra, E. Wilson, Neumann, Bock &c.) Later, Malassez ('Arch. de Phys.,' 1874) and after him Courrèges ('Thèse de Paris,' 1874) gave a new description of the parasites observed in this affection. According

to Malassez the parasite is found in the interior and on the surface of the epidermic cells and in their interstices. It does not penetrate the hair follicle, and is only accidentally met with on the hairs.

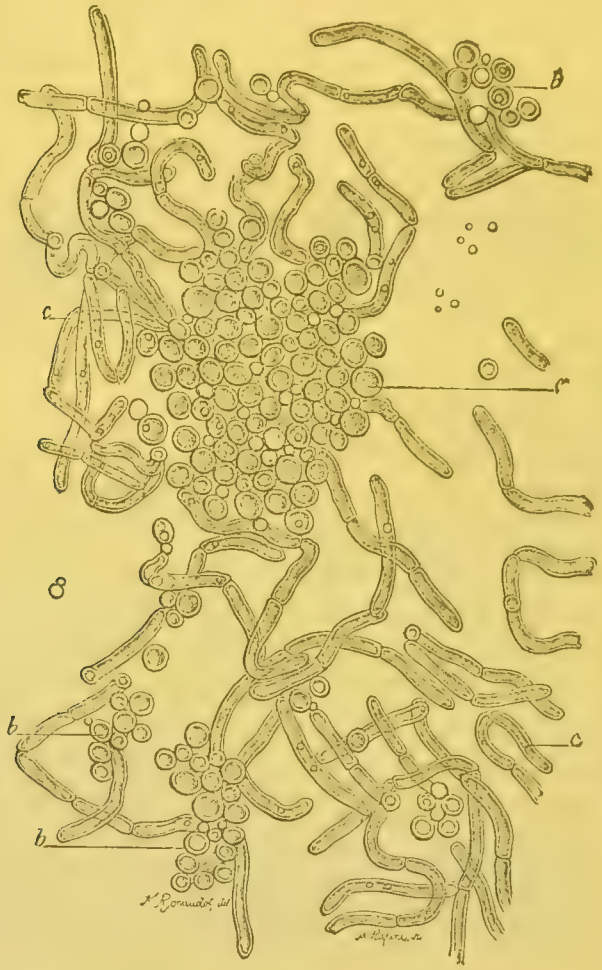

FIG. 291.—THE MICROSPORON FURFUR.

a, principal group of spores forming a round mass; *b*, *b*, *b*, small groups of spores; *c*, *c*, filaments of mycelium, formed of long, transparent and convoluted joints. Magnified 400 diameters.

In the latter case, it is fixed to pellicles probably detached from the cutaneous epidermis, and adhering by chance to the hair. The parasite is formed solely of spherical spores without any trace of mycelium. The largest spores measure from 4 μ to 5 μ in diameter and have a double contour. There are also smaller spores, measuring 2 μ in diameter or less. The parasite seems to multiply by budding. Gruby affirms that the *Microsporon Audouini* develops primarily on the surface of the hairs, at a distance of from 1 to 2 mm. from the skin, and that it sends ramifying fila-

ments into the tissue of the hairs. Malassez has not been able to verify any of these assertions. It seems certain that the para-

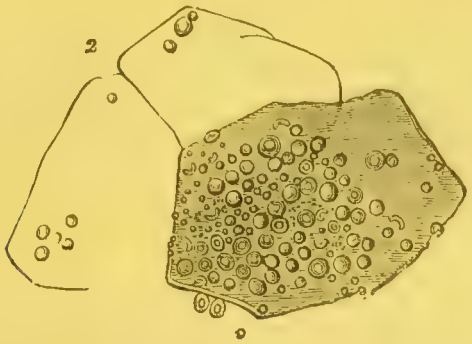

Fig. 292.—Epidermic Cells filled with Spores and taken from a Patch of Achromatic Alopecia. Magnified 500 diameters.

site described by Malassez is nothing else than that which is met with accidentally in varying quantity on the surface of the skin, and that it has no relation to alopecia. Many dermatologists place this affection among tropho-neuroses, and look upon it as

Fig. 293.—Hair from a case of Alopecia of Rapid Growth. It is surrounded by Epidermic Cells filled with Spores. Magnified 250 diameters.

a cutaneous achromatic atrophy. We should add that some observers have recently looked for the parasite of alopecia. Thus Büchner and recently Von Sehlen ('Fortschritte der Med.,' Dec. 1, 1883) have described small round micrococci measuring 1 μ in diameter, seated in the sheath, root and cuticle of the hair as

well as in the surrounding epidermis. But there is still nevertheless much doubt as to the parasitic character of *Alopecia areata*.

FIG. 294.—ISOLATED SPORES TAKEN FROM PATCHES OF ALOPECIA.

1, 2, 3, 4, large spores viewed from different points of sight; 5, budding spores; 6, 7, 8, large empty spores; 9, 10, 11, small spores; 12, minute spores. Magnified 1,000 diameters.

e. **The fungoid parasite of erythrasma** (*Microsporon minutissimum*).—Erythrasma is a more or less marked form of erythema situated in the inguino-crural region. It may become general. It causes slight thickening of the epidermis and small squamæ. It is caused by the presence in the horny layer of the epidermis of a fungus, the elements of which are extremely small, the *Microsporon minutissimum*. This parasite, described by Burchardt, Baerensprung and Köbner, has been often found in erythrasma by Balzer.[1] The spores are very small and round or slightly elliptical. The tubes are irregular, nodular, serpentine and curved in the form of S and U, and frequently ramify. They curl over the epidermic cells with which they are in contact. They resemble in size the filaments of *Leptothrix buccalis*, and like them they are formed of joints placed end to end and which are generally very short. In spite of their delicacy, the tubes of *Microsporon minutissimum* are regularly arranged like those of larger

[1] *Annales de Dermatologie et Syphiliographie*, December 25, 1883.

cutaneous fungi, *Trichophyton* and *Microsporon furfur* for example.

f. **The parasite of Pityriasis simplex.**—Malassez ('Arch. de Phys.,' 1874) has carefully described the parasites found in the epidermic scales of the scalp. They are seated in the horny layer of the epidermis between the cells. They penetrate into the hair follicles, but only near the point of emergence of the hair and not deeply, yet below the opening of the sebaceous gland. The growth is formed solely of spores, which are generally long and budding; the largest measure from 4 μ to 5 μ long and from 2 μ to 2·5 μ wide. The smallest are only 2 μ long. From the researches of

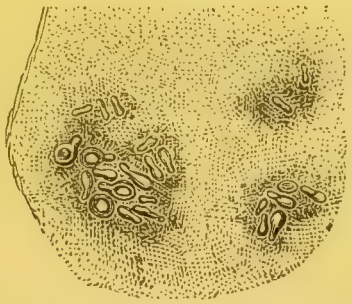

FIG. 295.—EPIDERMIC CELL OF THE SCALP AFFECTED WITH PITYRIASIS AND COVERED WITH SPORES

Malassez it appears that this parasite plays an important part in the production of pityriasic flakes. In this disease of the skin alopecia is produced by two causes: 1st, the mechanical action of the fungus, which dissociates the epithelial cells; 2nd, the

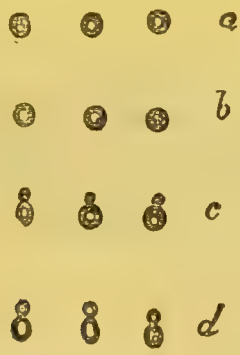

FIG. 296.—ISOLATED SPORES COLLECTED FROM THE FLAKES OF PITYRIASIS CAPITIS SIMPLEX.

a, round full spores; *b*, the same empty; *c*, budding, full spores; *d*, the same empty. Magnified 1,000 diameters.

part the parasite plays as a foreign body, which irritates the epidermis and leads to superactivity in the evolution of cells, dilatation

of the nucleolus, atrophy of the nucleus, which is pushed aside by this dilatation, and consequently incessant desquamation of the surface of the skin. Alopecia, which is the usual consequence of *Pityriasis simplex*, would also result, Malassez thinks, from obstruction of the part of the hair follicle near the orifice of the sebaceous glands. This obstruction would impede the regular growth of the hair; irritation of the follicle would follow, particularly of the parts near the bulb; here the wall of the follicle would undergo ascending hypertrophy, leading first to diminution of the calibre of the hair, and finally to obliteration of the follicle, which would be changed into a fibrous cord.

The methods by which the fungoid parasites of the skin are examined are very simple. The scales or hairs are removed and carefully washed in ether or absolute alcohol. At the end of one or two days, all the fat is dissolved and granules can no longer be mistaken for spores. The specimens should then be examined in glycerine or formic glycerine. Acetic acid, a forty per cent. solution of potash or ammonia, are useful to clarify the epidermic tissues, and to make the parasitic organism more evident. The spores and filaments can be as easily stained with hæmatoxylin as the nuclei of

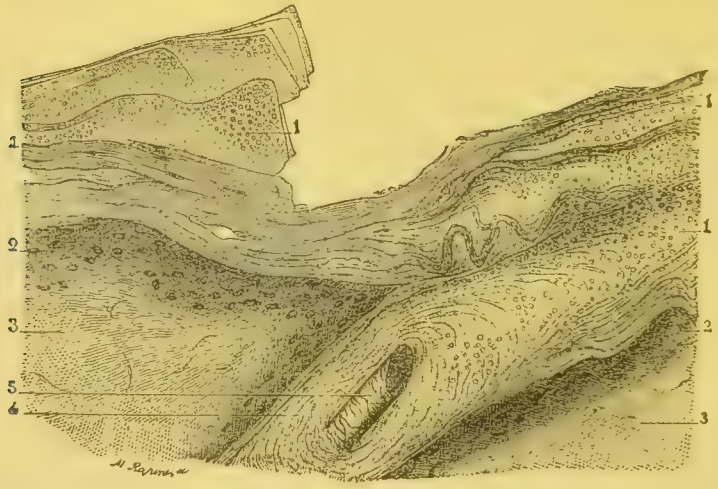

FIG. 297.—VERTICAL SECTION OF THE SKIN AFFECTED WITH SIMPLE PITYRIASIS.

1, horny layer of the epidermis dissociated into lamels infiltrated with spores; 2, Malpighian layer; 3, derma; 4, upper part of a hair follicle dilated by pityriasic squamæ; 5, atrophied hair. Magnified 250 diameters.

cells. Balzer uses eosine dissolved in alcohol, after treating the hairs and flakes with ether and absolute alcohol. The parts stained by the eosine are examined in a forty per cent. solution of potash. Von Sehlen has used with much success the following double staining for thin sections of the skin and hair. After removing the fat

from the sections by ether, they are placed in absolute alcohol and then in a weak solution of Ehrlich's fuchsin for twenty-four hours; they are washed with alcohol, then with weak hydrochloric acid, and finally with distilled water. The hairs and the epidermic scales only are coloured a deep red. The sections are then placed in a solution of methyl blue, or gentian violet, dehydrated with absolute alcohol, clarified with oil of cloves, and mounted in Canada balsam. The spores are stained blue and violet, while the hairs and epidermic scales are red.

BIBLIOGRAPHICAL REFERENCES TO TREATISES ON LESIONS OF THE ORGANS.

RESPIRATORY ORGANS. NASAL FOSSÆ.—SCHULTZE, *Unters. über den Bau der Nasenschleimhaut*, 1862. KÖLLIKER, *Human Histology*. STRICKER, *Handbuch der Lehre von den Geweben des Menschen und der Thiere*, 1868; *Larynx and Trachea*, by E. VERSON; *Lungen*, by Franz Eilhard SCHULZE. GIRALDÈS, *Mémoires de la Société de chirurgie*, 1853. MURON, *Structure des polypes naso-pharyngiens* (*Société de biologie*, 1870, p. 223). MEYER (of Copenhagen), *Ueber adenoïde Vegetationen in der Nasenrachenhöhle* (*Archiv für Ohrenheilkunde*). PEISSON, *Sur les tumeurs adénoïdes du pharynx nasal*, Thèse de Paris, 1883. CORNIL, *Note sur les tumeurs adénoïdes du pharynx nasal* (*Société anat.*, 1883, and *Journal de l'anatomie* of Robin, 1883); *Recherches histologiques sur l'action toxique de la cantharidine* (*Journal de l'anatomie et de la physiologie*, 1880, with 2 lith. plates).

LARYNX.—C. H. EHRMANN, *Histoire des polypes du larynx*, Strasburg, 1844 and 1850. TROUSSEAU and BELLOC, *De la phthisie laryngée* (*Mémoires de l'Académie royale de méd.*, vol. vi. 1837). BRETONNEAU, *Des inflammations spéciales du tissu muqueux*, Paris, 1826. COYNE, *Thèse de doctorat*, 1874. EBERTH, in RINDFLEISCH, *Treatise on Pathological Histology*. FOERSTER, *loc. cit.* LOUIS, *Recherches anatomiques, pathologiques et thérapeutiques sur la fièvre typhoïde*, Paris, 1840, 2 vols. in-8. MAURIN, *Des accidents laryngés de la fièvre typhoïde*, Thèse de Paris, 1865. KRISHABER and PETER, article LARYNX in the *Dictionnaire encyclopédique des sciences médicales*. CAUSIT, *Etudes sur les polypes du larynx chez les enfants et en particulier sur les polypes congénitaux*, Thèse de Paris, 1867. CH. FAUVEL, *Traité pratique des maladies du larynx*, Paris, 1866, in-8. KLEBS and H. EPPINGER, *Handbuch der patholog. Anatomie*, part 5, *Larynx und Trachea*, Berlin, 1880. ERNST ZIEGLER, *Lehrbuch der allgemeinen und speciellen pathologischen Anatomie*, 3rd edit. 1884, Jena, in-8, vol. ii. p. 440. M. MACKENZIE, *Essay on Growths in the Larynx*, London, 1876. KRISHABER, *Leçons sur le cancer du larynx* (*Annales des maladies de l'oreille et du larynx*, vol. v. July 1879). ZIEMSSEN, in *Ziemssen's Handb. der spec. Patholog.*, vol. iv. TURCK, *Klinik der Krankheiten des Kehlkopfes*.

BRONCHI AND LUNGS.—LAENNEC, *Traité d'auscultation médiate*, 2nd edit. 1826. CRUVEILHIER, *Atlas d'anatomie pathologique*, part 20. ANDRAL, *Clinique médicale*, 4th edit., and *Traité d'anat. path.*, 1829. BARTH, *Recherches sur la dilatation des bronches*, Paris, 1856. GOMBAULT, *Etudes sur l'anatomie pathologique de la dilatation des bronches*, Paris, 1858. RILLIET and BARTHEZ, *Traité des maladies des enfants*, 1843. FAUVEL, *Recherches sur la bronchite capillaire*, Paris, 1840. ROSSIGNOL, *Recherches anatomiques, etc., sur l'emphysème pulmonaire*, with plates, Brussels, 1849. BOUILLAUD, *Dictionnaire en 15 vol.*,

vol. vii. p. 121. SCHRADER, *Deutsche Klinik*, No. 18, 1854. LEROY, *Des concrétions bronchiques*, Thèse de doctorat, Paris, 1868. DUGUET, *De l'apoplexie pulmonaire*, Thèse d'agrégation, 1872. GAIRDNER, *Monthly Journ. of Med. Sc.*, vol. xiii. 1851 ; *On the Patholog. Anat. of Bronchitis*, Edinburgh, 1850. CORRIGAN, *Dublin Journal*, 1838, No. 38, and *Archives génér. de méd.*, 1838, vol. ii. 1854 ; *Dublin Hospital Gazette*, No. 24, 1857. CORNIL, *Leçons sur l'anat. patholog. et sur les signes fournis par l'auscultation dans les maladies du poumon*, in-8, 1874, and *Progrès méd.*, same year. SCHROEDER VAN DER KOLK, *Observations on Pathological, Anatomy* 1826. RAYMOND, *Thèse de Paris*, 1842. CHOMEL, *Nosographie de la pneumonie chronique, fondée sur huit faits*, 1845. CHARCOT, *De la pneumonie chronique*, Thèse d'agrégation, 1860. TRAUBE, *Deutsche Klinik*, 48, 49, 1849. GAVARRET, *De l'emphysème pulm.*, Thèse de Paris, 1843. VILLEMIN, *Recherches sur la vésicule pulmonaire et l'emphysème* (*Archives génér. de méd.*, 1886, vol. ii.) MAURICE RAYNAUD, *Mémoire sur l'angioleucite généralisée des poumons* (*Société médicale des hôpitaux*, March 13, 1874). FERRÉOL and THAON, *Société médicale des hôpitaux*, 1874. TROISIER, *Recherches sur les lymphangites pulmonaires*, Thèse de doctorat, 1874. CORNIL, *Note sur les lymphangites pulmonaires* (*Société médicale des hôpitaux*, May 22, 1874). LEGENDRE and BAILLY, *Nouvelles recherches sur quelques maladies du poumon* (*Archives génér. de méd.*, 4th series, vol. iv. 1844). LEGENDRE, *Recherches anatomo-path. sur quelques maladies des enfants*, Paris, 1846, in-8. RILLIET and BARTHEZ, *Mém. sur quelques parties de l'histoire de la bronchite et de la broncho-pneumonie chez les enfants* (*Archives génér. de méd.*, 4th series, vol. xxvii. 1851). ISAMBERT and ROBIN, *Soc. de biol.*, 1855–1866. GRISOLLE, *Traité de la pneumonie*, 1841 ; 2nd edit. 1864. VULPIAN, *Des pneumonies secondaires*, Thèse d'agrégation. SKODA, *Ueber chronische Pneumonie* (Vienna, 1868), Paris, 1860. CHARCOT, *Leçons cliniques sur les maladies des vieillards*, 1867, and 2nd edit. 1874 ; *Des pneumonokonioses*, by Gombault (*Revue mensuelle*, 1878) ; *Des pneumonies générales* (*cirrhoses du poumon*), by Balzer (*Revue mensuelle*, 1878). COLBERG, *Beiträge zur normalen und pathologischen Histologie der Lungen* (*Deutsches Archiv f. klinisch. Medicin*, Leipzig, 1867, vol. ii. p. 453). DAMASCHINO, *Des différentes formes de la pneumonie des enfants*, Thèse de doct., Paris, 1867. BALZER, *De la broncho-pneumonie*, Thèse de Paris, 1878. WYWODZOFF, *Die Lymphwege der Lungen* (*Oesterr. medic. Jahrbücher*, 1866, in-8 and plates). DYBKOWSKY, *Aufsaugung und Absonderung der Pleuravand* (*Arbeiten aus der physiolog. Anstalt zu Leipzig*, 1867, in-8, p. 40). GRANCHER, *Etude sur les lymphatiques du poumon* (*Société de biologie*, 1877). COHNHEIM, *Vorlesungen über allgemeine Pathologie*, vol. ii., *Luftwege*, p. 158, Berlin, 1880). GRANCHER, *De la pneumonie massive* (*Gazette médicale de Paris*, 1878). KLEIN, *The Anatomy of the Lymph. Syst.*, London, 1875. BUHL, *Lungenentzündung, Tuberculose und Schwindsucht*, 1872, and *Arbeiten a. d. path. Institut zu München*, 1878. JÜRGENSEN, *Die croupöse Pneumonie*, Tübingen, 1883. FRIEDLAENDER, *Die Mikrokokken der Pneumonie* (*Fortschritte der Medicin*, 1883).

TUBERCULOSIS.—BAYLE, *Recherches sur la phthisie*, 1810. LAENNEC, *loc. cit.* LOUIS, *Recherches sur la phthisie pulmonaire*, 1st edit. 1825 ; 2nd edit. 1843. KUSS, *Gazette médicale de Strasbourg*, 1847 and 1855. VIRCHOW, *Wiener med. Wochenschrift*, 1856, *Cellulary Pathologie.* MARTEL, *Thèse de Paris*, 1863. VILLEMIN, *Du tubercule* (*Gazette médicale de Strasbourg*, 1864) ; *Etudes sur la tuberculose*, Paris, 1868 ; *De la virulence et de la spécificité de la tuberculose* (*Bulletin de l'Académie de médecine* (vol. xxx. p. 76) ; *Discussion sur la tuberculose à l'Académie de méd.* (*Bulletin de l'Académie*, 1867 and 1868). EMPIS, *De la granulie*, Paris, 1865. HÉRARD and CORNIL, *De la phthisie pulmonaire*, Paris, 1867. LEBERT, *Physiologie pathologique*, 1856 ; *De l'anatomie pathologique, et de la pathogénie de la pneumonie disséminée et chronique et des tubercules* (*Gazette méd. de Paris*, 1867, p. 350). LÉPINE, *De la pneumonie caséeuse*, Thèse d'agré-

gation, 1872. THAON, *Recherches sur l'anatomie pathologique de la tuberculose*, 1873. GRANCHER, *De l'unité de la phthisie*, Thèse, 1873. NIEMEYER, *Clinical Lessons on Pulmonary Phthisis*. SCHUPPEL, *Observations on Tuberculosis of the Lymphatic Ganglions*, Tübingen, 1871. SANDERSON, *Report on the Inoculability and Development of Tubercle*. See also *Discussion on the Anatomical Relations of Pulmonary Phthisis with Tubercle of the Lung* (*Transact. Path. Society*, vol. xxiv. plates xii. xiii. xiv. and xv.) CARL FRIEDLAENDER, *Bemerkungen über Riesenzellen und ihr Verhältniss* (*Berliner Wochenschrift*, 1874, No. 37). MINTEGUYAGA, *Essai sur la séméiologie des crachats considérés surtout au point de vue microscopique*, Thèse de Paris, 1868. RASMUSSEN, *Continued Observations on Hæmoptysis*, translated into English by W. D. Moore, Edinburgh, 1870. FÉRÉOL, *Ulcération tuberculeuse de la langue* (Notes read at the Société Médicale des Hôpitaux, July 12 and October 25, 1872). JULLIARD, *Des ulcérations de la bouche et du pharynx dans la phthisie pulmonaire*, Thèse de Paris, 1865 (*Note sur l'ulcère tuberculeux de la bouche*, Lausanne, 1870). GOSSELIN, *Gazette des hôpitaux*, 1869. U. TRÉLAT, *Note sur l'ulcère tuberculeux de la bouche et en particulier de la langue* (*Acad. de méd.*, Nov. 27, 1869, and *Archives génér. de méd.*, 1870, vol. i. p. 35). LANDRIEUX, *Des pneumopathies syphilitiques*, Thèse, 1872. E. METZQUER, *Prophylaxie de la phthisie pulmonaire*, Strasburg, 1869. PUTÉGNAT, *Maladie des tailleurs de cristal de Baccarat* (*Bulletin de l'Acad. de méd.*, 1859). FELTZ, *Maladie des tailleurs de pierre* (*Gazette méd. de Strasbourg*, 1865, Nos. 2 and 3). GRAINGER STEWART, *On Dilatation of the Bronchi, or Bronchiectasis*, Edinburgh, 1867. AUFRECHT, *Die käsige Bronchopneumonie* (*Berlin. klin. Wochenschr.*, 1870). RINDFLEISCH, *Die chronische Lungen-Tuberculose* (*Deutsches Arch. für klin. Med.*, 1874). LEBERT, *Traité clinique et pratique de la phthisie pulmonaire*, 1879. BARD, *Phthisie fibreuse*, Thèse de Lyon, 1879. HIP. MARTIN, *Recherches anat.-path. et expérim. sur le tubercule*, Thèse de Paris, 1879. SPILMANN, *Thèse d'agrég.*, 1878. GRANCHER, *De la tuberculose pulmonaire* (*Archiv. de physiologie*, 1878); *De la dilatation bronchique chez les tuberculeux* (*Gaz. méd.*, 1878). BARTH, *De l'angine tuberculeuse*, Thèse, 1879. CHASSAIGNETTE, *De l'angine tuberculeuse*, Thèse de Paris, 1880. CHARCOT, *Anatomie pathologique de la phthisie pulmonaire* (*Revue mensuelle*, 1879). HANOT, *Phthisie pulmonaire* (*Nouveau dictionnaire*, edited by Jaccoud). HIRTZ, *De l'emphysème chez les tuberculeux*, Thèse de doctorat, 1878. REGINALD E. THOMSON, *On the Pathological Traces of Pulmonary Hæmorrhage* (*Medico-chirurg. Transactians*, vol. lxi.) MEYER, *De la formation et du rôle de l'hyaline dans les anévrysmes et dans les vaisseaux* (*Archives de Physiologie*, 2nd series, vol. vii.) WEIGERT, *Ueber Venentuberkel und ihre Beziehungen zur tuberculösen Blutinfection* (*Virchow's Archiv*, vol. lxxxviii., 1882, p. 307). J. RENAUT, *Note sur la tuberculose en général et les formes fibreuses pneumoniques en particulier* (*Soc. des scienc. méd.*, Lyon, March 26, 1879). JACCOUD, *Curabilité et traitement de la phthisie pulmonaire*, 1881. KRISHABER and DIEULAFOY, *Acad. de méd.*, 1881. RAYMOND and ARTHAUD, *Arch. gén. de méd.*, 1883. KOCH, *Berlin. klin. Wochenschr.*, April 10, 1882; *Mittheilungen des K. Gesundheitsamts*, Berlin, 1884. KIENER, *Des rapports de l'inflammation et de la tuberculose* (*Soc. méd. des hôpitaux*, 1883); *De la tuberculose dans les séreuses* (*Arch. de physiol.* and *Th. d'agrég. de Mairet*, 1878). HANOT, *Des rapports de l'inflammation avec la tuberculose*, Th. d'agr., Paris, 1883. QUINQUAUD, *De la scrofule dans ses rapports avec la phthisie pulmonaire*, Th. d'agrég., 1883. SCHMITT, *De la tuberculose expérimentale*, Th. d'agrég., Paris, 1883. BAUMGARTEN, *Centralbl. f. med. Wissenschaft.*, 1882, No. 15. LICHTHEIM, *Fortschritte der Medicin*. BALMER and FRAENTZEL, *Berliner klin. Wochenschr.*, 1882, No. 45, and *Deutsche med. Wochenschr.*, 1883, No. 17. CORNIL and BABES, *Communication to the Académie de Méd.*, April 1883; *Journal de l'Anatomie* of Robin, 1883. GERMAIN SÉE, *La phthisie bacillaire*, 1884, in-8.

DIGESTIVE ORGANS. MOUTH.—GIANUZZI, in *Sitzungsbericht der Süchs. Akademie*, Nov. 1865. DEBOVE, *Du psoriasis buccal*, Thèse de Paris, 1874. VANLAIR, *Du lichénoïde lingual* (*Revue mensuelle de méd. et de chir.*, 1880). DAVAINE, *Recherches sur les infusoires du sang dans la maladie connue sous le nom de sang de rate* (*Comptes rendus de l'Académie des sciences*, vol. lvii. pp. 220, 354, 386, 1863; vol. lix. pp. 393, 429, 1864, and vol. lx. p. 1296, 1865; vol. lxi. p. 3349). CHARCOT and VULPIAN, *Sur les lésions des nerfs dans la paralysie diphthéritique du voile du palais* (*Gazette hebdomadaire*, vol. ix. 1862, p. 368). DOLBEAU and GRANCHER, *Sur un cas d'éléphantiasis de la lèvre* (*Bulletin de thérapeutique*, 1874). GUYON and THIERRY, *Note sur l'existence temporaire de kystes épidermiques dans la cavité buccale chez le fœtus et le nouveau-né* (*Archives de physiologie*, 1869, pp. 368, 530). QUINQUAUD, *Nouvelles recherches sur le muguet* (*Archives de physiologie*, vol. i. 1868, p. 308). GUENEAU DE MUSSY, *Traité de l'angine glanduleuse*, Paris, 1858, in-8.

OBSERVATIONS ON ŒSOPHAGEAL SYPHILIS.—WEST, *Dublin Quarterly Journal*, Feb. 1869, and *Archives of Med.*, vol. i. p. 714, 1860; *Narrowing of the Syphilitic Œsophagus* (*The Lancet*, Aug. 9, 1872). FOLLIN, *Traité élémentaire de pathol. externe*, vol. i. p. 696, 1861. LANCEREAUX, *Traité historique et pratique de la syphilis*, 2nd edit. 1874.

DIPHTHERIA.—LABOULBÈNE, *Recherches cliniques et anatomiques sur les affections pseudo-membraneuses*, in-8, Paris, 1861. LETZERICH, *Ueber Diphtherie*, Berlin, Hirschwald, 1872. KLEBS, *Beiträge zur Kenntniss der Micrococcen*, 1873. CORNIL, *Observations histologiques sur l'inflammation diphthérique des amygdales* (*Archives de physiologie*, 2nd series, vol. viii. 1881, p. 372). LOEFFLER, *Observations on the Etiology of Diphtheria* (*Mittheilungen des K. Gesundheitsamts*, vol. ii., Berlin, 1884. BABES, *Observations sur quelques lésions infectieuses des muqueuses et de la peau, diphthérie, charbon, morve, choléra, fièvre typhoïde, verrues, etc.* (Robin's *Journal de l'anatomie*, 1884, with 4 plates).

ŒSOPHAGUS.—FOLLIN, *Rétrécissements de l'œsophage*, Paris, 1853. ZENKER and ZIEMSSEN, *Handbuch der specialen Pathol.*, vol. vii. ETERNOD, *Recherches sur les affections chroniques des ganglions trachéo-bronchiques*, Geneva, 1879. BARETY, *Adénopathie trachéo-bronchique*, Thèse de Paris, 1875. LANCEREAUX, *Atlas d'anat. pathol.*, 1871.

STOMACH.— For the normal histology of the cells and glands of the stomach, see HEIDENHAIN's description in Hermann's *Physiology*. BILLARD, *De la membrane muqueuse gastro-intestinale*, 1825. CRUVEILHIER, *Ramollissement de l'estomac*, mémoire read at the Institute in 1821; *Médecine pratique éclairée par l'anatomie et la physiologie pathologiques; Anat. path. générale*, p. 392. LOUIS, *Archives générales de médecine*, vol. v. RAYNAUD, *Sur un cas de gastrite phlegmoneuse* (*Société anat.*, 1860). CRUVEILHIER, *Anat. path.*, part 20, plates v. vi.; *Mémoire sur l'ulcère simple de l'estomac* (*Académie des sciences*, Jan. 21, 1856, and *Archives générales de médecine*, 1856, vol. i. pp. 149, 442. EBSTEIN, *Virchow's Archiv*, vol. xl. KRAUSS, *Das perforirende Geschwür im Duodenum*. V. CORNIL, *Note sur les polypes de l'estomac* (*Bullet. Soc. anat.*, 1863). LÉPINE, *Glandes à pepsine de l'estomac* (*Soc. de biologie*, 1873, p. 351). PENZOLDT, *Die Magenerweiterungen beim Kinde* (*Jahresbericht der Kinderspitales*, Bern, 1882). ROKITANSKI, *Lehrbuch der path. Anat.*, vol. ii. 3rd edit., 1861. MÜLLER, *Das corrosive Geschwür des Magens*, Erlangen, 1880. HENOCH, *Klinik der Unterleibs-Krankheiten*, Berlin, 1854. W. BRINTON, *Les maladies de l'estomac*, translated from the German of Bauer, 1862. WILSON FOX, *The Diseases of the Stomach*, London, 1872. V. CORNIL, *Fièvre typhoïde compliquée de gastrite* (*Soc. méd. des hôpitaux*, June 1880; *Empoisonnement par l'arsenic* (*Soc. méd. des hôpit.*, 1880). CHAUFFARD, *Etude sur les déterminations gastriques de la fièvre typhoïde*, Thèse de Paris, 1882. GAILLARD, *De l'ulcère simple de l'estomac*, Thèse de Paris, 1882.

HANOT and GOMBAULT, *De la gastrite chronique scléreuse* (*Arch. de physiolog.*, 1883). DAMASCHINO, *Maladies des voies digestives*, Paris, 1880. KUSSMAUL and MAIER, *Deutsch. Arch. f. kl. Med.*, iv.

INTESTINES.—VULPIAN, *Leçons sur l'appareil vaso-moteur*, 13th and 14th lessons, vol. i. 1875. HIS, in *Zeitschrift für wiss. Zoologie*, xi. p. 65; xii. p. 223; xiii. p. 455; xv. p. 127. TEICHMANN, *Das Saugadersystem, von anat. Standpunkt*, Leipzig, 1861. DEBOVE, *Archives de physiologie*, 1870. THIRY, *On a New Method of Isolating the Small Intestine* (*Wien. Sitzungsber.*, 1864). RADZIEJEWSKI, *Zur physiologischen Wirkung der Abführmittel* (*Reichert's und Dubois-Reymond's Archiv*, 1870, 1–67). A. MOREAU, *Expériences sur l'intestin* (Note communicated to the Acad. de Médecine, July 5, 1870).

DYSENTERY.—CHARCOT, *Recherches anatomo-pathologiques sur la dysenterie* (*Thèse de Sacher*, v., section iii. No. 3). CORNIL, *Sur l'anatomie pathologique des ulcérations intestinales dans la dysenterie* (*Archives de physiologie*, 1873, 311–218). KELSCH, *Contribution à l'anatomie path. de la dysenterie chronique* (*Ibid.*, pp. 406, 573); *Contribution à l'anatomie path. de la dysenterie aiguë* (*Ibid.*, p. 734).

CHOLERA.—HAYEM and RAYNAUD, *Société médicale des hôpitaux*, 1873, pp. 262, 267. PACINI, *On the Special Cause of Asiatic Cholera*, Florence, 1865. DAVAINE, article BACTÉRIE in the *Dict. encyclopédique des sciences médicales*; *Infusoires microscopiques dans les déjections des cholériques* (*Acad. des sciences*, April 23, 1849). KELSCH and J. RENAUT, *Progrès médical*, 1873, and *Journal des Connaissances pratiques*, 1873, p. 274. We give here the recent works on the bacteria of cholera, though not described in the text: KOCH, *Med. Wochenschr.*, 1883, Jan. 31 and March 26, 1884, Aug. 6 and 13, 1884. STRAUS, ROUX, NOCART, THUILLIER, *Arch. de physiol.*, 1884.

TREITZ, *Des affections urémiques de l'intestin* (*Prager Vierteljahrschrift*, vol. iv., and *Archives gén. de méd.*, 1860, vol. i.) LOUIS, *Recherches sur la fièvre typhoïde*, 1829. GAFKI, *Etiology of Typhoid Fever*, *Mittheilungen des Kaiserlichen Gesundheitsamts* (analysed in *Journal des Connaissances médicales*, April 1884). GOSSELIN, *De l'étranglement dans les hernies*, Thèse d'agrégation, Paris, 1864. NICAISE, *Des lésions de l'intestin dans les hernies*, Thèse, 1866. MALGAIGNE, *Mémoire sur les pseudo-étranglements et sur l'inflammation des hernies* (*Archives gén. de méd.*, 1841, and *Journal de chirurgie*, 1843, vol. i. p. 129). GOSSELIN and LABBÉ, *Leçons sur les hernies abdominales*, 1865. JOBERT, *Maladies du canal intestinal*, vol. ii. BROCA, *De l'étranglement dans les hernies*, Thèse d'agrégation, 1853. POZZI, *Etudes sur les fistules de l'espace pelvi-rectal supérieur*, Thèse de doctorat, 1873.

SYPHILITIC ULCERATION OF THE INTESTINES.—CULLÉRIER, *Union médicale*, 1854. FOERSTER, *Handbuch der speciellen pathol. Anatomie*, p. 841. MESCHEDE, *Virchow's Archiv*, vol. xxxvii. p. 565. EBERTH, *Ibid.*, vol. xl. p. 326. KLEBS, *Syphilitic Ulceration of the Intestines* (*Handbuch der pathologischen Anatomie*, p. 261).

LYMPHADENOMA.—DEMANGE, *Étude sur la lymphadénie*, etc., Thèse de doctorat, Paris, 1874. PICOT and RENDU, in the preceding thesis. KELSCH, *Société anatomique*, 1873. LANDOUZY, *Ibid.*, 1871. DEBOVE, *Ibid.*, 1872.

LIVER.—CRUVEILHIER, *Anat. path.*, b. xvi. pl. 3; b. xl. pl. 30. DANCE, *Archives gén. de médecine*, vol. xviii. 1828; vol. xix. 1829. LOUIS, *Recherches anat. path. sur diverses maladies* (*Mém. de la Société médicale d'observ.*, vol. ii.) BUDGE, *Ueber den Verlauf der Gallengänge* (*Müller's Arch.*, 1852, p. 642). ANDREJEVIÉ, *Ueber den feineren Bau der Leber* (*Wien. Sitzungsber.*, vol. liii. p. 379). MACGILLAVRY, *Wien. Sitzungsber.*, vol. lii. p. 207. EBERTH, *Med. Centralblatt*, 1866, No. 57, and *Virchow's Archiv*, vol. xxxix. p. 70. KÖLLIKER, *Elements of Human Histology*, 2nd French edit., p 552. SABOURIN, *La glande biliaire et l'évolution glandulaire graisseuse du foie* (*Revue mensuelle de méd.*, May 1883).

DUTROULEAU, *Traité des maladies des Européens dans les pays chauds*, Paris, 1861; *Archives générales*, 1853. GRIESINGER, *Treatise on Infectious Diseases.* FRERICHS, *Die Melanämie* (*Zeitschrift f. klinische Medicin*, Breslau, 1855); *Practical Treatise on Diseases of the Liver.* MURCHISON, *Treatise on Continued Fevers*, London, 1862. GARROD, *Treatise on Gout.* HASPEL, *Maladies de l'Algérie*, 2 vols. 1852. DE SINETY, *De l'état du foie chez les femelles en lactation*, Thèse de Paris, 1873. ROUIS, *Recherches sur les suppurations endémiques du foie*, 1860. SABOURIN, *Fièvre typhoïde, ictère grave, atrophie jaune aiguë du foie* (*Revue de méd.*, July 1882). CHARCOT and GOMBAULT, *Lésions consécutives à la ligature du canal cholédoque* (*Archives de physiologie*, 1876). VULPIAN, *Leçons professées à la Faculté de médecine* (*Journal de l'Ecole de médecine*, 1874). ARNOULD and COYNE, *Sur l'anatomie de l'ictère grave* (*Gazette médicale*, 1876). LIEBERMEISTER, *Klinik der Leberkrankheiten.* CIRRHOSIS.—BICHAT, *Dernier cours sur l'anatomie pathologique*, J. B. Baillière. LAENNEC, *Auscultation médicale*, 1st edit., obs. 25, 29, 35, 36; 2nd edit., obs. 35 and note to this case. BOULLAND, *Mém. de la Société médicale d'émulation*, vol. ix. p. 170, 1819. CRUVEILHIER, *Anatomie pathologique*, atlas, part 12, pl. 1; *Traité d'anatomie pathologique générale*, vol. iii. p. 210, 1856. ANDRAL, *Précis d'anatomie pathologique*, vol. ii. 2nd part, p. 583, Paris, 1829. BOUILLAUD, *Dictionnaire de médecine et de chirurgie pratique*, art. CIRRHOSE. BECQUEREL, *Recherches anatomo-pathologiques sur la cirrhose du foie* (*Archives générales de médecine*, April 1840). GUBLER, *Bullet. de la Société anatomique*, July and Aug. 1848, March 1849; *Thèse d'agrégation sur la théorie la plus rationnelle de la cirrhose*, 1853; *Gazette médicale de Paris*, 1852 and 1854. KIERNAN, *Philosophical Transactions*, 1833. ROKITANSKY, *Lehrbuch der path. Anatomie.* REQUIN, *Pathologie médicale*, vol. ii. p. 774, and *Supplément au Dictionnaire des Dictionnaires de médecine*, art. CIRRHOSE, 1851. SAPPEY, *Bull. de l'Acad. de Paris*, vol. xxiv. 1879. FRERICHS, *Practical Treatise on Diseases of the Liver.* DUPERRAY, *Thèse de Paris*, 1867. FOERSTER, *Handbuch der pathol. Anat.*, 2nd edit. 1862. RINDFLEISCH, *Lehrbuch der path. Anatomie.* KLEBS, *Handbuch der pathol. Anatomie*, 1868–73. CORNIL, *Note pour servir à l'histoire de la cirrhose hépatique* (*Archives de physiologie*, March 1874, and *Académie de médecine*, séance of Nov. 4, 1873). HAYEM, *Contribution à l'étude de l'hépatite interstitielle chronique avec hypertrophie* (*Archives de physiol.*, Jan. 1874). OLIVIER (P.), *Sur la cirrhose hypertrophique* (*Union médicale*, pp. 61, 71, 75, 1871). HANOT, *Etude sur une forme de cirrhose hypertrophique du foie*, Thèse de Paris, 1876 BERTRAND, *Etude sur le cancer de la vésicule biliaire*, Thèse de Paris, 1870. LANCEREAUX, *Contribution à l'étude de l'hépato-adénome* (*Gazette méd.*, 1868). EBERTH, *On Adenoma of the Ear Lobes* (*Virchow's Archiv*, vol. xliii.) KELSCH and KIENER, *Hépatite parenchymateuse nodulaire* (*Arch. de physiologie*, 1876, 1878, 1879 and 1880). DUBRAC, *Tumeurs adénoïdes du foie*, Thèse de Paris, 1872. SABOURIN, *Contribution à l'étude des lésions du parenchyme hépatique dans la cirrhose; Essai sur l'adénome du foie*, Thèse de Paris, 1881, 2 plates; *La cirrhose du système sus-hépatique d'origine cardiaque* (*Revue de méd.*, July 10, 1883); *Sur la cirrhose hypertrophique graisseuse* (*Arch. de physiologie*, 1880). HUTINEL, *Sur la cirrhose hypertrophique graisseuse* (*Société clinique*, 1880). DUPONT, *Hépatite interstitielle subaiguë*, Thèse de Paris, 1877. CHARCOT, *Leçons sur les maladies du foie et des reins*, 1877. MICATI and RICHOUD, *Travaux du laboratoire de la rue des Fabres, à Marseille*, 1881. ACKERMANN, *Virchow's Archiv*, vol. lxxx. SABOURIN, *Note sur l'oblitération des veines sus-hépatiques dans la cirrhose du foie* (*Revue de méd.*, Aug. 1882); *Du rôle que joue le système veineux sus-hépatique dans la topographie de la cirrhose du foie* (*Revue de méd.*, June 1882). HANOT, *Sur la cirrhose atrophique graisseuse* (*Arch. gén. de méd.*, 1883). SABOURIN, *Contribution à l'étude anatomo-pathol. des cirrhoses graisseuses* (*Revue de méd.*, Feb. 1884).

HANOT and CHAUFFARD, *Cyrrhose hypertrophique pigmentaire dans le diabète sucré* (*Revue de méd.*, May 1882).

PANCREAS.—VERNEUIL, *Mémoire sur l'anatomie du pancréas* (*Gazette méd.*, 1851). CL. BERNARD, *Mémoire sur le pancréas*, Paris, 1856, and *Cours de physiologie professé au Collège de France*, vol. ii. 1846. SAPPEY, *Traité d'anatomie*. EBERLE, *Physiologie der Verdauung*, Würzburg, 1834. BOUCHARDAT and SANDRAS, *Annuaire de thérapeutique*, 1843 and 1846. L. CORVISART, *Sur une fonction peu connue du pancréas*, 1857, and *Comptes rendus de l'Acad. des sciences*, 1859. KLOB, *Wiener Zeitschrift*, 1859. ARAN, *Arch. génér. de médecine*, 1846. WILLIGK, *Prag. Vierteljahrsschrift*, 1856. CORNIL and LÉPINE, *Société de biologie*, 1874. RECKLINGHAUSEN, *Virchow's Archiv*, vol. xxx. LUCKE and KLEBS, *Ibid.*, vol. xli. VIRCHOW, *Pathology of Tumours*, vol. i.

SPLEEN.—FREY, *Histology*. GERLACH, *Zeitschrift für rationnelle Medicin*, vol. vii. 1848. BILLROTH, *Virchow's Arch.*, vols. xx. and xxiii. SWEIGGER-SEIDEL, *Disquisitiones de liene. Halis*, 1861 (*Virchow's Archiv*, xxiii. and xxvii.) AXEL KEY, *Virchow's Archiv*, xxi. MÜLLER, *Ueber feineren Bau der Milz*. PELTIER, *Pathologie de la rate*, Thèse de Paris, 1872. LÉON COLIN, *Rapports qui existent entre la pigmentation splénique et celle des autres tissus dans la mélanémie* (*Société méd. des hôpitaux*, 1873). CARSWEL, *Abcès de la rate* (*Illustrat.*, fascicul. 8, pl. 3, fig. 6). BESNIER, art. RATE in the *Dictionnaire encyclopédique des sciences médicales*. PONFIK, *Studies on Recurrent Typhus* (*Virchow's Archiv*, May 1874). LEFEUVRE (Charles), *Etudes sur les infarctus viscéraux*, Thèse de Paris, 1867. BILLROTH, *Virchow's Archiv*, vol. xviii. VIRCHOW, *Pathology of Tumours*, vol. iii. GEE, *Enlargement of the Spleen in Hereditary Syphilis* (*Roy. Med. and Surg. Society*, 1867, and *Arch. de méd.*, 1867). PARROT, *Société de biologie*, Nov. 1872. SÉE, *Leçons de pathologie expérimentale*, 1866. ANDRAL, *Kystes de la rate* (*Anatomie path.*, vol. ii. p. 93). LEUDET, *Clinique méd. de l'Hôtel-Dieu de Rouen*, 1874. MAGDELAIN in PÉAN, *Ovariotomie et splénotomie*, Paris, 2nd edit., G. Baillière, 1869. ERNEST WAGNER, *Archiv der Heilkunde*, 1852, part 5.

SUPRARENAL CAPSULES.—OGLE, *Archives of Medicine*, vol. i. KUSSMAUL, *Würzburg. med. Zeitschrift*, 1863. DÆDERLEIN, *Inaugural Dissertation*, Erlangen, 1860. ADDISON, *On the Constitutional and Local Effects of Disease of the Suprarenal Capsules*, London, 1855. BÆRENSPRUNG, *Die hereditäre Syphilis*, Berlin, 1864. BÉHIER, *Leçons cliniques*. MARTINEAU, *Thèse de doctorat sur la maladie bronzée d'Addison*, 1864. JACCOUD, art. MALADIE D'ADDISON in the new *Dictionnaire de méd. et de chirurgie pratiques*. BALL, art. MALADIE BRONZÉE in the *Dictionnaire des sciences médicales*. LANCEREAUX, *Traité historique et pratique de la syphilis*, Paris, 1874, 2nd edit., and art. REIN et CAPSULES SURRÉNALES in the *Dictionnaire encyclopédique des sciences médicales*.

KIDNEYS.—KÖLLIKER, *loc. cit.* HENLE, *Zur Anatomie der Nieren*, Göttingen, 1862. LUDWIG, *Structure of the Kidney* (*Stricker's Handbuch der Lehre von den Geweben*, 1870). GROSS, *Essay on the Microscopical Structure of the Kidney*, Strasburg, 1868. CHARCOT, *Leçons professées en* 1874 *à l'Ecole de médecine sur les maladies du rein* (*Progrès médical*, 1874). KELSCH, *Revue critique et recherches anatomo-pathologiques sur la maladie de Bright* (*Arch. de physiologie*, September 1874). REINHARDT, *Annalen der Chariter zu Berlin*, 1851. FRERICHS, *Die Bright'sche Nierenkrankheit*. VIRCHOW, *Ueber parenchymatöse Entzündung* (*Arch. für path. Anatomie*, vol. iv. p. 260, 1852). JOHNSON (G.), *British and For. Med.-Chirurg. Review*, 1855; *Med. Soc. of London*, in *Lancet*, July 1858; *Medico-Chir. Transactions*, vol. xlvi. p. 154; vol. li. p. 57, 1868; *Medical Times and Gaz.*, April 1869; *Brit. Med. Journal*, April, 1870. GULL and SUTTON, *On the Pathology of the Morbid State commonly called Chronic Bright's Disease with Contracted Kidney* (*Arterio-Capillary Fibrosis*) (*Medico-Chirurg. Transactions*,

vol. lv. p. 273, 1872). GRAINGER-STEWART, *British Med. Journal*, July 1872, and *Brit. Rev.*, January 1867. HOOD, *Lancet*, Aug. 1872. TRAUBE, *Gesammte Abhandlungen*, vol. ii. WILKS (Samuel), *Cases of Bright's Disease* (*Guy's Hosp. Reports*, 2nd series, vol. viii., 1854). HANDFIELD JONES, *On the Curative Treatment of Chronic Morbus Brightii* (*Med. Times and Gaz.*, 1855). TODD, *Clinical Lectures on Certain Diseases of the Urinary Organs and on Dropsies*, London, 1857. ROSENSTEIN, *Practical Treatise on Diseases of the Kidneys.* CHARCOT and CORNIL, *Contribution à l'étude des altérations anatomiques du rein chez les goutteux* (*Société de biologie*, 1863). GARROD, *Treatise on Gout.* LÉCORCHÉ, *Traité des maladies des reins*, in-8, Masson, 1875. CORNIL, *Des différentes espèces de néphrites*, Thèse d'agrégation, 1869; *Note sur la dégénérescence amyloïde des organes étudiée au moyen de réactifs nouveaux* (*Arch. de physiologie*, 1875); *Etat des cellules du rein dans l'albuminurie* (*Journ. de l'Anatomie*, 1879, with 5 plates). BRAULT, *Contribution à l'étude des néphrites*, Thèse, 1881. BARTELS, *Treatise on Diseases of the Kidney.* CORNIL and BRAULT, *Etudes sur la pathologie du rein*, in-8, with 16 plates besides text, 1884.

In the latter part of this volume, in the chapters devoted to the genito-urinary organs and to the skin, we have given the bibliographical references in the text or in the foot notes; this dispenses with the necessity of repeating them here.

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