certain bacteria have been used, and Besançon used dead tubercle bacilli. Other investigators have employed vegetable alkaloids; for instance, Marckwald found that a cirrhosis followed the injection of antipyrin in frogs and rabbits.

From the organs of a guinea-pig that died without apparent cause Weaver isolated a bacillus belonging to the colon group, which, when injected into guinea-pigs, in doses not immediately fatal, caused a cirrhosis; bouillon cultures sterilized by heat caused similar alterations of the liver. Hektoen has produced a perilobular cirrhosis in guinea-pigs and rabbits by means of a bacillus of the pseudo-diphtheria group and also by cultures of the bacillus filtered through porcelain.

The above-named poisons, bacteria, and bacterial products have been administered with food, injected into the liver directly, or into the blood-vessels or body cavities.

The results of investigators in efforts to produce cirrhosis of the liver experimentally in animals have been varied; the production of cirrhoses which would serve as prototypes for those observed in man has been rarely accomplished. The results obtained by Boix with organic acids deserve special mention in this regard.

Kirkow has concluded, after a careful review of the literature, that degenerative processes and necrosis of the liver cells are not necessarily followed by cirrhosis, and that the important factor in the production of a cirrhosis is the repeated or continuous action of agents which produce such alterations—*i.e.*, agents which cause irritation.

In addition to such investigations with substances that act by destroying the parenchyma of the liver, efforts have also been made to produce cirrhosis by constricting the common bile duct or its branches, or by incomplete ligation of the main divisions or the branches of the hepatic artery or portal vein; the consequences of experimental hepatic embolism have also been studied.

Atrophic Cirrhosis.—This form of cirrhosis is the best and longest known; it is the commonest variety and has long enjoyed distinction under the names, "gin-drinkers' liver" and "hob-nailed liver"; it is also known as "Laënnec's cirrhosis" and "granular atrophy of the liver." In the liver it is the analogue of chronic interstitial nephritis or the "small granular kidney." The liver in this form of cirrhosis is lessened in size and weight; the diminution in size is often extreme in the left lobe, and this portion may appear simply as a short fibrous tag attached to the left border of the liver.

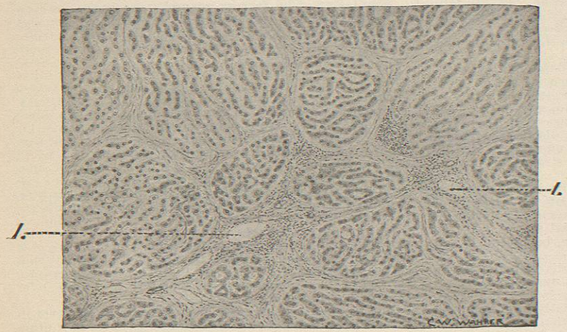

FIG. 3223.—Atrophic Cirrhosis. Great variation is shown in the size of the islands of liver cells and some are clearly too small to represent lobules (sublobular cirrhosis). At l are shown radicles of the portal vein. (Dr. Le Count's specimen.)

The weight is often reduced one-half and may be even less. The external surface, in place of the usual smooth and glistening appearance, possesses irregular rounded elevations that vary in size somewhat, but are distributed quite uniformly over all the exterior.

The elevations vary in color not only in different cases but also in the same liver; the presence of fat and the biliary pigments in different combinations produces tints of yellow and of yellowish-green or dark green. These elevations represent the remaining liver tissue, and some of them may correspond closely to the so-called adenomata or foci of nodular hyperplasia; to some extent, at least, most of these elevations on the external or cut surface represent efforts at regeneration on the part of liver cells and bile ducts.

Between the elevations there are furrows or linear and anastomosing depressions that are gray or reddish according to the embryonal or mature character of the granulation tissue composing them.

The elevations may be fairly uniform in size or they may vary from a barely visible size to that of a filbert; they are often best developed near the anterior margin or on the left lobe. That the contained liver cells are in a state of compression is rendered obvious by stripping off the capsule; the same fact is made apparent by sectioning the liver, when the islands of liver tissue are found projecting above the remainder of the cut surface. The liver is firm and cuts with increased resistance; the consistence may be like that of cartilage.

It is impossible to distinguish, on the cut surface, the "lobular markings" with any degree of certainty. It is not uncommon to see districts the seat of passive hyperæmia in which the "nutmeg appearance" of cyanotic atrophy is added to the changes caused by the cirrhosis. The histologic changes are as a rule confusing in that lobules are not readily found; difficulty is experienced in locating the central or intralobular veins, and lobules are often so cut up by bands of fibrous tissue that it may be impossible to locate their former limitations (Fig. 3223). It is not uncommon to find small groups of liver cells wholly within quite wide bands of fibrous tissue. As a rule, the liver cells are quite well preserved, although many may contain blood and bile pigments or may show signs of the former presence of fat droplets; occasionally fatty degeneration is very marked. The excess of connective tissue is most abundant about the portal vein radicles; in any well-developed case of atrophic cirrhosis there may be not only a large amount of fibrous tissue in these localities, but in other places there is also granulation tissue containing newly produced blood-vessels and accumulations of round cells, fibroblasts, and leucocytes. The vessels are outgrowths from the branches of the hepatic artery.

The occurrence of purely unilobular or of purely multilobular cirrhoses—the former with the increased tissue around each lobule, while in the latter it surrounds two or more lobules—is certainly quite rare; usually in any advanced case of atrophic cirrhosis the arrangement of the increased stroma is not limited to any single type. Flexner and his pupils and also Oliver have ascertained that both white fibrous and yellow elastic tissue are increased in amount in this form of cirrhosis (Fig. 3224). In the normal liver, according to Mall, there are three histological varieties of connective tissue serving as its stroma: the white fibrous, the yellow elastic, and reticulum; the last named existing chiefly within the lobules, while the yellow elastic tissue is to be found within and around the

blood-vessels. All three varieties may be increased in atrophic cirrhosis, but as concerns the reticulum the process seems to be an hypertrophy rather than an hyperplasia.

At the edges of the collections of liver cells representing lobules or portions of lobules and in the periportal newly formed connective tissue, there are present rows of cells that represent the attempt of the biliary channels to form new liver tissue. The continuity of some of these embryonic biliary canals with the older channels of the same kind has been proven by Ackermann, who succeeded in injecting them. It is also thought that some of them may represent a reversion of the liver cells to an embryonic type. Many of these rows of cells are continuous with the cords of liver cells.

There are certain sequential and incidental changes in other viscera and in other parts of the body that are more or less characteristic and constant accompaniments of atrophic cirrhosis and deserve consideration.

The spleen is usually enlarged and it may attain twice or even three times its normal size. This enlargement is usually ascribed to passive hyperæmia, and yet the claims of Oestreich are frequently quoted. From the study of a number of cases he was led to believe that the enlargement is mainly of an inflammatory character and that during the early stages of the cirrhosis the pulp of the spleen undergoes an hyperplasia which may persist, or later suffer induration or atrophy. Oestreich believes that the splenitis is due to the same irritants as those which produce the cirrhosis, and, like Ackermann, he is of the opinion that they may reach the liver by the arterial circulation.

The absence of valves in the portal vein and its branches facilitates collateral circulation, which, however, is seldom if ever completely established; and, in consequence of this, peculiar and interesting alterations result. The classical so-called "caput Medusæ" is perhaps of more clinical significance but certainly not more interesting than some of the more deeply seated disturbances of the circulation and blood-vessels, that owe their origin to a similar cause. The writer once met with multiple dilatations of the mesenteric veins in a necropsy held at the Cook County Hospital in Chicago, upon the body of a man who, previously to his death from atrophic cirrhosis, had suffered from numerous intestinal hemorrhages. The dilatations were located at the junction of the mesentery and bowel, were usually circular in contour, varied in size from a buck-shot to a small hickory nut, and were most numerous in the upper part of the bowel, decreasing in frequency toward the colon. Many of these had ruptured into the bowel and formed false diverticula; others were filled with dark blood or thrombi and looked not unlike a string of small grapes that formed a fringe to the intestine at its mesenteric attachment.

Dilated and tortuous veins occur in all the ligaments of the liver; in the round ligament a dilated vein is occasionally found as large as the finger. In the lower end of the œsophagus dilated veins are practically always present in marked cases of atrophic cirrhosis. Stockton, of Buffalo, has pointed out an important connection between ascites and the establishment of collateral circulation in that the latter may prevent the occurrence of the former. Such an influence of dilated œsophageal veins in compensating for the obstructed portal circulation has also been emphasized by Preble, who, in a valuable contribution to the literature of cirrhosis, analyzes sixty cases of fatal gastro-intestinal hemorrhage due to cirrhosis. He found that of these, only six per cent. showed ascites, enlarged spleen, and subcutaneous abdominal varices.

Icterus may occur with atrophic cirrhosis, and not only is the color of the liver thereby modified but the adipose tissue and lining membranes of the heart and blood-vessels are also tinted yellow.

Fibrous adhesions about the liver are not uncommon. Associated with ascites there are frequently œdema and serous atrophy of the subperitoneal and perinephric adipose tissue. Catarrhal inflammations of the stomach and intestines are also frequent in atrophic cirrhosis, and in the kidneys there is often found an interstitial inflammation comparable to that in the liver.

The diminution in length of the small intestine is a sequel to atrophic cirrhosis that many authors fail to mention; from the usual 7 to 8 metres, the length is reduced to 5 or 6 metres or even less. Gratia mentions one case in which it was reduced to 3.55 metres. The colon is also shortened and both large and small bowel undergo a diminution in calibre. The mesentery also becomes shortened. These changes in the alimentary canal and the mesentery are worthy of further investigation.

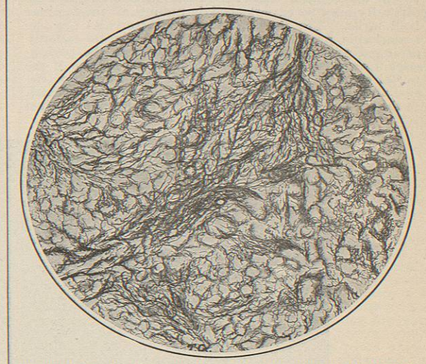

FIG. 3224.—Drawing from a Section of Atrophic Cirrhosis, after the Removal of the Parenchyma and Elastic Tissue by Digestion. Through the centre a vertical band of white fibrous tissue extends, and on either side the reticulum, which is also increased, is well shown. (From the collection of Dr. Oliver, of Chicago.)

Hypertrophic Cirrhosis.—On account of its infrequent occurrence and the fewer opportunities for studying it, less is known about this form of cirrhosis than about the preceding. According to Hanot hypertrophic cirrhosis occurs in young and feeble men, beginning with an attack of pain in the right hypochondrium and being associated with symptoms of disturbed digestion. After two or three such attacks jaundice appears and gradually increases. There are few other symptoms; attacks of indigestion and pain are accompanied by enlargement of the liver and spleen, and both viscera finally attain enormous sizes.

The liver weighs from 2 to 4 kgm.; it is finely granular externally, but on the whole it is smooth when contrasted with the liver of atrophic cirrhosis. Fibrous adhesions may exist, binding it to the diaphragm, peritoneum, or neighboring viscera. The size of the liver causes displacement of the costal arch and ribs on the right side forward and outward, and an increased width of the lower part of the thorax. Its lower margin is often to the left of the umbilicus and below, and in contact with the crest of the ilium on the right side. The color of the organ is usually yellowish-green or dark olive green or mottled with patches of both. The biliary channels are all patent, so far as the gross examination goes. The lobular markings, viewed externally or on the cut surface, are obscure or indistinguishable and in their place are innumerable small, rounded, and irregular elevations; occasionally these are not at all striking and both the external surface and that exposed by sectioning may be quite smooth. The consistency of the liver is increased.

While the changes in the minute anatomy of the liver are quite different from those ordinarily found in atrophic

cirrhosis, it would nevertheless be hazardous in all cases to attempt to distinguish the two forms of cirrhosis from one another by the histologic alterations alone; occasional examples would prove very puzzling (Fig. 3225). In typical instances the limitations of the lobules may be located by the interlobular vessels and bile ducts, although some difficulty may be experienced in finding all the familiar landmarks. The most marked characteristics are the remarkable proliferation of the bile ducts, the radially arranged growth of connective tissue from the peripheries toward the centres of the lobules, the failure of the portal veins to become involved in the granulation tissue, and the general absence of perilobular hyperplasia of the stroma. The borders of the lobules are notched

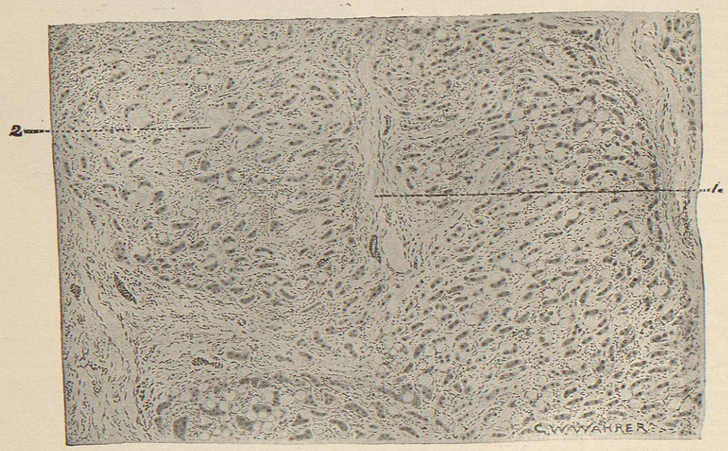

FIG. 3225.—Hypertrophic Cirrhosis. The band of tissue shown at 1 is interlobular connective tissue; there is a lobule to the right of this and one to the left; at 2 is the central vein of the latter, and below 2 are numerous small groups of liver cells isolated from the main part of the lobule by intralobular extension of small bands of embryonal connective tissue. (Dr. Le Count's specimen.)

with small processes of connective tissue which, extending into the lobules, separate more or less completely single liver cells or groups of them from their respective cords and columns. Such isolated liver cells often contain bile pigment in rounded and club-shaped masses or branching plugs moulded to the shape of the biliary canaliculi. These isolated liver cells are directly continuous with the newly grown bile ducts. These last formations are very numerous, and from the small size of some of them it is difficult to believe that they possess distinct channels. Around the larger bile ducts there are both the mature and the hyaline forms of connective tissue, in excess of the normal amount, and also granulation tissue and collections of leucocytes (Heineke). The liver cells are but slightly altered; the great increase in size and weight of the organ, it has been suggested, may be due to an increase in the parenchyma; be this as it may, it is certain that hyperplastic cirrhosis would be a more appropriate name than the one in present use.

The etiology of this form of cirrhosis is not definitely known, but there is a general disposition to connect the process with the pericholangitis which constitutes such a conspicuous feature of its minute anatomy. The view at present held by the French school of pathologists is that hypertrophic cirrhosis, or Hanot's cirrhosis, is due primarily to an infection that invades the liver by way of the bile ducts.

The enlargement of the spleen, which may reach a weight of 1 kgm. or more, is due to an hyperplasia of the lymphoid tissue. The general nutrition is maintained for a long time in this form of cirrhosis, cachexia rarely appearing until the disease has been established for several years. Ascites, if present at all, makes its appearance toward the end; it may be entirely absent and is never considerable in amount. The entire course of the illness may extend over a period of from five to ten years.

Obstructive Biliary Cirrhosis.—The extrahepatic ducts may be obstructed in various ways. Following the general law that the parenchyma of the gland disappears when its excretory canal is closed, cirrhosis of the liver takes place as an accompaniment of atrophy of the gland tissue proper. Such cirrhoses may follow congenital absence, malformation, or occlusion of the bile ducts. Death occurs before any considerable shrinkage has taken place, for the livers of such infants are found greatly enlarged, firm, deeply jaundiced, granular externally, and quite resistant to the knife.

Histologic examination reveals an interlobular cirrhosis with extensive formation of embryonic biliary channels. It is not known whether the cirrhosis is due to the obstruction to the outflow of the bile or to the same causes that produced the malformation of the ducts in these cases.

That cirrhosis would ultimately occur is borne out both by experiments upon animals and by the cases reported in which cirrhosis affected one lobe in which calculi have been found obstructing the corresponding branch of the hepatic duct.

Ford has collected the cases of obstructive biliary cirrhosis that have accumulated in medical literature since the compilation of Mangelsdorff in 1882. He was able to find twenty-one and to these he added three.

As concerns the pathological anatomy and histology of this form of cirrhosis, there is less to mark it as a distinct

form than is found in the etiology and clinical course of the affection. The liver may be greatly enlarged or it may approach in size and appearance the ordinary atrophic cirrhosis; it should be remembered, however, that, in the latter, icterus is usually absent entirely or at least is not marked; whereas in obstructive biliary cirrhosis the liver will be deeply pigmented. A further difference in the morbid anatomy is afforded by the occurrence of numerous biliary retention cysts in the obstructive form; these are usually small, rarely larger than a pea, frequently smaller, and contain dark green or inspissated bile. In this form of cirrhosis the extrahepatic ducts are dilated and in any given case the obstruction might be still demonstrable.

The liver is often found enlarged in obstructive biliary cirrhosis, and in two of those considered by Ford (one reported originally by Boinet) it weighed over 4 kgm. It is hard, rough externally, and adherent to the surrounding structures.

It is cut with difficulty and, in addition to the retention cysts mentioned, the cut surface shows an increase in connective tissue. If the cases did not run such an acute course it is likely that the resemblance to Laënnec's cirrhosis would prevail in all cases; as it is, however, there is a great similarity to the hypertrophic biliary cirrhosis of Hanot. The appended table, taken from the article by Ford, illustrates well the differences between the two as well as some further analogies between obstructive biliary cirrhosis and atrophic cirrhosis. There is no doubt that this form of cirrhosis is worthy of consideration as a distinct morbid entity.

Symptoms.	Hanot's cirrhosis.	Obstructive cirrhosis.
Course of disease	Chronic	Acute.
General health	Good	Poor.
Emaciation	Slow	Rapid.
Loss of weight	Slow	Rapid.
Intermission of symptoms.	Common	Does not occur.
Fever	Common	Rare.
Anorexia	Rare	Common.
Good appetite	Common	Rare.
Vomiting	Rare	Common.
Jaundice	Slight at first, increasing.	Deep from the first.
Clay-colored stools	Rare	Constant.
Bile-stained urine	Common	Constant.
Enlargement of liver	Common	Common.
Contraction of liver	Rare	Common.
Ascites	Rare	Common.
Œdema of extremities	Rare	Common.
Caput Medusæ	Rare	Common.

Pigmentary Cirrhosis.—In 1891 Welch described a condition of cirrhosis due to the presence of particles of coal. Numerous small black specks and streaks were visible both externally and on the cut surface; they were scattered at irregular intervals of not more than 0.5 to 1 mm.; around many of them the liver possessed a grayish color, although the prevailing color was yellowish-brown.

The chemical examination of the pigment revealed no difference between it and the coal pigment found so commonly in the lungs and bronchial lymph glands. The histologic examination showed, as the prevailing condition, the presence of rounded masses of fibrous tissue averaging from one-sixth to one-eighth the diameter of a liver lobule; they were located most frequently in the interlobular tissue and were composed of dense fibrous tissue. These fibrous patches were also found within the lobules and surrounding the central veins; they were so numerous that with low powers of the microscope many were seen to be present in any single field. They all contained large amounts of black coal pigment.

The cirrhosis differed greatly from any of the ordinary forms in the circumscribed and focal character of the lesions.

Welch named the condition "cirrhosis hepatis anthracotica," and references to his description are often met with in the literature of cirrhosis of the liver. As an etiological and pathological entity this variety deserves recognition.

Another form of cirrhosis due to deposits of pigment has attracted considerable attention within recent years, and it possesses the merit of manifesting clinical characteristics, in addition to etiological and pathological features, that serve to distinguish it; it is the pigmentary cirrhosis of bronzed diabetes.

In a necropsy held by me in the Cook County Hospital upon a case of this character the liver weighed 2.7 kgm. and was at once remarkable for its color, a yellowish-brown or ochre-yellow—a pigmentation never simulated by the biliary pigments. There were no tints of green present. The liver had preserved its form; the external surface was finely granular; the consistence markedly increased; and, on the surfaces exposed by sectioning, the lobules were plainly distinguishable, projecting slightly above the surface and surrounded by reddish or darker-colored sunken stroma. The gall bladder was distended by thick dark bile and the ducts were patulous.

This case has been reported in full by Condon, and at the time of its publication it was the third necropsy upon this form of cirrhosis recorded in America. The liver in the case reported by Opie answered to a very similar description, as will be seen by the following:

"Weight 2,270 gm. The surface is of a deep reddish-brown color of a peculiar character, resembling that of iron rust. The surface of the left lobe, more markedly than that of the right, is superficially nodular and puckered, presenting in moderate degree the appearance of a hob-nail liver. On section islands of lighter brown parenchyma, representing one or several lobules, are surrounded by fibrous stroma of a deeper brown color. Sparsely scattered are opaque yellowish-white areas, often 1.5 mm. across. The gall bladder, distended by thin green bile, measures 12 cm. in length."

The histological changes in this form of cirrhosis are truly remarkable on account of the excessive amount of hæmatogenous pigment present everywhere. The points where it is accumulated in greatest amount are in the fibrous tissue, but large amounts also occur in the liver cells, in the endothelial cells of the capillaries, and in Kupffer's cells; it is also found entirely free. Newly formed bile ducts occur in the cicatricial tissue as well as in embryonal blood-vessels. The perilobular type of cirrhosis is followed for the main part, but the groups of segregated liver cells are often smaller than lobules.

Whatever may be the final outcome of the present speculations as to the relationship between the generalized hæmochromatosis, the diabetes, and this form of cirrhosis,—for all three usually occur together,—it is proper to consider this form of cirrhosis a distinct type of disease of the liver in its pathogenesis, morbid anatomy, and histology.

A most thorough review of the entire subject has been made by Anschütz; in it he analyzes twenty-four cases. Different theories have been advanced by the different writers. One view is, that the diabetes is primary, and that hæmolysis and pigmentation, with interstitial inflammations in various viscera, occur secondarily; some of the adherents to the foregoing theory believe that the pigment is formed where it is found, while others maintain that it is deposited there subsequently to its formation. Other writers have advanced the proposition that the hæmolysis is primary, the diabetes resulting from pigmentary cirrhosis of the pancreas, and the cirrhosis of the liver from the deposition of pigment there. "It may be stated that the deposition of pigment in the liver is now universally regarded as the existing cause of the liver changes" (Futcher).

A cirrhosis due to pigmentation has also been described in malarial infections; but, since considerable pigmentation may take place without any marked cirrhosis in malarial infections of a chronic type and in malarial cachexia, the origin of the cirrhosis occasionally met with has been questioned. The pigment is deposited in the endothelial cells and in Kupffer's cells, but is rarely found within the liver cells; and since a prerequisite for the development of a cirrhosis seems to be a destruction of the parenchyma cells, a cirrhosis of the liver due to

the deposition there of pigment formed during malarial infections may justly be considered rare.

Other Forms of Cirrhosis.—Certain other forms of cirrhosis possess a distinct etiology and some a definite histology, but few of these at the same time have associated syndromes or morbid anatomy that would permit of their recognition either clinically or at post-mortem examinations. An exception to this statement perhaps occurs in the coarsely nodular cirrhosis due to syphilis, which in some instances is associated with gummata.

The cirrhosis of congenital syphilis has been described as diffuse and "pericellular" in type. The cirrhosis caused by long-standing passive hyperæmia, which is in reality much more uncommon than is generally supposed, possesses a distinct histology; this was well illustrated by a case studied in the Pathological Laboratory of Rush Medical College by Mr. Dryer, whose report was embodied in the article by Herrick on "Pericarditic Pseudo-Cirrhosis of the Liver."

The liver weighed 2,235 gm., and, aside from the very evident cirrhosis, showed miliary tubercles and foci of nodular hyperplasia. Although, in the gross inspection of the liver, there were no signs to indicate the pathogenesis of the cirrhosis, the study, by serial sections, of the minute anatomy revealed the fact that the proliferation of connective tissue was most marked about the central veins, and that from here the lobules and interlobular structures were involved.

The descriptions of Parmentier do not make it apparent that "cirrhose cardiaque" could be easily recognized from its gross anatomy alone.

The termination of acute yellow atrophy in "multiple nodular hyperplasia" has afforded opportunity for many publications and lengthy discussions; for the most part they have been directed to the relationship of the so-called "adenoma" formations to tumor growth, rather than to that which such processes of regeneration bear to cirrhosis.

Finally, there is mentioned in some text-books a form of cirrhosis, "Glissonian cirrhosis," that has been supposed to have its origin in a perihepatitis.

The insufficient grounds upon which such ideas have rested is well shown by Nicholls in his recent monograph on "Chronic Inflammation of the Serous Membranes." After a careful consideration of all the published cases of chronic perihepatitis ("Zuckergussleber") Nicholls writes: "Our recorded cases clearly prove that cirrhosis of the liver is by no means a frequent accompaniment of hyaline perihepatitis." *E. R. Le Count.*

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LIVER, DISEASES OF: CIRRHOSIS. (II. CLINICAL).

—The classical division into two classes: (1) Portal cirrhosis (synonyms: Laënnec's cirrhosis, hob-nailed liver, atrophic cirrhosis) and (2) biliary cirrhosis (synonyms: Hanot's cirrhosis, hypertrophic biliary cirrhosis) will be preserved here, but with the distinct explanation that the clear-cut distinction which the two terms seem to imply cannot always be made out, as the symptoms of the two varieties run into each other almost inextricably in many of the cases. However, the two classes named above enable us theoretically better to understand the disease.

1. Portal or Atrophic Cirrhosis.—The symptoms of the first stage are not at all characteristic of the disease, but are due to the action upon the stomach and intestines of the most frequent cause of the hepatitis, *i.e.*, alcohol. There may be morning retching or vomiting, with discharge of mucus, in conjunction with other symptoms of gastric catarrh, such as loss of appetite, nausea, sensations of weight and distention after meals, gaseous eructations, disagreeable taste in mouth, temporary and slight elevations of temperature, irregularity of the bowels,—at one time costive, at another time loose,—a tendency to hemorrhoids, etc. Perhaps a slightly yellowish color of the conjunctivæ may be noticed from time to time. Examination may elicit tenderness in the epigastrium and sensitiveness over the liver, which by percussion and palpation may be found somewhat enlarged. These symptoms are obstinate, and yield only slightly to treatment, and when such is the case in a person who has for a long period of time been addicted to alcohol, our suspicions may be aroused as to the presence of cirrhosis of the liver in an early stage.

The second stage, as the morbid process in the liver progresses, presents a very definite train of signs and symptoms which are due to (1) the portal obstruction, and (2) the impairment of the hepatic function brought about by the destruction of the liver cells.

1. The obstruction to the portal capillaries, so soon as the collateral circulation is not sufficient to carry the portal blood to the heart, produces serious symptoms. There is a chronic hyperæmia of the gastro-intestinal tract causing an intensification of the already existing gastric and intestinal symptoms (as above). Ascites makes its appearance in at least eighty per cent. of the cases, and it may be the first symptom noticed by the patient. It is usually slow in development, but may assume enormous proportions so soon as the collateral circulation becomes inadequate to carry the portal blood to the heart. This collateral circulation is given by Osler as follows: "1. The accessory portal system of Sappey, of which important branches pass in the round and suspensory ligaments and unite with the epigastric and mammary systems. These vessels are numerous and small. Occasionally a single large vein (parumbilical) or several smaller ones may run from the left division of the portal vein, in the round ligament, alongside the obliterated umbilical vein, to the umbilicus, where they communicate with the epigastric system. There may be produced about the navel a large bunch of varices: the so-called caput Medusæ. Other branches of this system occur in the gastro-epiploic omentum, about the gall bladder, and, most important of all, in the suspensory ligament. These latter form large branches, which anastomose freely with the diaphragmatic veins, and so unite with the vena azygos. 2. By the anastomosis between the œsophageal and gastric veins, the veins at the lower end of the œsophagus may be enormously enlarged, producing varices which project on the mucous membrane. 3. The communications between the hemorrhoidal and inferior mesenteric veins. The freedom of this communication is very variable. 4. The veins of Retzius, which unite the radicles of the portal branches in the intestines and mesentery with the inferior vena cava and its branches, to which system belong the whole group of retroperitoneal veins. Œdema of the legs and feet, of the external genitals, and of dependent parts of the abdominal walls is frequent in the later stages of the disease, and is due to the pressure of the distended abdominal contents upon the veins coming from the lower extremities, as well as to the enfeeblement of the general circulation, and malnutrition of the patient."

Hemorrhages may take place from the gastro-intestinal tract at any time, either from the stomach or from the intestine. The smaller ones are probably due to the bursting of congested capillaries. Larger hemorrhages are due to the ulceration or rupture of one of the varicose, dilated veins lying in the cardiac end of the stomach and the lower part of the œsophagus. The hemorrhage may be very profuse and quickly fatal. Epistaxis and cutaneous hemorrhages may occur later in the disease. Hemorrhoids are frequent and readily bleed. The gastro-intestinal hemorrhages often give temporary relief to the digestive disturbances. Pain and tenderness over the region of the liver and spleen may also be complained of at various times, and these attacks are doubtless due to attacks of local peritonitis. Pain may also be referred to the angle of the scapula, and to the tip of the right shoulder. An adequate explanation of these referred pains cannot be given at the present time (Schaefer). There is no fever in this variety of cirrhosis, and when present, it is due to complications. The spleen is enlarged in all but one-quarter of the cases, and is probably caused by not only the portal obstruction, but also by the absorption of toxins from the intestinal tract.

2. Symptoms referable to disturbed hepatic function. In pure portal or atrophic cirrhosis jaundice is not the rule, and, if present, is usually light and due to the duodenal catarrh. Digestive disturbances become more extreme, and malnutrition and loss of flesh and strength are pronounced. The patient becomes nervous and irritable. The heart's action is enfeebled, the respiration labored and accelerated, in part from the elevated condition of the diaphragm due to the abdominal distention. The urine is often diminished in amount, and presents an abundance of urates and sometimes bile pigment. The urea may be found decreased. Albumin and casts indicate coincident disease of the kidneys. In rare instances it may contain sugar. The condition of the blood is not characteristic. There is no increase in the leucocytes, no extensive diminution either of the hæmoglobin or of the number of the red corpuscles, but epistaxis and petechiæ in connection with the general, as opposed to the portal, circulation would seem to indicate that the blood is either of poor quality, or else contains toxic substances capable of producing degeneration of the capillary walls. The occasional occurrence of œdema preceding ascites is another indication of this toxic or impoverished condition of the blood.

Physical Examination.—There may be a faint, and perhaps recurrent, yellowish tint of the conjunctivæ and skin, or this latter has an earthy, ashen look, and is dry and scaly, often with eruptions. The venules on the nose and cheeks are distended. The face assumes a characteristic appearance. It is thin, the eyes are sunken, and the malar bones are very prominent. The tongue is dry and coated. The distended abdomen contrasts sharply with the greatly emaciated chest. The navel protrudes, and the superficial capillaries and veins are prominent (caput Medusæ). Œdema of the extremities is likely to appear. The physical signs of ascites are usually typical. There may be some tenderness over the liver and spleen. These two organs may not be palpable until paracentesis is performed, when the liver may be found moderately enlarged (in the early stages or when combined with fatty infiltration), or, what is more characteristic, small, hard, nodular, and contracted. The edge of the spleen is readily felt, and the organ may be doubled or tripled in size, and is dense. There may be a systolic functional murmur at the apex of the heart, and a venous hum in the epigastrium.

Complications may coexist and give appropriate physical signs and symptoms, such as pleurisy with effusion, emphysema, endocarditis, myocarditis, pericarditis, arteritis, cirrhotic nephritis, chronic pachymeningitis, tuberculosis, peripheral neuritis, thrombosis of the portal vein, etc.

Course, Duration, and Prognosis.—After ascites or hemorrhages have made their appearance, the course is usually rapid, and the end is reached within a year. In many cases the course may be protracted over a long period, or even altogether arrested in a few cases, if the diagnosis be made early, the causes avoided, and the treatment initiated before the alterations have become considerable. Death usually results from intercurrent disease or from progressive exhaustion. In not a few cases cerebral symptoms occur suddenly — delirium, stupor, convulsions, coma, and death.

2. Hypertrophic Cirrhosis.—This so-called biliary cirrhosis is a distinct disease, and in typical cases presents many points of marked contrast with the preceding variety. In the first place, while in the majority of cases there is a definite history of hard drinking, yet from the fact that in other cases there is no such history, we must conclude that alcohol is not always the immediate cause. There is increasing evidence in favor of regarding this form as definitely of infectious origin. There is often a history of gall stones, or of obstruction of the duct from other causes. Then, again, the greater number of cases occur in young adults. The early symptoms do not amount to more than a general failure of health, loss of appetite, slight weakness, and perhaps a sensation of weight in the right hypochondrium. The onset of jaundice is often the first real symptom. With this there is frequently a series of attacks of pain in the region of the liver, with tenderness, and with each of these attacks the jaundice becomes more marked. Jaundice increases and persists throughout the course of the disease. The number of leucocytes in the blood may be found increased. The abdomen enlarges, as a result of the increased size of the liver, whose surface is smooth and indurated. The liver remains large throughout the disease and does not contract. The jaundice is commonly intense, but bile is very rarely absent from the stools. Ascites and hemorrhages are either entirely absent or else slight. There are no evidences of portal obstruction. These patients are liable to severe attacks of gastro-duodenitis with jaundice, attended with fever and cerebral symptoms. These attacks are often fatal. Enlargement of the spleen is very common throughout the disease. The occurrence of fever is an important feature of the disease, being thus unlike portal cirrhosis. There is often an afternoon rise of temperature which, during the severe attacks, may run high, to assume a hectic type suggestive of hepatic abscess or pylephlebitis. These attacks behave like a bad obstructive jaundice, although the hepatic and common bile ducts are pervious. The patients have pain over the liver, vomiting, constipation, intense and increasing jaundice, high fever, emaciation, rapid pulse, delirium, convulsions, coma, and death.

The *prognosis* is unfavorable, but yet in many cases the course of the disease is slow, and in some it is arrested altogether, the patients having no symptoms, although the cirrhosis still exists.

The *diagnosis* is often difficult. Gradual and continued jaundice without cause, continuing for a long time, associated with persistent enlargement of the liver and spleen