with a few flakes of fibrin. There is a similar reddening and swelling of the mucous membrane fading away towards the stomach. No trace of tumour near the line of incision, or in any other part of the stomach."

"Microscopic Examination.—The growth is a carcinoma, which appears to have originated in the alveoli of the pyloric glands. The transition from the normal to the abnormal epithelium is sudden, the cells being at once reduced to half their size. While their granular protoplasm is retained, the nuclei are spherical and centrally placed. Still, in all parts of the tumour isolated cells are observable, with flattened peripherally situated nuclei and clear contents. The tumour penetrates the muscularis mucosæ, and extends horizontally beneath it, so as to undermine the healthy mucosa; it insinuates itself between the bundles of the muscular coat, and even penetrates them. The alveolar structure is most marked in the upper portion of the growth, the cells being here contained in long narrow spaces, some of which are provided with a lumen. In the submucosa and muscularis the alveoli are much smaller, irregular in shape, and with very little interstitial substance. The ulceration is extensive, and in places extends as far as the muscularis mucosæ."

REMARKS

ON

BILIARY OR "HYPERTROPHIC" CIRRHOSIS, WITH A CASE IN WHICH THERE WAS ATROPHY OF LIVER.

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THE following is an account of the case:—M. C., aged 37, married. Family history good. She has had eight children, of whom five are alive and well and three died of measles. She has had no bad illness and has always been healthy though delicate. She has always been strictly temperate, and there is no history of syphilis. She has had a great deal of trouble and lately has suffered from nervous depression. Her last confinement occurred two years previously. She gave no history of illness following any of her confinements. The present illness began 15 months ago with jaundice, which has been worse at intervals and has never entirely disappeared. On her admission it was said to be more marked than ever before. She complained often of pain in the right side, suffered from violent attacks of vomiting at times, but never brought up any blood nor passed any in the stools. About once in every two months she noticed that she passed a small quantity of water for some days, and this would be followed by a copious flow. She had always suffered from constipation, and since the appearance of the jaundice from dyspepsia. She had never had fits nor convulsions of any kind. Lately her manner has been strange, and she did not always seem conscious of her surroundings, for instance, whilst carrying food to her mouth she would let it drop without appearing to notice that she had done so. On August 29th, 1889, she was lightheaded, and her friends brought her to the hospital. This was all the history that could be obtained from her friends; the patient herself was incapable of giving us much information. She was admitted on August 30th; her manner was dull and heavy, she allowed her friends to answer all questions addressed to herself, and gave the porter a lozenge under the impression that it was a sixpence. She sat up in bed and talked all the night, and from time to time had violent fits of yawning. She refused her medicine, but took milk and beef tea.

When I saw her on August 31st the patient was sitting up in bed and talking to herself; she did not answer questions unless spoken to loudly, and it was found on subsequent inquiry of her friends that the answers she did make were not altogether correct. She was very weak, rather emaciated, and deeply jaundiced. On examination a soft systolic murmur was audible over the præcordial area, the lungs were healthy, the liver dulness extended in the nipple line from the sixth rib above to a point about half an

inch above the lower border of the ribs. The edge of the liver could not be felt, there was no tenderness over it. The urine contained much bile-pigment, a trace of albumen, and some crystals, which looked like leucin plates, but I was not absolutely sure that they were leucin. Specific gravity, 1020. There were also renal epithelial cells and some epithelial and hyaline casts.

On September 2nd the patient was partly comatose, the motions were passed into the bed: they were green in colour and mixed with about 10 ounces of dark blood. The urine was retained, and 12 ounces were drawn off by catheter: it had the character above mentioned and contained 0.6 to 0.7 per cent. of urea, estimated by Russell and West's process. She answered sensibly when spoken to, and said that she was in no pain. A few small petechial spots on the chest; respiration regular, deep, and sighing; tongue covered with thick yellow fur, sordes on teeth and lips, and odour of breath very offensive. No liver dulness detected, apparently from distension of intestines.

On September 3rd her general condition was much the same; the liver dulness was now distinctly made out to be two inches in the nipple line. Examination of the urine showed well-marked crystals of leucin and tyrosin, the leucin plates being the more numerous; there was, as before, much bile-pigment and a trace of albumen; there were renal cells and epithelial casts. On examining a specimen of the blood a few crystals of hæmoglobin were seen lying in the plasma, the red corpuscles did not form rouleaux readily, the red and white discs were in the normal proportion. A small motion containing a little blood was passed in the evening. No vomiting, but violent fits of yawning from time to time.

September 4th. Jaundice more intense; patient much emaciated and in a comatose state, from which she could not be roused. A small motion, not green in colour and not containing blood, was passed. The fits of yawning had ceased; head and face covered with cold sweat. Respiration sighing, 24 to minute; pulse 140, very small and weak; liver dulness two inches in nipple line; tongue dry and foul, and teeth covered with sordes. Throughout the patient had no convulsions and no vomiting. The temperature was normal to the last day of life, when it rose to 100° in the evening, and remained at this level till death. Urine: Specific gravity 1030, no sugar, acid, large trace of albumen, much bile pigment, large crystals of oxalates, bundles of tyrosin crystals, and greasy-looking plates of leucin were all seen in great abundance. The amount of urea estimated by Russell and West's method was only 0.3 per cent.; the quantity passed in the twenty-four hours cannot be exactly stated, as the whole of the urine passed could not be obtained. Death occurred in coma on September 5th.

Necropsy Twenty-six Hours after Death.—Body emaciated; rigor mortis present in legs; a few small, scattered, petechial spots on legs and upper part of chest. The skin and the organs generally, with the exception of the brain, were bile-stained. There were recent adhesions over the greater part of the lung; both lungs were somewhat emphysematous, and a large hæmorrhage had taken place into the lower lobe of the right lung; right lung, 19 ounces; left, 10½ ounces. Heart normal; its muscle was not fatty. The blood was everywhere perfectly fluid, and almost black in colour. No crystals were seen in the portal blood. On opening the abdomen, the peritoneum was normal; no ascites; duodenum distended with gas, and contained, together with partially digested food, some large drops of oil. The opening of the bile duct was patent, and a few drops of very dark bile escaped on pressing the gall bladder. The liver weighed 21½ oz.; it was very small and somewhat flabby to the touch. The capsule was not particularly wrinkled; the surface was smooth, and the shape of the organ normal. On section, the left lobe was in colour a bright canary, firm in consistence, the surface finely granular, the lobules being raised above the level of the section, their outlines rounded, perhaps fused into groups, stained deep yellow, and plainly demarcated from each other by a paler tissue that lay between them. In the right lobe the appearances were much the same, with the exception that there was a large area of dark red material occupying the mesial portion, and similar smaller areas in other parts of it; in these dilated vessels were observed. These changes extended throughout the liver, but were less noticeable in a zone, which was, however, yellowish in colour, about a quarter of an inch in depth, along the posterior border. The spleen weighed 3½ oz., dark and soft. Kidneys: capsules stripped easily, leaving a smooth surface; parenchyma of cortex soft and pale. The pyramids showed deep purple congestion, the venæ rectæ prominent and full of dark blood; ratio of cortex to pyramids normal. Intestines normal; contained some

hard scybala, mostly yellowish in colour, and apparently composed largely of fatty matter. Brain small; weighed $36\frac{1}{2}$ oz., otherwise with the membranes it was normal. Pancreas and suprarenals normal. Uterus contained one small intramural fibroid.

The following is an account of the histological changes in the liver. There is new formation of fibrous connective tissue, rather loose in texture, for the most part richly nucleated and abundantly supplied with vessels, forming interlobular tracts, separating the individual lobules from each other by narrower or broader bands of connective tissue. Within the lobules between the columns of liver cells and also between the individual cells is a more delicate tissue, hyaline in appearance. This is most abundant and more fibrous at the periphery of the lobules. The lobules in the early stages retain the general arrangement of their cells, but in more advanced parts the cells are irregularly arranged, and often widely separated from each other by the intervening new growth. In other parts there is a very abundant infiltration of round cells between and around the liver cells, accompanying a similar round-celled infiltration in the interlobular tissue. The amount of this connective tissue varies much in different fields. In some the whole field is occupied by fibrous tissue with a few scattered remnants of liver cells, or total disappearance of these, and there is every degree of variation from this extreme to fields in which the lobules are well marked and preserve their normal arrangement, but are separated from each other by abnormally wide septa of connective tissue with finer intralobular hyaline growth. The degree of atrophy of the liver cells themselves showed corresponding variation; in the less advanced parts they looked fairly healthy. Where round-celled infiltration was marked the nuclei of the liver cells were proliferating; in other parts the cells were atrophied or in process of disappearing, containing pigment and other granules in the protoplasm, and very rarely fat droplets. Fatty degeneration may be said, however, to be entirely absent throughout the liver. In the interlobular connective tissue generally, and especially in those spots in which the nuclear growth is rich, there are seen in abundance the double rows of nuclei usually taken to represent small biliary ducts. They appear to branch and form networks, and in most places their epithelium is undergoing desquamation, the lumen of the tubes in cross section being choked with products of cell proliferation. I could nowhere detect transformation of liver cells into connective tissue. The branches of the portal vein showed some dilatation and thickening of their walls.

Hypertrophic cirrhosis: showing interlobular connective tissue in early stage; it is invading chiefly the periphery of the lobules, and the hepatic cells are becoming atrophied in places; the intercellular new growth is well marked, as are the biliary ducts in the interlobular tissue (aa).

In sections taken through the red areas the changes differ some-

what from the foregoing. They consist of large areas composed almost entirely of round cells, amongst which no liver cells can be distinguished, accompanied by extensive hæmorrhages. In many of these areas the small biliary channels above mentioned are especially thick set and conspicuous, and the cubical cells lining them in active proliferation; in some places they run parallel to one another, suggesting that they represent the remnants of atrophied lobules. Generally speaking the destruction of the hepatic cells is complete in these areas, but in parts they can be distinguished, and present somewhat different changes to those found in the other parts of the liver; their protoplasm is swollen, clouded, and finely granular, so that their outlines are obscured, and their nuclei invisible.

In the kidneys the epithelial cells of the convoluted tubes had lost their contour, were swollen, with granular protoplasm entirely obscuring the nuclei, which were indistinguishable; no lumen could be detected in the tubes which were filled by the swollen epithelium. In some of the loops of Henle there are similar changes in the epithelium, but this is not universal as in the convoluted tubes. Some of the loops showed earlier changes, consisting of proliferation of nuclei and a granular appearance of the protoplasm. In some of the glomeruli the nuclei were, perhaps, abnormally abundant, otherwise the glomeruli were healthy. In all other respects kidneys quite normal, as were also the heart, spleen, and suprarenals.

From the symptoms observed during the short time that the patient was under my care, the diagnosis made was acute yellow atrophy of liver, supervening on jaundice of some duration. The diminished size of the liver, jaundice, deepening coma, hæmorrhages, presence of leucin and tyrosin in the urine, with failing excretion of urea, pointed to this. At the necropsy the naked-eye appearances in the liver did not correspond with the changes found in acute yellow atrophy; the smooth unwrinkled capsule, the granular section, bright yellow colour and firm consistence, are the chief points of difference. Microscopic examination cleared up the diagnosis by showing that the morbid change in the liver consisted in a new formation of connective tissue around the lobules (monolobular), with round-celled infiltration in parts of it, and of the same growth within the lobules between the liver cells (intracellular); in addition the little channels lined with cubical epithelium which lie in the interlobular tissue, and are generally held to be biliary ducts, were exceedingly numerous, and their epithelium appeared to be proliferating. As to the origin of these little ducts in such cases, there is considerable difference of opinion amongst authors. It is considered by some that they form the essential element in the morbid anatomy of hypertrophic cirrhosis, but it has been shown that they are also present (though not so numerous) in the ordinary forms of cirrhosis, and cannot, therefore, be held to be a distinguishing characteristic of any one variety. Certainly they are more abundant and conspicuous in this case than in sections of ordinary alcoholic cirrhosis. Goodhart is of opinion that there is no new formation of ducts, and quotes Cornil and Ranvier to the same effect, namely, that the increase of biliary ducts is due, not only to the abnormal prominence of those already in existence, but to the conversion of the bile-capillaries into ducts by the extension onwards of the duct epithelium.¹ In this case they are most prominent in situations where the hepatic cells are most extensively destroyed; I could not distinctly make out ducts in process of formation. A more characteristic feature than the presence of these ducts in the interlobular tissue—numerous though they are—and one which gives the sections a quite different appearance to those of the ordinary form of cirrhosis, is the intralobular formation of connective tissue separating the cells from each other. As to the mode of origin of the newly formed tissue, whether within the lobules or growing into them from without, the more advanced change in the periphery of the lobule is in favour of the latter view being the correct one. I think that the "red patches" must have occurred quite late in the disease, towards the end of the illness, when the morbid process was intensified, giving rise to hæmorrhages and rapid round-celled infiltration.

The minute changes in the liver mark the case as one of intracellular or biliary (hypertrophic) cirrhosis, according to the ordinary classification, or adopting Mr. Munro Smith's² division of cases of cirrhosis into two groups, obstructive and irritative, it falls under his first subdivision of obstructive cirrhosis. It is sufficient to state that the entire absence of any evidence or his-

¹ *Atlas of Pathology*, New Syd. Soc., fascic. iv, p. 35.

² *JOURNAL*, 1888, vol. i, p. 1381.

tory of syphilis excludes this as a cause of the condition; and the changes present do not resemble those found in the red atrophy of liver of British authors. In classifying the case, however, one must take into consideration the clinical symptoms as well as the anatomical changes. These symptoms afford a marked contrast to those of hobnailed cirrhosis; there was no alcoholic taint, no ascites, no enlargement of spleen, nor dilatation of abdominal veins. On the other hand, jaundice was present to a degree most unusual in ordinary cirrhosis, and death took place with symptoms of malignant jaundice. The hæmorrhages which occurred late in the case may reasonably be attributed to the profound blood changes then present, and not as in hobnailed cirrhosis, to obstruction to the blood flow through the portal system. Both on clinical and anatomical grounds, then, the case corresponds to hypertrophic or biliary cirrhosis, "*cirrhose hypertrophique avec ictère*" of the French, except that there was no hypertrophy, but instead atrophy of liver. Whether there had been hypertrophy at some time in the period of fifteen months during which jaundice and other symptoms were present, it is impossible to say; the patient frequently complained in the earlier stages of pains in the hepatic region; pain is more commonly present in enlargement than in contraction of the liver, and so far as this symptom goes it is in favour of an antecedent hypertrophy. With regard to this point, I may here quote a case of Murchison's³ which strongly resembles my patient's. The patient was a girl, aged 12. At the age of 6, she contracted a severe chill from sea bathing; her illness began four years later with jaundice; the liver at that time "reached down almost to the pubes;" later on it was not enlarged. There was at this time slight jaundice and enlargement of the spleen, but no ascites. She died after two years' illness, with symptoms of acute yellow atrophy. At the necropsy, the liver was small and rounded, puckered and irregular on the surface, and weighed only 16 ounces. Comparing this case with that of my patient, there is close correspondence as regards long duration of symptoms, termination by icterus gravis, and *post-mortem* changes. In the former there was great enlargement of the liver at one stage of the illness, and this affords some ground for supposing that enlargement of the liver was the cause of the pain from which M. C. suffered.

The question here arises as to whether "hypertrophic" as a distinguishing term for this form of cirrhosis is not a misnomer, as hypertrophy is not a constant feature of the disease. The size of the liver varies much in individual instances of all kinds of cirrhosis, and it is doubtful whether it is desirable to make hypertrophy an essential characteristic of one variety. On referring to the literature of hypertrophic cirrhosis, I find that nearly all the textbooks describe it as being attended with great increase in the size of the liver, but that they are silent as to subsequent changes in the direction of atrophy that may ensue in cases where life is prolonged beyond the usual period in this disease. Strümpell, however, states "that too much stress has been laid upon this point. If in many cases of hypertrophic cirrhosis the liver has remained large to the end, this is probably in part due to an early death, before there was opportunity for much shrinkage. Cases that lasted longer have presented a contracted liver."⁴ He does not, however, give any references to such cases, and after careful search I can only find accounts of two cases that correspond to the one above reported. One is given by Dr. West;⁵ the patient was a boy, aged 2; the final illness lasted nearly four weeks; the diagnosis during life was acute yellow atrophy; he had had a severe scald of the abdomen four months previously, from which the illness may have dated. The liver was thought to be enlarged a few days before death, but at the necropsy it is stated to be small in size; the weight is not given. Both naked-eye and microscopical appearances exactly tally with those found in my patient; there was here also cloudy swelling of the renal cortex; it would be interesting to know if this is a constant change in such cases. The other case is the one of Murchison's already referred to, and which Dr. West also cites.

These instances, I think, show that if the term "hypertrophic" is applied to this form of cirrhosis, it is well to bear in mind that hypertrophy is not necessarily present in all stages of the disease, and possibly may not occur at all in some cases, at any rate to a degree capable of clinical recognition. This point is not without its practical bearing, for if in a case of atrophy of liver with jaundice the diagnosis was satisfactorily made of intracellular (hyper-

trophic) cirrhosis, the prognosis with regard to immediate danger to life would be more grave than if the alternative lesion, hobnailed cirrhosis with jaundice, were present, for if in the former case atrophy of the liver has occurred to a sufficient extent to be recognised clinically, the symptoms of icterus gravis may at any time supervene, and speedily prove fatal.

The termination by icterus gravis seems to be characteristic of the course of the disease; the distinction from acute yellow atrophy and phosphorus poisoning, in which the same symptoms are present, lies in the fact that in those maladies these symptoms come on in persons in whom there is no evidence of previous liver disease, while in hypertrophic cirrhosis there is a history of jaundice for some time before their onset. The symptoms of jaundice, etc., in the early stages are probably caused by reabsorption of bile from obstruction to its flow, owing to the changes in the minute biliary passages. As the disease progresses, partly from irritation by the retained bile, partly from the increasing atrophy of the hepatic cells, both the final stages of the manufacture of bile by the liver are imperfectly performed, and also the nitrogenous tissue waste fails to be completely converted by it into a form fit for elimination by the kidneys. So long as the kidneys act well grave symptoms may not arise, but after a time the continued passage through the renal circulation of abnormal (toxic) material irritates the renal epithelium, and elimination by these organs becomes more and more faulty.

In this way the cloudy swelling of the epithelium of the convoluted tubes may be supposed to be originated. Finally, renal excretion is reduced to a minimum, the toxic products arising from reabsorption of bile, from mal-dissimilation of nitrogenous tissue waste by the liver, and non-elimination of it by the kidney, accumulate in the blood, and death takes place from the poisonous action of these upon the central nervous system.

THE RELATIONS OF SUBDIAPHRAGMATIC ABSCESS TO THE THORACIC VISCERA; WITH THREE ILLUSTRATIVE CASES.

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THE separation of the thoracic from the abdominal viscera by means of the diaphragm is incomplete or imperfect at two points: Anteriorly, between the margins of the muscular fibres arising from the ensiform cartilage and the adjoining costal cartilages, the fibres of the diaphragm are scanty or altogether wanting, and the space is filled with connective tissue having in relation with its superior or thoracic aspect the pleura, and with its inferior or abdominal surface the peritoneum. It is at this point, therefore, that we meet with phrenic or diaphragmatic hernia, and it is by this channel that occasionally pus will find its way from the mediastinum to the abdomen or the reverse direction. In 115 cases of suppurative mediastinal disease collected by Hare, three were of this character; in one the pus made its way upward from the abdomen, in two it burrowed downward into an adherent liver.

Posteriorly, the arch of the internal ligament affording passage for the great psoas muscle affords another channel for the passage of fluids upwards or downwards. On its upper surface the diaphragm is in contact with three serous membranes, the bases of the pleura on either side and in the middle, covering the tendinous centre, the pericardium. On its lower surface is found a portion of the general parietal peritoneum.

The viscera in relation with it are the bases of the two lungs and the heart above; the liver, spleen, and both kidneys (particularly the left) beneath; the large end of the stomach is also in contact with it. As a result of these relations it is by no means uncommon to find suppurative disease traversing these boundaries either by means of the weak points already described or by setting up adhesive inflammation followed by perforation. Circumscribed peritoneal abscesses frequently occupy the right and left hypochondria, and Dr. Fagge has described¹ sixteen cases of this sort. In one of them the abscess was on the convex surface of the left lobe of the liver, and there was a perforation through the diaphragm leading into the left pleural cavity. In a very

³ Diseases of Liver, Case CLXXIX.

⁴ Textbook of Medicine, p. 454.

⁵ St. Bartholomew's Hospital Reports, vol. xliii, p. 224.

¹ Guy's Hospital Reports, vol. 19, p. 213.