here there is no tumour we may take the tenth rib for a landmark, for, as Tillaux has pointed out, its tip can be felt to be prominent and movable, and a sense of grating is experienced when it is moved against the ninth rib, to which it is attached by a short ligament.

On opening the peritoneal cavity the fundus of the gall bladder presented, partly overlapped by a linguiform process of liver, and having numerous adhesions to the colon below. The significance of the linguiform process and of the adhesions has already been referred to. The forefinger was then passed along the ducts up to the foramen of Winslow, which could only just be reached, but as it was not necessary—for reasons already given—to make a thorough examination of the common duct, there was no need to enlarge the incision for this purpose. So far as the finger could examine the ducts, no stone was felt.

The gall bladder—after placing a sponge below it to prevent the escape of any fluid into the peritoneal cavity—was aspirated, and 7 ounces of an opalescent mucoid fluid were withdrawn. This fluid was alkaline, had a specific gravity of 1.010, was not ropy, and showed no trace of bile. This last fact need cause no surprise, for in cases of blocking of the cystic duct (which we are considering) no bile can enter the gall bladder, and the distension of that organ is brought about by the gradual accumulation of the secretion of the mucous membrane with which it is lined.

After the withdrawal of the fluid the gall bladder was incised at the end of the fundus, this spot being chosen because the gall bladder is often considerably drawn up under the liver after it has been emptied of its contents, and unless the incision is low down there would be a difficulty in attaching the gall bladder to the parietal wound. The forefinger was then passed into the gall bladder to explore it, and the ducts were again examined outside, but no sign of stone could be detected except some slight brownish *débris* from the neighbourhood of the orifice of the cystic duct. A probe was passed through the opening in the gall bladder and along the cystic duct, and by this means it was made clear that there was no organic stricture.

It was probable, therefore, that the obstruction of the cystic duct had been brought about by the dragging on the gall bladder caused by the adhesions to the colon which have already been described. That these adhesions may have been caused by the existence of gall stones at some time or other is probable, though I could discover none at the time of operation.

The case then proved to be one of simple hydrops of the gall bladder caused by some kinking of the cystic duct from the adhesions between the colon and the gall bladder. I therefore determined to attach the opening of the fundus of the gall bladder high up in the parietal incision—to prevent, if possible, any further dragging upon the organ and a recurrence of the mischief. At the same time the gall bladder was drained in order to carry away any fluids that might collect after operation, and which might otherwise escape into the general peritoneal cavity. The gall bladder was sewn to the peritoneum and transversalis fascia only, by a running catgut stitch which when pulled tight fitted closely round the drainage tube which had been placed within the gall bladder. The opening in the gall bladder should never be brought up to the skin, as under such circumstances a fistula is likely to form and to necessitate an operation for its closure.

The rest of the wound was closed with silkworm-gut stitches in the ordinary way. The tube in the gall bladder was left long, so that its outer end might be conducted to a wide-mouthed bottle kept by the side of the patient. The wound itself was thus kept dry and free from the discharges from the gall bladder which escaped into the bottle through the tube. It is now four days since cholecystomy was performed, and bile-stained fluid has been flowing through the drainage tube ever since. This fact is most important, for it shows that the cystic duct is patent, and that the theory of kinking of the duct from the dragging of the adhesions on the gall bladder was probably correct.

You will notice that the patient presents a slight icteric tint. This came on the day after operation, and is already rapidly disappearing. It was doubtless due to the manipulation of the ducts during their examination at the time of operation.

The drainage tube will be kept in the gall bladder for about a week; when, if all goes on favourably as at present, it will be removed, and the fistula allowed to close gradually.

This case was a very ordinary one of distended gall bladder, but it was produced, as we have seen, by a most unusual cause. Almost all such cases are dependent upon the presence of gall stones in the cystic duct; but I have here a collection of twenty-eight gall stones which I removed from a patient a few months ago, and in which case one of the largest stones was firmly impacted in the cystic duct, from which it was removed with some difficulty. In this instance a lady 63 years of age had had a swelling of the gall bladder for nearly twenty years, but about three weeks before I saw her the swelling had begun to enlarge rapidly, and rigors and high temperature had supervened. In short, an inflammatory condition had been set up in the quiescent hydrops of the gall bladder, suppuration followed, and a condition known as empyema of the gall bladder was established. Such a condition, unless speedily operated upon, is fraught with danger, and the case serves to exemplify one of the risks of an apparently simple disease. After the removal of 9 ounces of thin pus and the twenty-eight gall stones the gall bladder was drained for eight days. The fistula itself healed in the course of a month, and the patient has been well ever since. Cultures from the pus in this case at the time of operation showed numerous colonies of the bacillus coli communis, which probably served as the immediate cause of the suppuration. It is interesting to note that in this case also the linguiform process of liver, to which reference has been made, was present.

[Note.—The tube in the case which forms the basis of this lecture was removed on the eighth day after operation. The patient got up on the fourteenth day, and went home with the fistula healed on the twenty-first day. Bile was discharged through the tube or wound for about a fortnight after operation. Some time later Dr. Swinhoe reported that the patient was continuing in perfect health.—J. S.]

REMARKS ON THE PATHOLOGY OF ACUTE YELLOW ATROPHY OF THE LIVER.

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THE following clinical note of the case of acute yellow atrophy of the liver on which this paper is founded is by Dr. D. C. McVail, Physician to the Glasgow Royal Infirmary.

Lizzie J., aged 15, was admitted to the Glasgow Royal Infirmary on September 16th, 1899. She had general dropsy—excluding the face—and ascites. She had always been delicate, and had had measles six years previously. In February, 1899, her eyes became "jaundiced" and her urine brown in colour. She had swelling of the feet at that time which disappeared in a few weeks, but returned again two months ago after a chill, and has remained till the present. Diarrhoea set in a month ago and has been severe. There is no history of rheumatism. Patient is the eldest of her family, of whom the others are healthy. Her father and mother living and well.

State on September 17th.—She is thin and very weak, but not suffering from headache or other pain; she is rather deaf, although she has never had aurial discharge. She is slow at answering questions. Her tongue is red and dry; diarrhoea is frequent; she had twelve motions last night, all of which were small and fluid. Her urine is dark-coloured; the motions and urine are passed into the bed. There is no renal tenderness. There is considerable dependent oedema the abdomen is distended with fluid. There is oedema of the chest wall, and there are dilated veins on the abdomen and chest. There is no oedema of the face. The conjunctivae are somewhat yellow, but the complexion is pale. Her gums bleed slightly. There is no blood in the motions. The abdomen measures 29½ inches at its largest circumference; its surface blistered in two places from application of mustard. The lungs are resonant to percussion except at the bases behind, and laterally there is a curved line of fluid dullness on both sides, its highest point being at the level of the eighth dorsal spine. The respiratory murmur is deficient here, and also deficient over the whole of the right lung. There is no respiratory distress. The cardiac apex is in the fifth space; there is no murmur. The pulse tension is low; a tracing shows hyperdicrotism, with the respiratory curve plainly marked. The diarrhoea, under treatment, had lessened. No specimen of urine was obtained.

Vomited three times on the morning of September 18th. The abdomen was tapped and 6½ ounces of clear, greenish-yellow coloured fluid were withdrawn, containing a moderate amount of albumen, 5 per cent. of urea, and sufficient peptones to give the biuret reaction. No bile was present, but chlorides were abundant. The temperature on admission was 100°, but it sank to subnormal on the evening of the 18th, with a rising pulse and irregular breathing. At 9 P.M. on the 18th the patient was very grey-looking and cold; she had slight external strabismus of

the right eye. There were no twitches. A vapour bath was given for twenty minutes, the temperature half an hour afterwards rose to 100°. Brandy was given hypodermically on account of gastric irritability. Death took place early on the morning of September 19th from respiratory failure.

The post-mortem examination was conducted thirty-two hours and a half after death. Permission was not obtained to open the head.

External Appearances.—The body is much emaciated. The pupils are dilated and equal. Rigor mortis has completely passed off, and there is considerable post-mortem lividity of the abdomen and the whole posterior surface of the body. There is well-marked oedema of the legs, and over their outer and posterior aspects is seen an eruption of purpuric spots, with much brown pigmentation. The abdomen is swollen. On reflecting the skin the subcutaneous fat in the chest wall and abdominal parietes is found to be in very small amount.

Thorax.—The pericardium contains about 1 ounce of clear yellowish fluid. The heart is small, weighing only 4 oz., and there is an entire absence of the normal subpericardial fat. There is no abnormality of the valvular orifices or curtains. The ventricles are somewhat dilated. The muscular tissue is flabby, shows slight "thrush breast" appearance, and on section is pale and distinctly greasy. The coronary arteries are normal. No hæmorrhages are seen under either the visceral or parietal layers of the pericardium.

The right lung weighs 1½ oz., and is in an extreme condition of oedema, with marked hypostatic congestion of its inferior lobe. This lobe is loosely adherent to the diaphragm and lowest part of the costal pleura by a recent gelatinous exudation. There is no fluid in the right pleural cavity. About 12 ounces of blood-coloured fluid are present in the left pleural cavity, and old adhesions bind down the lower lobe of the left lung to the diaphragm and chest wall. There are a few ecchymosed patches under the costal pleura. The upper lobe of the left lung—like that on the right side—is oedematous, while the lower is completely carnified and sinks in water. The left lung weighs 11 oz.

Abdomen.—Twenty ounces of a clear, yellow-coloured fluid are present in the peritoneal cavity. The spleen is enlarged, weighs 6 ounces, and is of firmer consistence than normal. Its edges are sharp and well defined, and the capsule appears somewhat thickened. The kidneys together weigh 6½ ounces. The capsules are very easily removed, and the surface is pale, mottled, and somewhat yellow. On section the cortex appears pale and granular, while fatty streaks and, here and there, small hæmorrhagic spots are seen. The medulla is deeply congested. The kidneys, in fact, present the features of an acute tubular nephritis. The bladder and pelvic organs are healthy. The stomach is dilated, and shows some congestion and swelling of its mucous membrane, and there is a considerable quantity of glairy mucus present. The duodenum contains bile-stained mucus, and pressure on the gall bladder readily permits the bile to flow along the common bile duct through the biliary papilla into the duodenum. There is no obstruction of the common bile duct, though the structures entering the portal fissure of the liver are surrounded by a considerable amount of dense fibrous tissue. About 1 ounce of dark-green bile of a syrupy consistence is found in the gall bladder.

The liver is much diminished in size, and weighs only 2½ oz. Its greatest transverse diameter is 5½ inches, while a slice taken through the middle of the organ shows at its greatest depth a measurement of a little over 3½ inches. The capsule is thickened and in places roughened and granular, while an old fibrous adhesion exists between the right lobe and the hepatic flexure of the colon. The liver is of very firm consistence, more tough to cut than normal, and its edges are unusually sharp. On section the organ is found divided into two portions, a red and a yellow. The left lobe is very small, and is throughout of a red colour, and penetrating this red area is a fine greyish-coloured network. The right lobe is much mottled, and presents in the main an orange yellow colour. The yellow is in the form of irregular patches dotted and streaked throughout with red spots and bands. When freshly cut the yellow parts stand out more prominently than the red, giving to the cut surface a coarsely granular look and feel. No distinct lobulation can be made out in this yellow area, though, where Glisson's capsule is not thickened, the fine lobulation can be distinctly seen as areas of a fainter or darker yellow separated by red lines. In that part of the right lobe which is continuous with the left there is a thin rind of this red substance just under the capsule of Glisson. On the under surface of the right lobe two yellow nodules, about the size of a horse bean, stand out above the general level. The portal vein is seen to be distinctly corrugated, and its larger branches show this same feature with considerable distortion of the lumen in places.

The pancreas is of firm consistence. The mesenteric glands are enlarged and firm, but show no caseous or calcareous areas. The intestines are normal in appearance, apart from a marked swelling and congestion of the Peyer's patches and solitary glands. No ulcers or cicatrices are seen.

Microscopic Examination.—**The Heart:** Portions from both ventricles show slight fatty degeneration. This condition is pretty general, though more marked in some places than in others. **The Spleen:** There is a fibroid change present, as evidenced by the thickening of the capsule, the trabeculae, and the adventitial coats of the blood vessels. The walls of the pulp sinuses are thickened, and there is a large amount of hæmatoidin scattered throughout the organ. The kidneys show a very evident catarrh. The convoluted tubules, with scarcely an exception, contain swollen granular cells no longer capable of taking up nuclear stains, or only able to do so slightly. In transverse sections the convoluted tubules show a diminished lumen and the stellate fissure so characteristic of catarrh, while fatty granules and globules of small size are seen, on staining with osmic acid, in the basal parts of the secreting epithelium. The loops of Henle and the straight tubules have suffered much less than the convoluted tubes. It is to be noted, however, that even in the medulla, many of the former show extensive fatty degeneration, as evidenced by the numerous small fatty granules distributed through the epithelial cells, and by a loss of nuclear staining. Hæmatoidin or biliary granules in considerable amount are found in the epithelium of both the secreting and conducting tubules, while desquamated epithelium and fatty debris are found in the lumina of both the straight and the convo-

luted tubules. The Malpighian bodies and the remaining healthy straight tubules stand out in marked relief from the other opaque and granular structures, and apart from a few fat granules in the epithelium lining Bowman's capsule and scattered through the glomeruli, these bodies are healthy. Already there is a commencing increase of the interstitial tissue, as shown by the larger numbers of nuclei in the glomeruli and between the convoluted tubules.

The Liver: The surface of the liver shows numerous microscopical elevations and depressions, caused by the contraction of the dense fibrous tissue composing the capsule. Beneath this thickened capsule are large numbers of thin-walled, and evidently new-formed, blood vessels, lying around and between which are many formative cells or fibroblasts with old and young fibrous tissue. Several recent small hæmorrhages are present (as, indeed, they are throughout the greater part of the red substance), and there are evidences of older hæmorrhages in the shape of small accumulations of hæmatoidin granules. Where a yellow patch abuts on the capsule, the liver is seen to be divided up into irregularly-shaped and differently-sized areas by tracts of connective tissue, which contain fully formed connective-tissue fibres, numerous connective-tissue cells or fibroblasts and round cells. The latter occur in little heaps or accumulations here and there in the region of blood vessels, but are never very abundant. This fibrous or granulation tissue is continuous with that of the capsule, and the little islets of hepatic tissue lying between these fibrous bands are found to be in a state of very advanced degeneration, and show extreme fatty changes. In not a single section, taken from any part of the liver, was a healthy liver lobule to be found; all, though in varying amounts, presented an extreme degree of fatty change. The hepatic cells, with few exceptions, contain fatty granules and globules, or may be distended beyond recognition with a single large globule of fat. The hepatic cells which have most retained their form are to be found along the margins of the lobules. In many cases the degenerate liver cell has broken down, and numerous fine fatty granules and small fat globules are seen lying free amidst the liver cells. It is to be noted that the fibrous tissue formation has followed no very definite plan, though the older and more dense connective tissue formations are in the region of the portal systems, as in the multilobular type of cirrhosis. In some places two or three lobules are isolated by the connective tissue, while alongside such a condition a single lobule may be found divided up into several portions.

There is a very considerable quantity of fully-formed fibrous tissue in the portal systems, leading to great separation of the artery, duct, and vein from one another, and often bringing about considerable distortion and narrowing of the vein. Inside this general thickening a special vestment of fibrous tissue surrounds each tube. In the case of the arteries this new connective-tissue formation has occurred in the adventitial layer only, the intima and the media being perfectly healthy. The portal, interlobular or sublobular, and even the small central veins show, in addition to what may be termed an adventitial thickening, well-marked nodules projecting into the lumina of the vessels and composed of proliferated endothelial cells; there is here, in short, an endophlebitis. In some of the lobules a great dilatation of the capillaries passing to the central vein exists, giving rise to an imperfect type of the so-called "nutmeg liver," dependent, no doubt, on the narrowing of the central or sublobular veins. There is, however, no thickening of the capillary wall. Though surrounded by much dense connective tissue, the bile ducts themselves, with few exceptions, are quite healthy. Their layer of cubical or columnar cells is regular and perfect, and the lumen contains no foreign elements. Only very occasionally a duct is seen showing evidence of catarrh. In these cases—perhaps more frequent in the red than in the yellow substance—the lumen is filled with debris and desquamated epithelial cells of a globose or irregular form, while even at the basement membrane no cubical or columnar cells can be detected.

The small bile ducts in the interlobular spaces appear to be more numerous than normal at those points where the connective tissue is invading the lobule from its margin. Here it may be seen that the young

Fig. 1.—Proliferating hepatic cells from margin of a lobule.

connective tissue shaves off successive layers of hepatic cells, and small collections of these cells are found isolated from their lobule by fibrous tissue. It has already been shown that the healthiest cells exist at the periphery of the lobule, and from this point to the central part of the interlobular connective tissue—where true ducts are met with—there is evidently a gradual transition from these clumps of liver cells to the duct-like columns of hepatic cells or so-called new duct formations. At

the margin of a lobule, perhaps separated by only a single row of spindle-shaped connective tissue corpuscles, exists a small collection of hepatic cells. These cells are large and some contain many nuclei, two to five, while others exhibit a single large nucleus double the normal size. (Fig. 1.) There can be no doubt that these are proliferating hepatic cells. As we pass towards the centre of the interlobular space the cells, still proliferating as shown by abundant and double nuclei, arrange themselves in more definite columns, become smaller in size with smaller nuclei, but neither do they lose their original polygonal shape nor do they cease to be solid columns of cells. They may approach very closely the normal duct appearance, but invariably the polygonal shape of the cell and the large oval and more faintly staining nucleus suffice to distinguish these pseudo-ducts from the true ducts, which have smaller rounder and more deeply staining nuclei, and exhibit a more definite cubical shape (Fig. 2). Occasionally the lobule seems to be broken up

Fig. 2.—A, peripheral part of a lobule showing degenerated and fatty hepatic cells and at extreme margin healthy multi-nucleated cells; B, hepatic cells cut off from their lobule; C, columns of hepatic cells or so-called pseudo-ducts; D, columns of hepatic cells still more closely resembling bile ducts; E, true bile ducts.

into columns of hepatic cells by invasion of the connective tissue in a radial rather than in a concentric fashion, but the latter is decidedly the more common. In places numerous round cells are found insinuating themselves between the columns of hepatic cells, more especially when the latter are observed to be breaking down. These columns of hepatic cells may contain in their interior few and small fat globules, but never extreme fatty changes. Here and there a few fat globules are seen in the blood vessels lying in the interlobular connective tissue, while similar globules are observed in what I take to be lymph channels in the same area.

The red area, or "red substance of Zenker," merely represents a further stage of the condition found developing in the interlobular spaces between the degenerated and fatty liver lobules constituting the yellow area. Here practically all the fatty tissue has been got rid of, presumably that through the agency of the leucocytes. The fatty debris is not discharged by the bile ducts, since not even in tissues prepared by means of Professor Workman's gelatine method, to prevent the duct contents from being shaken out during the processes of cutting and washing after freezing, could fatty matters be observed in either the larger or the smaller bile ducts.

The connective tissue in the red area has still further increased, and, apart from a very occasional remnant of a degenerated and fatty lobule, there is no true hepatic tissue to be seen. Very few round cells are present here, but there are very numerous connective tissue corpuscles along with old and more recently formed fibrous tissue. Amidst this connective

tissue are many large and thin-walled blood vessels, giving rise here and there to an angiomatous appearance. In places vessels are seen in process of formation from flattened endothelial or large fibroplastic corpuscles, and many of the large, thin-walled blood vessels are of this origin. Some of them, however, must be regarded as the original capillaries and vessels, which were seen in process of dilatation in the "nutmeg"-like portions of the liver in the yellow area, and which by an extension of the same process have assumed angiomatous characters.

If a portal system is examined, it is found to be surrounded by a very considerable amount of dense fibrous tissue, while just beyond this appear columns of hepatic cells, radiating out in all directions. These columns, however, though alike in the size and shape of their cells, are not of such simple structure as in the yellow portion of the liver. They are now seen to branch, and show at their extremities club shaped formations consisting of cells with dividing nuclei. Further, these cylinders have anastomosed with neighbouring columns of cells to form an irregular network, and from the cords of this network solid sprouts are again being given off. It may be mentioned that there is nothing here to suggest that these networks are really branching ducts; no basement membrane can be detected, while such a membrane can be demonstrated even in the most minute of the bile ducts. Apart from these columns of hepatic cells, though sometimes in continuity with them, are epithelial or hepatic cells arranged in an irregular fashion, while isolated hepatic cells are also to be recognised lying amidst connective tissue. No crystals of leucine or tyrosine were observed in sections of the liver, nor could these substances be obtained by evaporating down extracts of the liver substance.

PATHOLOGICAL CONCLUSIONS.

Most pathologists are agreed that in cases of this nature the principal lesion is fatty degeneration of the liver cells, following which is an increase of the interstitial connective tissue. While admitting that the degeneration of the hepatic cells occurs before the overgrowth of connective tissue, Levitski and Brodowski¹ maintain that there is, prior to the cell degeneration, a cell proliferation in parts of the liver parenchyma not yet degenerated. Distinct evidences of proliferation and division of the hepatic cells were noted by me in the peripheral parts of the lobule, but such proliferation is, in my opinion, a forerunner not of degeneration but of regeneration of the proper hepatic tissue. On the other hand, Winiwarter² thinks that the first change consists in an inflammatory process in the interlobular areolar tissue, which only secondarily causes fatty degeneration of the liver lobules. It seems to me clear that the fatty degeneration of the hepatic cells is the primary lesion, and that the connective tissue increase is secondary. There is not a single lobule in the liver free from advanced fatty changes, and yet many show a comparative freedom from the invading connective tissue. Moreover, inflammatory changes are only to be seen where there is work for the leucocytes to do in the shape of broken-down liver cells to be removed. These same round cells diminish in number with the laying down of the new-formed connective tissue, and are practically absent by the time that the granulation tissue has been converted into distinct fibrous tissue. I may allude here to the fact that this new-formed connective tissue is exceedingly vascular, and cannot therefore interfere with the nutrition of the liver cells, and, moreover, cannot exercise any great devitalising power by crushing the cells themselves, else we should never find proliferating hepatic cells and tubules in those very parts where the connective tissue is strongest and oldest, namely, at the periphery of the hepatic lobule. This contention is further supported by the observation that very acute cases only show fatty degeneration or yellow atrophy, while, according to Zenker,³ a certain degree of chronicity is requisite for the development of the cirrhotic bands and patches. In a very rapid case, reported by Dreschfeld⁴ the bulk of the liver was in a diseased state from fat infiltration, and nowhere was there embryonic connective tissue. It has been already pointed out that no sharp line can be drawn between the red and the yellow substance. The two conditions merge gradually into one another, and the widened interlobular areas in the yellow substance must be regarded as the red substance of Zenker in an early stage. But over and above the fatty degeneration and increase of connective tissue, there is distinct evidence of an attempt at regeneration on the part of the surviving liver cells. This is shown by the presence of solid columns of hepatic cells in the interlobular connective tissue, where the resemblance to glandular tubes is very marked. At one stage of development the liver in the embryo is a tubular gland, and these solid columns of hepatic cells must be regarded, as Obrzut and others maintain, in the light of reversions to the embryonic type. "As the process of development proceeds, however, an important change arises in that the cylinders unite and

anastomose with one another everywhere to form a close network."⁵ This further stage can be followed in our case, and is the very evident explanation of the branching and complicated networks of hepatic cells in the red substance of Zenker.

The formation of these solid columns of liver cells, or so-called pseudo-bile ducts, from the surviving hepatic cells is, to me, quite apparent—a view already supported by Ziegler,⁷ Obrzut,⁸ Nicati and Richaud,⁹ and others. These columns of cells are attempting to form a compound gland, and it is in places very clearly brought out from the apparent convergence of the cylinders towards a portal canal that the true centre of the lobule is, as Delépine⁹ and Sabourin¹⁰ hold, the portal canal and not the central lobular vein. These duct-like formations, moreover, are not the persisting excretory ducts which have survived the deleterious agent—whatever it may be—to which the more delicate secreting structures have succumbed, as Coats¹¹ has suggested. They are new-formed beyond a doubt. Further, they cannot be regarded as proliferating bile ducts (Cornil and Ranvier).¹² They are not ducts at all in the true sense, and it is not correct to talk of hepatic cells reverting to their embryonic or epithelial type to form ducts (Dreschfeld), for ducts they do not form. Nor are these columns of hepatic cells due to sprouts from the bile ducts, though "some observers attribute the new formation, after injury, to outgrowths of the epithelial cells of the bile ducts."¹³ Occasionally even small bile ducts may be found with very short lateral branches, but there is no reason to regard these as other than normal. This new-formed hepatic tissue often grows into relation with the true bile ducts, and I have succeeded in demonstrating the connection of these columns of hepatic cells with unequivocal bile ducts. Dreschfeld⁴ and Obrzut,⁸ though obtaining a negative result, hold that such connection cannot be excluded. "Kelsch, Keener, and Brieger have observed such cells to pass gradually into the true epithelial cells of the biliary duct; and Dreschfeld himself has traced such a connection in the monolobular form of cirrhosis."¹⁴

It has been pointed out by Delépine⁹ that, "in the development of the liver nearly the whole of the mesoblast becomes converted into veins full of blood. In other glands only a small portion of such tissue is transformed into veins, the greater part remaining in the shape of the interlobular and intralobular tissue. In the liver, therefore, the hepatic veins take the place of the greater part of the stroma of other glands. It is only around the oldest hypoblastic tubes, which become ultimately ducts, and at the periphery of the organ, that a little mesoblastic tissue becomes transformed into fibrous connective tissue (Glisson's capsule)." Now this peculiarity of the mesoblastic tissue of the liver in the embryo is a quality that the structure seems to possess throughout life, and, in my opinion, this particular faculty goes far to explain the extremely vascular condition of the new-formed connective tissue, and the persistent vascularity and angiomatic appearances amidst even fully-formed fibrous tissue, which in other structures and organs would have gone on to form a vascular or cicatricial tissue. Catarrh of the bile ducts was only seen in a few and widely separated instances, the majority of the ducts being perfectly healthy. This accounts for the complete, or almost complete, absence of jaundice in this case, and shows that the symptom of jaundice is an accident and not a necessary concomitant of yellow atrophy.

The macroscopic and microscopic appearances of the liver itself, together with the associated changes in the other organs throughout the body, make up a very complete pathological picture, and give sufficient justification for classifying this as an example of yellow atrophy of the liver. It might be called by some acute yellow atrophy, but, since the course of the disease was somewhat too long for an acute yellow atrophy, it seems more accurate to follow the precedent of Hlava and Eppinger, and designate it chronic yellow atrophy of the liver. But before going further, it may perhaps not be out of place to inquire if we really can justifiably term yellow atrophy of the liver a distinct pathological entity? I think not. In 1886 Obrzut⁸ published a paper entitled "Chronische gelbe Leberatrophie oder acute Lebercirrhose," wherein he contends that all cases identical with his—as our case is—may be called acute atrophic cirrhosis, which title agrees best, not

only with the histological appearances, but also with the clinical phenomena. He further points out that no difference in kind exists between his case, the atrophic cirrhosis of Laennec, and the hypertrophic cirrhosis of Hanot, Charcot, and Sabourin. This case of ours—as also Obrzut's—shows how slender is the basis (namely, the arrangement of the fibrous tissue) on which the different forms of cirrhosis are classified. Many pathologists refuse to accept any such classification, and, as Obrzut remarks, "quantitative differences no doubt exist, but quantitative histogenetic differences there are none."

When Dr. Lindsay Steven¹⁴ supported these views the late Professor Coats objected that "it was not right to compare acute cirrhosis with acute yellow atrophy, because acute cirrhosis was specifically a disease of the liver, while the other was a general disease." That yellow atrophy of the liver is a general disease is insisted on by almost every writer on the subject,¹⁵ but herein it differs in no way from ordinary cirrhosis, as shown most perfectly by the necropsies of those who have died from their cirrhosis, and not from some inter-current disease. In this connection, too, it may be mentioned that for many years Professor Workman has taught that, in cases of cirrhosis of the liver, the liver is not the only organ in the body showing cirrhotic changes, and he frequently, indeed almost invariably, finds cirrhosis of the kidneys with fibrosis of the heart and lungs. In this case we already saw that there was a commencing, though very slight, increase of the connective tissue of the kidney, and perhaps also of the heart, associated with the marked fatty changes in these organs. Had time permitted—or, in other words, had this cirrhosis of the liver been chronic instead of acute—there seems no reason to doubt but that a cirrhotic kidney would have resulted. At the same time, it might be contended that alcoholic or ordinary cirrhosis is essentially a disease of the interstitial tissue, while yellow atrophy, as shown here, is primarily a morbid change of the hepatic cells themselves. Still, there remains considerable room for doubt as to whether or not cirrhosis of the liver really owes its commencement to connective tissue changes; and "the view that fibrosis is secondary has been supported by Wickham Legg, Charcot, and Gombault, Ackermann, Hamilton, and many others. Moreover, Lafitte has found in rabbits that alcohol directly affects the hepatic cell and leads to its atrophy, while Mertens has shown in rabbits caused to live in an atmosphere containing vaporised alcohol that the liver shows a marked increase of fibrous tissue if the animals live long enough (a year), and that in these cases the liver cells are but slightly altered. When the animals succumb after a few months there is no increase of connective tissue, but the liver cells are greatly degenerated."¹⁶ Divergence of result is admitted, still Lazarus-Barlow¹⁶ holds that the balance of evidence goes to show that agents such as alcohol, chloroform, ether, phosphorus, etc., act primarily on the cells, and that the fibrosis is secondary.

It must be admitted, I think, that all these facts and opinions go to support the contention of Obrzut that chronic yellow atrophy is nothing more than an acute cirrhosis of the liver, differing from other cirrhoses in quantitative histogenetic changes. In yellow atrophy the degeneration of the hepatic cell is more extreme than in the ordinary types of cirrhosis, tending more frequently to death than to recovery of the cell. The connective tissue formation differs little from what we find in other cirrhoses, but the regeneration of the hepatic tissue—as evidenced by the very numerous columns of hepatic cells—has gone much further than in ordinary cirrhosis, and has even outdone the so-called hypertrophic or biliary cirrhosis in what is regarded by some as its special feature.

MICRO-ORGANISMS.

Unfortunately no cultures were taken from the liver or other organs.

In a small branch of the portal vein, and lying between the hepatic cells in the yellow area, there were seen a few large bacilli, which stained deeply with thionine. Dr. McCrorie, to whom I submitted the specimen, thought that most probably this organism was the bacillus coli communis, which it resembled. In the kidney, numerous shorter rods or diplococci were found arranged in capillaries, and even inside the cells of the convoluted tubules. In the spleen

few short rods or diplococci were observed. I could find no evidences of organisms in the heart.

Klebs, Waldeyer, and Eppinger⁷ have published papers on a micrococcus found in this disease, and Dreschfeld¹⁷ has observed micrococci in one out of the three cases he has investigated. The majority of workers in this field have failed to satisfy themselves of the presence of any microbe in the liver, and I have been unable to find any record of a culture obtained from the liver. Hunter,¹⁵ moreover, has expressed the opinion that "the widespread character of the liver change, and the rapidity with which it usually occurs, suggest the action of a circulating toxin rather than a local invasion by micro-organisms."

I do not know how much importance, if any, attaches to the finding of these bacilli in the liver, spleen, and kidneys; for during the thirty-two and a-half hours between death and the post-mortem examination, there was ample opportunity for the organisms to emigrate from the intestine, and to make their way into these organs along the route of the blood vessels. No unequivocal bacilli were seen inside the liver cells, though such were found in the epithelium of the convoluted tubules of the kidney. If these be really colon bacilli, it is not improbable, in the light of Adami's researches,¹⁸ that the micrococci of other observers merely represent different forms of the same colon bacillus. Adami has found typical colon bacilli in the liver not only in cases of cirrhosis, but also in cases in which no cirrhosis could be detected. I could not see in the liver cells the diplococcus-like bodies staining deeply (modified form of the colon bacillus), though such was probably present in the kidney. Neither could I see the remains of dead or degenerate forms of dying bacilli which Adami has observed in the hepatic cell.

I take this opportunity of expressing my indebtedness to Professor Workman for allowing me to make use of this material, and must thank him for much valuable advice, ungrudgingly given, during the progress of my research.

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CHRONIC BRASS POISONING.*

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INTRODUCTION.

In large metal manufacturing centres like Birmingham a complaint is frequently to be met with which is apt to be not a little puzzling to a stranger. Its most prominent characteristics may be illustrated by the following clinical picture:

The patient is a young workman. As he enters the consulting room you notice that his expression is more or less anxious, his face thin and haggard, his complexion sallow, unhealthy, and consumptive looking. He complains of gradual loss of strength, with dry hacking cough, cold sweats, and possibly hæmoptysis. Pains in the chest, loss of appetite, and progressive emaciation in addition lead one instinctively to the suspicion of phthisis, but a careful examination of the chest fails to reveal any pulmonary lesions beyond, perhaps, those of a slight bronchial catarrh. A tentative diagnosis is arrived at, and the patient is sent away with a tonic or expectorant prescription, and instructions to return in a week. In due course he makes his appearance, with the statement that he is not a bit better, or only slightly so. This time the urine is examined, but no abnormality observed. The com-

plaint is labelled "debility," and there the matter ends, with no advantage to the patient.

In the meantime other similar cases begin to crop up, and one is compelled to admit that there is something in the distinctive character of the symptoms requiring explanation. Inquiry into the occupation of such patients appears at first to afford little assistance, as they describe themselves variously—some as stampers, others as metal finishers, others as polishers, etc.; but further investigation elicits the important fact that the one feature common to the entire class is the metal in which they work—namely, brass. The large proportion of copper in this metal immediately suggests an inspection of the teeth, where we find the almost inevitable green line.

The mystery is now solved, and in course of time we become so familiar with the recital of grave general symptoms unaccompanied by correspondingly serious local signs, that we can almost unhesitatingly prophesy an occupation concerned in the manipulation of raw brass, and a green line at the bases of the teeth.

We now turn for assistance to the literature on this subject, and find it surprisingly scanty and unsatisfying. Practically the first investigation into the effects of brass was made by Dr. Headlam Greenhow nearly forty years ago, although some thirty years previously allusion was made to the subject by Thackrah in his *Essay on the Effects of Arts, Trades, and Professions on Health and Longevity*. Greenhow's conclusions supply the material of a paper on Brassfounders' Ague, published in the *Medico Chirurgical Transactions* (1862), in which he describes a form of ague that attacks the casters or founders, who work the metal in its molten state. His description is graphic and interesting, but, as shown by Dr. Simon and others, by no means accurate. There is no doubt that brassfounders do occasionally suffer from attacks exhibiting symptoms which, as Dr. Simon says, "are just such as would be caused by the ingestion of a quantity of an irritant metal sufficiently large to cause vomiting and its attendant depression;" but this is not the occasion, even if one had the necessary information, on which to discuss what is really a form of acute poisoning. Before leaving the subject, however, I should like to remark that this brassfounders' ague, of which so little is known, is just one of those conditions in which we must look for instruction from the private practitioner. The onset is so sudden, and the symptoms so evanescent, that the patient has no time to arrange for treatment at the hospital or dispensary, and presumably he sends for the nearest medical man. Are such cases common? And, if so, how many are correctly diagnosed?

Not until 1887 was any serious attempt made to describe the complaints affecting brassworkers not engaged in casting. In that year Dr. Hogben, of the Queen's Hospital, published in the *Birmingham Medical Review* an article on Brassworkers' Disease, which contains practically all that is known on the subject. The *BRITISH MEDICAL JOURNAL* of the following year has a contribution by Dr. Simon, of Birmingham (Remarks on Brassworkers' Diseases) discussing the conclusions of Greenhow and Hogben, with some original observations; while, later still, seven years ago, a summary of these appeared in the work of the late Dr. Arlidge, *On the Diseases of Occupation*.

SYMPTOMS.

A person may be employed for months or years filing, polishing, or otherwise manipulating brass, even under adverse conditions, without suffering any ill-effects, and many appear to enjoy a permanent immunity; but, on the other hand, there are individuals whose health begins to become affected almost from the commencement of their occupation, while others, again, exhibit symptoms only after many years. These symptoms are by no means uniform; and considerable difference exists between those manifested in the early stages of absorption and those of a more advanced period.

Early Symptoms.

I am convinced that in a large proportion of cases the first indication of poisoning is the existence of anæmia. The frequency with which anæmic patients, particularly young women, turn out to be brassworkers, and exhibit a green line at the bases of the teeth, suggests this, while the hypothesis is to some extent supported by the occasional state-

* Delivered before the Midland Medical Society.