I fully realize that this paper is iconoclastic, but I feel that the evidence which I have given is already strong from facts already collected. The directions from which further evidence will come are also plain. From the trend of the writings of those authors whom I have quoted and of others from whom I have not quoted it is shown that medical thought is focusing towards this idea and that the evidence merely needs to be correlated and then substantiated by crucial experiments.

Dwight demonstrated but did not observe this condition because he did not think of the change from the horizontal to the vertical animal. His admirable work was pure, descriptive anatomy.

Cannon has done much to show us the physiology of the duodenum, but has worked with the horizontal animal and therefore not appreciated the clinical importance of the root of the mesentery in man.

Weinland gave us evidence of the anti-ferments, but was so imbued with the traditional dread of acid that he failed to perform the crucial test of cross experiments.

Türk, in order to keep the stomach and duodenum exposed to bacteria, took the trouble to feed dogs constantly for months with cultures of bacteria. Perhaps he might have produced an artificial stenosis of the duodenum by sewing down the mesentery and have kept his stock culture in the duodenum itself.

Ochsner observed cases of dilatation of the duodenum on the operating table and vaguely appreciated their clinical importance, but erroneously supposed the condition to be due to an imaginary sphincter.

Laffer, Finney, Ordway and the numerous writers and experimenters on acute gastro-mesenteric ileus have been so engaged with the acute condition that they have not realized the importance of the chronic but more common condition produced by the same cause. Bloodgood is the only one whom I have read who has even devoted one sentence to the chronic condition. Doubtless others whom I have not read have spoken of it.

Those interested in this subject will find the literature of the acute condition admirably reviewed by Laffer in the *Annals of Surgery*, for February and April of this year. Laffer's paper is a landmark in the study of this subject.

KAISER WILHELM PROFESSOR AT COLUMBIA UNIVERSITY. -- At a meeting of the trustees of Columbia University, held on April 6, Dr. Max Verworm, director of the Physiological Institute of the University of Göttingen, who had been nominated for the position by the Prussian Ministry of Education, was appointed Kaiser Wilhelm Professor for the season of 1908-9. His lectures will be given both in the medical department of Columbia and in that of pure science.

ACUTE YELLOW ATROPHY OF THE LIVER. A REPORT OF TWO CASES, ONE WITH ASCITES.*

BY WILDER TILESTON, M.D., BOSTON.

IN spite of the large number of cases of acute yellow atrophy of the liver already published, the subject remains a dark one and there are still many points to be explained. The following two cases present certain features which are rather unusual and have therefore seemed worthy of being placed on record.

CASE I. *Woman, twenty-nine years old. Vague gastro-intestinal symptoms of some months' duration. Jaundice soon after an attack of "grippe." On the eighteenth day of jaundice persistent vomiting, followed by severe abdominal pain, distention and ascites. Delirium and stupor on twenty-fifth day of jaundice; on the following day laparotomy and death. At autopsy, typical acute yellow atrophy.*

H. McC., twenty-nine years old, single, a domestic servant. The past and family history could not be obtained. Her last employer states that the patient came to work with her in August, 1907. She did not seem well, was inclined to be drowsy, and easily tired. Her complexion was sallow, and at times "decidedly jaundiced." Her appetite was capricious, and though she felt very hungry before meals, a few mouthfuls would satisfy her. About Christmas, 1907, she had the "grippe"; the symptoms were severe cough with fever, accompanied by inflammation of the middle ear without suppuration. She recovered in two weeks, except that she did not wholly regain her strength. On Feb. 1, 1908, she called in Dr. G. W. Nickerson, of Stoneham, complaining of jaundice of two weeks' duration. She showed then an intense icterus, which was thought to be catarrhal. Two days later, she had a chill, and began to vomit. The next morning she had another chill. When seen again by Dr. Nickerson, on Feb. 5, she complained of frequent vomiting and thirst. There was no pain, the temperature was normal and the pulse 74 to 80. He found the abdomen free from distention, and thought that he could feel the gall bladder. Three days later severe abdominal pain set in, and Dr. Nickerson found the abdomen distended. On Feb. 11, 1908, she was admitted to the Massachusetts General Hospital (Record No. 156,996) to the service of Dr. J. G. Mumford, to whom I owe thanks for placing the case at my disposal. She was too confused to give a good history; she complained of abdominal pain, vomiting and constipation.

Physical examination. — A well developed and fairly nourished woman of medium stature. Marked jaundice. There is an odor of acetone on the breath. The chest negative. The abdomen distended, the muscles held rigidly. On percussion there is dullness in both flanks, shifting with change of position; in the center the note is tympanitic. The liver dullness extends from the fifth space to two fingers above the costal margin. Marked tenderness about the navel, and towards the right iliac fossa; none over the gall bladder. The patient is evidently suffering severe pain, and keeps her hand applied to the tender area. The urine, withdrawn by catheter, contains bile and acetone, but no sugar. Two small evacuations of the bowels were obtained after enemata; the feces were clay-colored. Temperature 98.6°, pulse 110.

Subsequent course. — The patient became delirious on the night of admission, and the next day (Feb. 12) was in a state of stupor. She reacted somewhat to

* Read at a meeting of the Medical Board, Massachusetts General Hospital, March 13, 1908.

stimuli, but would not reply to questions. The leucocyte count was 34,000. Differential count, 400 leucocytes: polynuclear neutrophils 82.5%; small lymphocytes 15.5%; large lymphocytes .75%; mononuclear and transitional, 1%; eosinophiles, 0%; mast cells .25%. Iodophilia present. Red cells normal. She was seen by several consultants, but no definite diagnosis was made. As her chances without operation were evidently of the worst, it was decided to open the abdomen. Dr. Greenough kindly asked me to see her just before the operation; examination showed the abdomen much distended, with a high degree of ascites; the upper limit of the liver dullness at the fifth rib, the lower border somewhat above the costal margin; the epigastrium tympanitic. The spleen was not palpable, and the splenic dullness was obliterated. The possibility of acute yellow atrophy was considered, but the marked tympanites was considered sufficient cause for the decrease of the hepatic dullness below, and for the absence of splenic dullness.

Operation, Dr. R. B. Greenough, 1 p.m., Feb. 12. On opening the peritoneum a large amount of clear dark-colored fluid escaped. The small intestine was a good deal distended, especially the duodenum. The stomach was likewise larger than normal. The gall bladder was somewhat distended, its walls normal, however, and no stone could be felt. The liver was palpated, and did not seem abnormal. Exploration revealing nothing which could be helped by surgical measures, the wound was closed. The patient's condition rapidly became worse, her temperature fell to 97.2°, and she died in coma at 8 p.m. the same day.

Autopsy No. 2,084, Feb. 13, 1908. — Dr. Oscar Richardson. (The following is an abstract of the autopsy protocol, unessential details being omitted.)

A woman, 167 cm. long, well developed and nourished. No subcutaneous edema. Head not examined. The skin and conjunctiva yellow, with a few minute brownish-red macules. The peritoneal cavity contains a moderate amount of reddish fluid. (Most of the ascitic fluid had been evacuated during the operation.) The peritoneum in many places shows smaller and larger irregular red spots. Similar hemorrhagic areas are found in the pleuræ, the mucosa of the intestine, the lungs and in some of the muscles. The anterior margin of the right lobe of the liver is four fingers' breadths above the costal border in the mammillary line. Diaphragm on the right at the third rib, on the left at the third interspace. The pleural cavities contain a slight amount of reddish fluid. The lungs show no consolidation; in one bronchial gland a small fibro-calcareous nodule (obsolete tuberculosis). The heart weighs 238 gm.; myocardium firm, brownish red, rather pale. Valves and cavities not remarkable. The gall bladder contains a small amount of dark, thick bile, but no stones. Bile ducts free. The pancreas not remarkable; the duct of Wirsung is free. The spleen weighs 130 gm.; on section slightly soft, with visible follicles and trabeculae. Kidneys: combined weight, 260 gm.; the color pale brownish-yellow, otherwise not remarkable. The adrenals, bladder, uterus, tubes and ovaries are normal. The stomach not abnormally large, the mucous membrane normal; the duodenum also not distended. The intestines normal except for the small hemorrhagic areas in the mucous membrane, already mentioned; the contents not hemorrhagic. The retroperitoneal glands near the head of the pancreas moderately enlarged, but without signs of tuberculosis.

Liver. — Weight, 645 gms. It is greatly reduced in size. From side to side it measures 18 cm., from top to bottom 13 cm.; the right lobe measures from side to side 13 cm., and the left 5 cm. The right lobe measures about 5 cm. at its thickest portion. The organ is

symmetrical and its contours are fairly well preserved. It is extremely flaccid, so that when supported on the tips of the fingers it falls over them like a cap. The surface generally is fairly smooth, and of a pale brownish-yellow color, tinged with red in places. Along the upper border of the right lobe are a number of yellowish nodules projecting above the surface, and about the size of a split pea. On section the tissue is somewhat leathery and flabby. The section surfaces generally show a pale, brownish-yellow homogeneous tissue mottled with small reddish areas, giving somewhat of a nutmeg appearance. In places there are pale brownish-yellow areas, in which there are minute yellowish spots. There are also areas which are pale red and homogeneous. The hepatic bile ducts not remarkable. The portal vein is free and its walls are normal. The perivascular tissue along the portal spaces is well marked.

Bacteriological report. — Cultures on blood serum from the heart's blood and spleen show a scum of growth of colon-like bacilli, with streptococci in the water of condensation.

Microscopical examination. Liver. — The original parenchyma has been very extensively destroyed. The greatest part of all sections is made up of connective tissue. Scattered through the section are rather numerous areas rich in blood, which under the high power are seen to consist of capillaries close together, separated by a thin reticulum of connective tissue. In some of them there are red cells apparently free in the tissue. These areas are the red spots seen in the gross specimen. Here and there are groups of liver cells with atypical arrangement, often in parallel columns. The cells are of varying size, some larger, some smaller than normal. The nuclei are well stained, the protoplasm contains a moderate amount of fat. These groups are considered areas of regeneration, probably from pre-existing liver cells. In places there are small patches of liver cells separated the one from the other by detritus, without definite arrangement; these cells are of various shapes, rounded, elongated, or polygonal; they take a deeper stain with eosin than those in the regenerating areas. Some are quite small, and loaded with brown pigment (bile pigment). The bile ducts in the connective tissue portions are much more numerous than normal. There is a marked infiltration with lymphoid cells in some of the portal spaces, with a few plasma cells. Sections stained with Mallory's connective tissue stain do not show any considerable new formation of connective tissue; the apparent increase of the latter seems to be due mostly to collapse of the liver tissue, consequent on the destruction and removal of the parenchyma. About some of the larger bile ducts, however, there is a distinct increase of connective tissue. Sections hardened in Flemming's solution and stained with safranin show a moderate number of fat droplets in the liver cells, and much bile pigment, partly within the cells, partly in small masses apparently within bile ducts. There is no evidence of an antecedent cirrhosis.

Kidneys. — The glomeruli and interstitial tissue normal. Sections stained with osmic acid show extensive fatty degeneration situated chiefly in the convoluted tubules.

Spleen. — The spleen shows nothing of importance histologically.

The above description was kindly verified for me by Drs. J. H. Wright and Oscar Richardson.

Examination of the urine. — A specimen of urine was obtained just before the operation, with the intention of looking for leucin and tyrosin, but owing to circumstances I could not examine it until after the autopsy. Bile, acetone and a trace of albumin were present. The

sediment showed a few typical leucin crystals, but no tyrosin. Leucin and tyrosin were further searched for by Frerichs' method. The syrup thus obtained showed numerous characteristic crystals of leucin, and many large needles thought to be tyrosin, but not aggregated in rosettes. The syrup gave all the tests for tyrosin which were tried, viz., Millon's, Pyria's, Denigé's and Scherer's. The small amount of material at hand made it impossible to separate the two substances, and the tests for leucin, which require the presence of that body in a pure state, were therefore unsatisfactory.

Toxicological examination, by Dr. W. F. Boos. Aqueous extracts from the liver, kidneys and blood, freed from albumin, were concentrated at a temperature of 70° C., and samples of each were given to rabbits intravenously, and to frogs, but produced no effect. Dr. Boos had previously found that similar extracts from the organs of eclamptic patients exhibited a marked toxic action. This is interesting in connection with the relation which has been assumed by some to exist between eclampsia and acute yellow atrophy.

This case presents in most respects the usual picture of acute atrophy of the liver. The ascites, however, is quite exceptional and requires a separate discussion. A fairly thorough search of the literature has brought to light only seven cases with ascites, in which the diagnosis of a primary acute atrophy of the liver seems certain. Those instances of atrophy secondary to cirrhosis are naturally to be excluded.

The study of these cases shows that they have several features in common. A comparatively long course (usually about two months) is almost invariable, and in the only exception (MacCallum's case), the acute changes in the liver could be dated back with probability to an attack of dysentery six months previous. The ascites is usually of unknown duration, but may appear early, as much as two months before death. The spleen was enlarged at autopsy in all but the present case, and usually much enlarged (up to 1,200 gm.). Cerebral symptoms are generally absent till near the close of life, in spite of the fact that the acute process in the liver has evidently taken place a considerable time before.

A very remarkable feature in this group of cases is the regeneration of the liver, which in several instances (Marchand, MacCallum, Schöppler) took on the form of a nodular hyperplasia very suggestive of adenoma.

As a rule no explanation of the ascites has been sought for; Schöppler attributed it to a coincident nephritis and Marchand to portal obstruction due to the extensive destruction of liver tissue. A careful perusal of the microscopical descriptions leads me to the belief that the ascites has been due in all these cases to changes in the circulation within the liver. In those cases where the new formation of connective tissue has been great, the ascites was probably due to the same causes that produce ascites in ordinary cirrhosis of the liver. In my case the connective tissue increase was but slight, and it seems more reasonable to attribute the ascites to the profound circulatory disturbance which must necessarily accompany the destruction and removal of such large areas of liver substance. F. C. Herrick

has recently shown that, for some cases at least, there is no portal obstruction in the ordinary cirrhosis of the liver, but an abnormally free communication between the radicals of the portal vein and those of the hepatic artery, with consequent increase of the portal pressure. A similar abnormality in the circulation might well arise in the type of acute yellow atrophy under consideration, and would account in a satisfactory way for the ascites.

A second point of considerable interest in the present case is the dilatation of the duodenum which was found at the operation, and which considerably exceeded the distention present in other parts of the intestine. This feature, with the accompanying dilatation of the stomach, suggested the possibility of a so-called gastro-mesenteric ileus. This condition, to which a good deal of attention has been paid lately, may, according to some authors, be chronic in certain cases. Such a chronic dilatation of the stomach and intestine would favor catarrhal inflammation of the duodenum, and might in this way have acted as a predisposing factor in the production of icterus and the acute atrophy of the liver which followed. Dilatation of the duodenum has not been noted in other cases of acute yellow atrophy, but the stomach has often been described as "large" at the autopsy, and dilatation of the duodenum might have been present in life, and, as in the present case, not have been demonstrable at the autopsy. It is possible, of course, that the dilatation may have developed as the consequence of a terminal gastro-mesenteric ileus, the result of the persistent vomiting, or that it may have been due to atony. The above suggestion, for which Dr. E. A. Codman is responsible, is therefore offered purely as an hypothesis.

CASE II. Boy, nine years old. Sympathetic ophthalmia following injury to the eye. Inunctions of mercury for fifty-three days, then nausea and vomiting, tenderness at navel. Six days later jaundice; delirium beginning on eleventh day of jaundice; enlargement of spleen. Liver dullness normal in size; rapid decrease only on day preceding death. Death in coma on seventeenth day of jaundice. No autopsy.

T. B., a boy, nine years of age, on Feb. 18, 1907, received an injury to the left eye from a knife. Early in April the sight in the other eye began to fail, and on the 12th he was admitted to the Massachusetts Charitable Eye and Ear Infirmary, to the service of Dr. E. E. Jack, to whom I owe thanks for placing the hospital records at my disposal. The family and previous history were negative. Examinations of the eyes showed panophthalmitis on both sides, with small irregular pupils, irresponsive to light. Daily inunctions of mercury (Ung. hydrargyri, half strength) were prescribed, for antiphlogistic purposes. There was no history of syphilis. The mercurial treatment was continued for nearly two months without intermission. During this time the temperature was normal, there was no pain, and the child seemed healthy except for the eye condition. Mercurial stomatitis was not observed. On May 4 and 6 tuberculin was administered for diagnostic purposes, in doses of 1-10 and 5 mgm. respectively. There was no reaction. On June 4 there was nausea and vomiting, with tenderness just

above the navel, and the inunctions were omitted. These symptoms persisted, and six days later jaundice appeared, and rapidly became intense. I was called to see the patient in consultation on June 20. Examination showed a well developed and nourished boy with marked icterus. Temperature normal, pulse 90. Chest negative; the liver palpable at the costal margin, the spleen not enlarged. Psyche normal. A diagnosis of catarrhal jaundice was made. At my next visit on June 25, the liver flatness began at the sixth rib and reached to the costal margin; the spleen was now enlarged to percussion, though not palpable, the splenic dullness extending above to the seventh space, and forwards nearly to the mammillary line. The patient had been delirious at night for four days, and markedly so for the last two nights. He talked to himself, got out of bed at night, and tried to lie on the table, pounded a hole in the wall, etc. In the daytime he was depressed, and had a delusion that his mother was dead. There had been daily vomiting, usually at 5 A.M. The vomitus consisted of food. The stools were not observed. The jaundice was so intense that the water of his bath was stained yellow (excretion of bile by the sweat). There was retention of urine, rendering catheterization necessary. The temperature was never over 99°, and reached 97° twice. The pulse was extremely labile, rising to 135 at times, though usually between 80 and 90. The urine was dark, bile-stained; specific gravity 1.020; it contained a trace of albumin but no sugar. The sediment showed a fair number of hyaline and fine granular casts, with a few small round cells adherent; numerous small granules of bilirubin. I was unable to find crystals of leucin or tyrosin, but did not employ chemical methods for the detection of these substances.

The patient was transferred the same day (June 25) to the Children's Hospital, where he was under the care of Dr. H. I. Bowditch, to whom I am indebted for further notes. He became unconscious that afternoon. The white count was 23,000; lumbar puncture was performed, and 60 ccm. of a clear fluid under low pressure escaped; smears of the sediment showed no cells or organisms. The next day there was frequent vomiting of a coffee-grounds material; the feces (obtained after enemata,) were clay-colored. *The liver flatness was now decreased*, extending from the seventh space to just above the costal margin. The urine showed no leucin or tyrosin in the sediment. The temperature rose to 103.5° in the last hours of life. Death took place on the 27th, at 4 A.M. Autopsy was refused.

The foregoing case is so typical of acute yellow atrophy that the diagnosis may be considered certain, even in the absence of autopsy. None of the usual features was absent, except the demonstration of leucin and tyrosin in the urine. But these bodies may be absent in acute yellow atrophy, and they may have been present in the case in question, for chemical methods of examination may reveal them where they are not present in a crystalline form in the sediment. Phosphorus poisoning may be excluded by the course of the disease, and Weil's disease by the lack of fever and of enlargement of the liver.

The chief importance of this case lies in its bearing on the etiology of acute yellow atrophy. So far as I can ascertain, it is the first in which mercurial poisoning could be thought of as the sole predisposing cause. In all the other cases where the administration of mercury has preceded acute yellow atrophy, the drug has been given in

the treatment of secondary syphilis. Because of the fact that acute yellow atrophy has occurred in some cases where no mercury had been given, the writers on the subject have denied that mercurial poisoning had any part in the process. In the present case, however, there can be no question of syphilis. Kobert¹ states that mercury may cause fatty degeneration of the liver and sometimes jaundice. And C. W. Miller and Edsall² have shown that mercury increases autolysis, a factor to which much importance is now ascribed in acute yellow atrophy. Bandler has collected a number of cases of acute yellow atrophy following chloroform narcosis, and has shown experimentally that chloroform may cause marked lesions of the liver. If, however, a single chloroform narcosis may cause acute yellow atrophy, it is by no means impossible that the prolonged use of mercury might have a similar effect. The fact that ptialism was not noted in the present case is of no great importance, for it was not especially looked for, and it may be absent in cases of chronic mercurial poisoning.

For the above reasons I believe that the prolonged use of mercury *may* have acted as a predisposing factor in the production of acute yellow atrophy in the case in question, and that it may have been of some etiological importance, in conjunction with syphilitic toxins, in many of the reported cases of acute yellow atrophy associated with syphilis.

In conclusion, the high leucocyte count in these two cases is worthy of remark. In the first, the hyperleucocytosis was shown to be due to an increase in the polynuclear neutrophiles. The few previous reports of the blood findings in this disease usually show a leucocytosis, the character of which is seldom mentioned. Leucocytosis, relative or absolute, could probably be found nearly always after the advent of cerebral symptoms, if looked for.

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ON THE SIGNIFICANCE OF CLINICAL HISTORIES BEFORE AND AFTER OPERATIVE DEMONSTRATION OF THE REAL LESION.

BY MAURICE H. RICHARDSON, M.D.,
 Moseley Professor of Surgery, Harvard University.

(Concluded from No. 15, p. 473.)

At the Quincy Hospital on Thursday, Dec. 8, 1906, I saw a man of fifty who was suffering from an attack of epigastric pain, tenderness, rigidity and distention. He had had a similar attack on Nov. 2, beginning in the night and accompanied by vomiting and severe abdominal pain. Distention followed, with a bad condition of the heart. A year before this he had had an attack associated with a very irregular heart. The

¹ Kobert, R.: Lehrbuch der Intoxicationen, 1902, Bd. ii, pp. 329, 331.

² D. L. Edsall: in Osler's "Modern Medicine," vol. i, p. 126.