Two cases of acute haemorrhagic pancreatitis / by J.H. Bryant.

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TWO CASES OF

ACUTE HÆMORRHAGIC PANCREATITIS

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TWO CASES OF ACUTE HÆMORRHAGIC PANCREATITIS.

I PUBLISH these two cases as they present some curious features which I have not been able to find recorded before. If perchance I have missed any case in which similar changes have been noted I take this opportunity of apologising to the author or authors for claiming them as new. In Case 1 when performing the necropsy I found marked fat necrosis of the mediastinal and pericardial fat and in both cases at the time of the operation the peritoneal cavity was found to be distended with large quantities of bile-stained serous fluid.

CASE 1.—The patient, a bandmaster, aged 36 years, was admitted into Luke Ward at Guy's Hospital on May 31st, 1899, under the care of Mr. L. A. Dunn, for excruciating pain in the abdomen. On Sunday evening, May 28th, he was playing in a band at Portsmouth and felt quite well and later in the evening he partook of some pigeon-pie for supper. On coming up to London in the train on the same night he was seized with violent pain in his abdomen and was sick. He went to a medical man who gave him an injection of morphia and he passed a very fair night. On the 29th the pain was just as bad and the medical man gave him another morphia injection, but he had a bad night. His bowels were fairly well opened. On the 30th the pain had much increased. He was very sick, he brought up a quantity of gas, and he passed a very bad night. On the 31st he was in a very collapsed condition; he was in great pain and was unable to take any food. He was removed to the hospital in the evening.

On admission the patient was found to be very collapsed. The pulse was 144 and feeble. He was in great pain and could not bear to be touched. He was soon afterwards seen by Mr. Dunn and myself. We ascertained that for some years he had suffered from attacks of abdominal pain and sickness, points which materially influenced our diagnosis.

An examination of the abdomen showed it to be rather distended, especially in the upper part between the umbilicus and the ensiform cartilage. There was no pain, tenderness, or tumour in the right iliac fossa. The abdomen was most tender

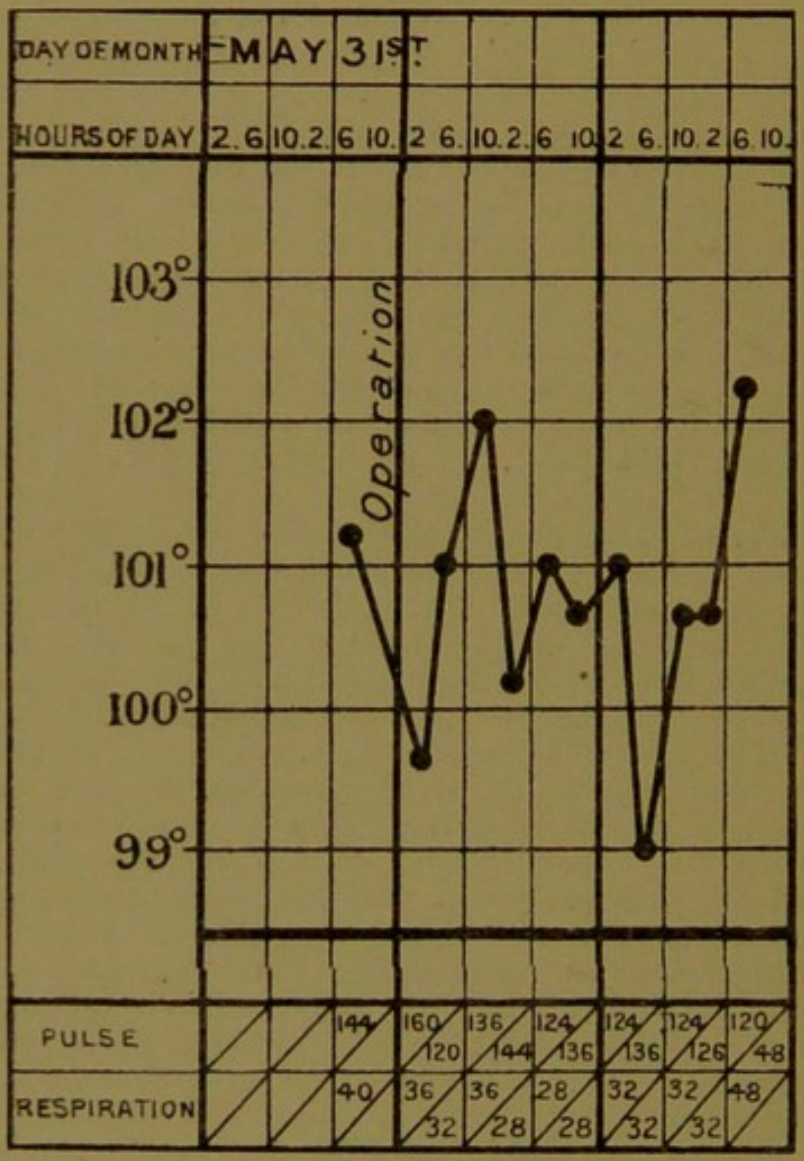


Chart showing course of temperature.

between the umbilicus and the ensiform cartilage, and the wall in this part was very resistant. The abdomen was dull on percussion. He vomited some bile-stained matter and brought up a lot of foul-smelling gas. We came to the conclusion,

taking into consideration the previous history of abdominal pain and vomiting, the sudden onset, and the position of the pain and tenderness, that the most likely diagnosis was one of perforating gastric ulcer. The possibility of acute hæmorrhagic pancreatitis was mentioned, but we thought that perforating gastric ulcer was more likely to be correct.

At 8.30 P.M. on May 31st Mr. Dunn performed laparotomy. The stomach and duodenum were found to be quite healthy. Patches of fat necrosis were discovered in the sub-peritoneal fat and in the mesenteric and omental fat. A large hard mass was felt in the region of the pancreas and a diagnosis of acute hæmorrhagic pancreatitis was made. On exploring the pancreas a large quantity of clear, dark-brown, bile-stained serous fluid escaped from the lesser peritoneal cavity and later from the general peritoneal cavity. The abdominal cavity was flushed out with hot saline solution, a drainage-tube one inch in diameter was inserted, and the abdomen was closed. During the night he became very restless. On June 1st in the morning he appeared to be better and was able to take some nourishment. On the 2nd he was worse; at two o'clock on that day the pulse was 126 and was very feeble in character. He took nourishment up to 1 P.M., but after that he refused it; at 6 P.M. his temperature rose to 102·2° F. and he died.

At the necropsy, which was performed by me on June 3rd, the body was found to be very well nourished. The complexion was dark. There was no anasarca. The brain was not examined. The thyroid was much larger than normal, but on section it had a perfectly normal appearance. There was no pleurisy. The lungs were engorged with blood, but there was no pneumonic change. The mucous membrane of the trachea and bronchi was much congested. The mediastinal fat and the intra-pericardial fat showed a number of opaque, milky-looking spots of undoubted fat necrosis. There was no direct communication between the peritoneal and pericardial cavities. There was no pericarditis. The heart weighed eight ounces. The myocardium was soft and flabby. The left ventricle was dilated. The endocardial lining was stained a deep red on both sides. Frothy blood was found in the right ventricle. The valves were healthy except for their colour. The intima of the blood-vessels was stained a similar colour. The mucous membrane of the œsophagus was deeply stained with bile. The stomach was congested. The duodenum presented a normal appearance and there were no signs of catarrh. Areas of fat necrosis,

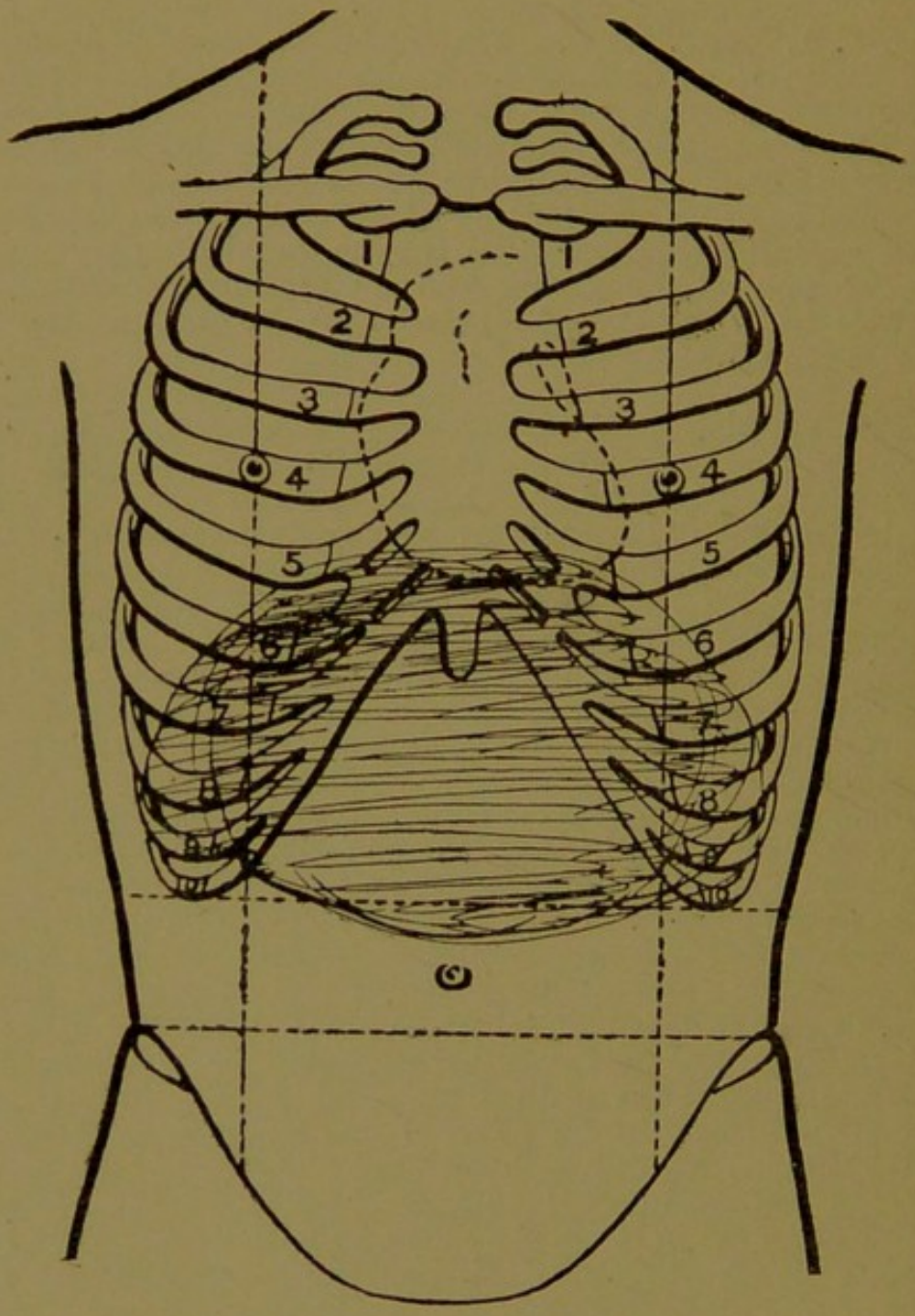
varying in size from minute, almost imperceptible spots to others one-sixth of an inch in diameter, some a dead white, some a golden yellow, others a greyish yellow, and some a milky white, were seen throughout the peritoneal cavity wherever fat was situated. The peritoneal cavity contained a good deal of blood-stained fluid. There was no peritonitis. In the position of the pancreas a large hard mass about three or four times as large as a normal pancreas was found, which appeared to be chiefly made up of blood of a dark chocolate colour. On section very little trace of any normal-looking pancreatic tissue could be seen; the whole organ was infiltrated with, and appeared to be tightly distended with, blood. In places dark-brownish breaking-down necrotic areas were seen, the largest being about a quarter of an inch in diameter. The inter-acinous, inter-lobular, and peri-pancreatic tissues all appeared to be infiltrated with blood. The head of the pancreas appeared to be the most thickened part of that organ; it measured 4·2 centimetres in the antero-posterior diameter. The gall-bladder was thickened; it contained several gall-stones and a thick brownish fluid. The liver weighed 60 ounces and it was normal. The spleen also was normal; it weighed four and a half ounces. An examination of the pancreas and its adjacent tissues some time after it had been lying in formalin solution showed some reddish areas of hæmorrhage in the fat of the mesentery similar in size and form to the areas of fat necrosis and suggested that the earliest change which took place in the fat was one of hæmorrhage. The kidneys were normal; they weighed 10 ounces. There was a considerable amount of hæmorrhage into the perinephric tissues and in the fat numerous points of fat necrosis were seen.

On microscopical examination sections of the pancreas showed marked inflammatory changes. The outlines of the acini were just visible; the nuclei of the cells lining the acini were, however, unstained and were almost indistinguishable from the protoplasm of the cells which was granular and cloudy in appearance. In places no traces whatever of the normal pancreatic structure could be seen, it being replaced by a structureless granular débris. No marked blood extravasations were visible; the blood-vessels generally were very distended with blood. The fat in the interlobular tissue showed many areas of fat necrosis. The increase in the size of the pancreas was more apparent than real, as the blood was almost entirely effused into the peri-pancreatic tissues. The mediastinal and pericardial fat showed typical fat necrosis.

CASE 2.—The patient, a man, aged 22 years, was admitted into John Ward, Guy's Hospital, under my care on Sept. 16th, 1899, suffering from abdominal pain. The clinical clerk was Mr. A. A. Miller. The patient had had an attack of jaundice on the previous Christmas. He had frequently had attacks of abdominal pain since, which he ascribed to indigestion, and for a few days he had noticed that his urine was very dark in colour. Two days before his admission into the hospital he had a severe attack of abdominal pain. He went to a medical man who noticed that he was slightly jaundiced and thought that the case was one of biliary colic. The bowels had been opened regularly. As he became worse he was sent to the hospital and admitted.

The following was his condition on admission. The pulse was 140 and was very soft and compressible and the temperature was 97·6° F. He complained of pain in the abdomen, but did not appear to be much distressed. His colour was good and he was not jaundiced. The tongue was slightly furred. There was some distinct fulness in the upper part of the abdomen between the umbilicus and the ensiform cartilage. There was also a little fulness in the left hypochondriac region. The abdomen moved hardly at all on respiration. There was tenderness over the upper part of the abdomen, but it was not very intense. There was a curious area of dulness extending from the ensiform cartilage to the umbilicus and on each side to a point about an inch outside the nipple lines (see Figure). The heart and lungs were normal. I saw him very soon after his admission and thought the diagnosis rested between acute hæmorrhagic pancreatitis and perforating gastric ulcer. Mr. Dunn was called in to see him and he agreed with the diagnosis, but as he was rather collapsed he decided not to operate until some stimulants had been administered. Tincture of digitalis (15 minims) and solution of strychnia (five minims) were given hypodermically and a saline enema of one pint was injected, with the result that the patient's pulse improved in rate and volume, being 128 per minute just before the operation. A.C.E. was administered and he took the anæsthetic well.

After the patient had been carefully prepared to prevent any risk of sepsis Mr. Dunn made an incision in the middle line of the epigastrium and opened the peritoneal cavity. Some bulging was found in the region of the small omentum. Mr. Dunn therefore opened the lesser sac, when a large



The shaded part represents the area of dulness.

amount of clear bile-stained fluid flowed out. The gall-bladder was felt to be full, but no rupture of that organ or of the ducts could be discovered, nor was there any perforation of the duodenum or of the stomach. The pancreas did not appear to be enlarged. Some parts of the small intestine appeared to be a little collapsed. Fat necrosis was carefully looked for but none was found. It was at first thought that the bile-stained fluid was confined to the lesser peritoneal cavity, but a second incision was made below the umbilicus and bile-stained fluid flowed away from here also. Two drainage-tubes were inserted into the upper opening and one into the lower opening and the upper wound was partially closed with a double row of sutures. The operation did not clear up the diagnosis. As the pancreas did not feel enlarged and as there was no fat necrosis visible the diagnosis of acute hæmorrhagic pancreatitis was given up. The cystic duct was intact but the bile duct and hepatic ducts could not be satisfactorily examined.

The patient was put back to bed and was placed on his left side. A port wine enema was given immediately and about one and a half pints of saline solution were infused into the axilla. He came round well from the anæsthetic and was very little sick. The pulse was almost imperceptible at 11.20 P.M. and the hands were very cold. Twenty minims of brandy were given hypodermically and the saline enema was repeated. This caused a decided improvement in the pulse. The dressings were changed at this time. He subsequently became very restless, and one-sixth of a grain of morphia was given hypodermically but had no effect, and at 2 A.M. on the 17th the pulse again became very bad. The dressings were changed. The pulse continued very rapid in the early morning but improved later. He was of a good colour and the tongue was clean. The hands were cold, but other parts were warm. He was again very restless, and at 12.10 P.M. an injection of a quarter of a grain of hydrochlorate of morphia was given. This gave him about half an hour's sleep, and another injection of hydrochlorate of morphia (one-sixth of a grain) was given at 9.50 P.M. He was dressed twice, the dressings on both occasions being saturated with bile-stained fluid. On the 18th the abdomen became more distended and was tender. Sickness commenced in the morning and the patient complained much of flatulency. He was fed on albumin water. He was very restless and could not keep still. The sickness increased in the afternoon and at 4 P.M.

he became very collapsed and he died at 5.30 P.M. The cause of death was considered to be peritonitis and the primary condition was thought to be rupture of the common bile duct or of one of the hepatic ducts. The fluid obtained at the operation contained a large quantity of bile. Cultures were taken and proved to be sterile both under aerobic and anaerobic conditions. No micro-organisms could be detected on microscopical examination of the fluid.

The necropsy was made 20 hours after death when rigor mortis was well marked. The body was anæmic but it was not wasted. The conjunctivæ were slightly tinged with yellow. The brain was not examined. There was no pleurisy but there were numerous sub-pleural petechiæ. The lungs were normal. The heart weighed nine ounces and was normal. General acute peritonitis was found, the peritoneum being injected and covered with flakes of yellow bile-stained lymph. At the time of the operation there was no peritonitis, so that it must have followed the draining of the peritoneal cavity. The coils of intestine were found adhering to each other. There was a good deal of turbid bile-stained fluid in the peritoneal cavity. The peritoneal blood-vessels were much congested. The stomach and duodenum were quite normal; there was no ulceration or perforation and the mucous membrane presented quite a healthy appearance. The small and large intestines were also quite normal in appearance. The pancreas was much enlarged, feeling about one and a half times as large as it should have been under normal conditions. It was adherent to the adjacent structures and it was covered with lymph which was deeply stained with bile. The under-surface of the liver was covered with lymph and the connective tissue in the portal fissure had a sodden appearance and was deeply stained with bile. Bile could be squeezed from the gall-bladder into the duodenum. The gall-bladder was not abnormally large, but its walls were œdematous. The common duct was patent and its mucous membrane was bile-stained; it was not ulcerated and there was no fistulous opening. The hepatic ducts were normal, so also was the cystic duct. A small calculus of about the size of a pea was found in the common duct resting in a fold of mucous membrane just where the cystic duct joined it. The fat in the neighbourhood of the pancreas showed spots and patches of fat necrosis. The pancreas was firm and hard. There were many little infiltrations of blood either into the tissues of the pancreas or into the adjacent tissues. The parenchyma had

a swollen, pink, and sodden appearance. I could not trace any direct cause for the bile-stained peritoneal fluid. There certainly was no fistulous communication between the gall-bladder, the cystic duct, the common or hepatic ducts and the peritoneal cavity, but the tissues in the neighbourhood of the bile passages and pancreas had a sodden appearance and were all deeply stained with bile. There were no signs of general biliary pigmentation, although the urine contained a large amount of bile, a condition which was noted before death. The liver weighed 51 ounces. A depressed, wedge-shaped, dull yellowish-looking area was found at the edge of the left lobe extending upwards for about half an inch and being about a quarter of an inch in thickness. In appearance it resembled an infarct more than anything else. The kidneys weighed eight ounces. The left kidney was normal. The perinephric fat surrounding the right kidney was bile-stained and showed numerous opaque, milk-white, and orange-yellow spots and patches of fat necrosis. The spleen weighed three and a half ounces. It was quite healthy. The suprarenals were normal.

Sections from different parts of the pancreas were examined under the microscope. It was found that the pancreas was not involved throughout. All the sections examined showed areas where the acini and their cells appeared to be quite normal. Irregular-shaped areas were also seen, the central parts of which appeared to be made up of a granular débris, no outline at all of the acini or their epithelial cells being visible. Dotted about in this granular débris were a number of polymorpho-nuclear leucocytes. There were also several patches where this granular débris was stained a bright golden colour (? bilirubin). In places effusion of blood could be seen into the inter-lobular tissue. The blood-vessels generally were distended with blood and some of the smaller ones were filled with thrombi partially organised. At the periphery of the necrosed areas the outline of the acini and their cells could be seen, but the protoplasm of the cells had a very granular appearance and their nuclei were not stained. Some of these cells were stained a bright golden colour and contained granules of this pigment. Outside these the cells were faintly stained and outside these again the acini appeared to be normal. There was undoubted parenchymatous inflammation, necrosis of the glandular tissue, pigmentation, and blood effusion and infiltration. Numerous patches of fat necrosis were seen also in the interlobular connective

tissues. Sections stained with carbol thionin blue and examined with a $\frac{1}{12}$th oil immersion did not show the presence of micro-organisms. Cultures were taken and a pure growth of the bacillus coli communis was obtained.

Remarks.—Case 1 was not diagnosed during life. The history of previous attacks of abdominal pain and indigestion spreading over several years, and the acute onset of severe abdominal pain after a late meal of pigeon-pie, seemed to point to perforating gastric ulcer as the most likely explanation of the patient's condition when he was seen on his admission into the hospital. A satisfactory elucidation, however, of the cause of these attacks of pain was found at the necropsy in the gall-bladder, which contained several calculi. A small calculus was also found in the other case, lying in a fold of mucous membrane in the common duct close to the opening of the cystic duct. This association of gall-stones with acute hæmorrhagic pancreatitis is far from being uncommon. If the calculi are formed as a result of changes in the ducts and gall-bladder produced by an invasion of the bacillus coli communis, and as in nearly all of the cases of pancreatitis which have been examined bacteriologically the bacillus coli communis has been found, the invasion of the organ by this organism may have been the cause of this disease, for if the bacillus has ascended the bile duct, the cystic duct, and the hepatic duct it might at the same time just as easily have invaded the pancreas by means of the duct of Wirsung. The diagnosis was cleared up by the operation, fat necrosis being found. The bile-stained peritoneal fluid I shall refer to when discussing Case 2.

The chief point of interest in Case 1 was the finding of fat necrosis outside the peritoneal cavity. No mention of such a possibility is mentioned either in Osler's, Taylor's, or Allbutt's "System of Medicine." Osler[1] writes: "A point of interest is the relation of fat necrosis to pancreatic disease. The areas are found in the interlobular pancreatic tissue, in the mesentery, in the omentum, and in the abdominal fatty tissue generally." Fitz, in his article in Clifford Allbutt's "System of Medicine," chiefly draws attention to sub-peritoneal fat necrosis.

A good deal of experimental work has been done on fat

[1] The Principles and Practice of Medicine, p. 494.

necrosis, but I have not been able to find any note of it as having occurred outside the peritoneal cavity. Flexner[2] and Williams[3] have published the results of their work on the pathology of this curious change in the fat and they both give important summaries of the work of other pathologists. The first pathologist who directed attention to fat necrosis was Balser[4] in 1882; he found it either within the inter-acinous tissues of the pancreas or in the adjacent and distant fat. Langerhans[5] injected the sterilised pulp of fresh pancreas into the peritoneal tissues of rabbits and inflammation resulted with evidence of fat necrosis. He, however, only had one successful experiment out of 12. He satisfied himself that a decomposition of the fat molecule occurred with liberation of the fatty acids and considered that it was due to the action of the fat-splitting ferment. Dettner[6] experimented with pure trypsin which produced a sero-hæmorrhagic effusion in the peritoneal cavity but no fat necrosis. Hildebrand[7] suggested that the hæmorrhage in acute hæmorrhagic pancreatitis was due to trypsin and that the fat necrosis was caused by the action of the fat-splitting ferment. Hlava[8] produced hæmorrhagic pancreatitis and fat necrosis by injecting Klebs-Löffler bacilli into the pancreas after a laparotomy. Rosenbach and Jung[9] experimented with trypsin and with portions of pancreas which they introduced into the abdominal cavities of rabbits. They obtained fat necrosis with pieces of pancreas once out of four times. Flexner's conclusions are as follows:—
1. In peritoneal fat necrosis the fat-splitting ferment is demonstrable at certain stages of the pathological process. 2. It is present in greatest amount in the early stages and may disappear in the later ones when the healing is well advanced. 3. Although it cannot be affirmed that steapsin is the direct cause of the necrosis of tissue such an assumption is rendered highly probable by its constant occurrence in the diseased areas, its absence from the healthy fat, and the

[2] Journal of Experimental Medicine, 1897, vol. xi., pp. 413 to 425.
[3] Boston Medical and Surgical Journal, 1897, vol. i., pp. 345 to 348, and 1898, vol. i., 342.
[4] Virchow's Archiv, 1882, Band xc., p. 520.
[5] Experimenteller Beitrag zur Fettgewebsnekrose, Virchow's Fortschrift.
[6] Inaugural Dissertation, Göttingen, 1895.
[7] Centralblatt für Chirurgie, 1895, Band xxii., p. 297.
[8] Centralblatt für Pathologie, 1897, Band viii., p. 792.
[9] Inaugural Dissertation, Göttingen, 1895.

nature of the pathological changes. 4. The escape of the pancreatic secretion into the peri-pancreatic and pancreatic tissues is the origin of the necrosis and this escape is facilitated chiefly by lesions of the pancreas itself, but also by disturbances in its circulation. Williams concluded that there was some substance in the pancreatic tissue, probably the fat-splitting ferment, which had the power of producing changes in fat similar to those found in fat necrosis.

It will be seen from the above that experimental evidence goes to show that fat necrosis is caused by an escape of the pancreatic secretion into the peri-pancreatic and pancreatic tissues. The changes in the mediastinal and pericardial fat could not be explained exactly in this way, as there was certainly no direct communication between the peritoneal cavity and the pericardial sac. If fat necrosis is due to the action of the fat-splitting ferment of the pancreatic secretion it must have been carried to the pericardial and mediastinal fat by the blood, or by the lymphatic vessels, or by both. It is a well-known fact that a pericarditis or pleurisy may proceed from a peritonitis and that the channel of infection is along the blood-vessels or lymphatics, and I see no reason why the pancreatic secretion should not be carried in a similar manner. The reddish areas of hæmorrhage which were noted in the fat of the mesentery, which were similar in size and form to the areas of fat necrosis, suggested that the factor causing the fat necrosis was carried in the blood-vessels.

In Case 2 the previous history of abdominal pain and indigestion and the acute onset with pain suggested perforating gastric ulcer as the most likely diagnosis to explain his symptoms and condition. The fulness in the upper part of the abdomen, the tenderness situated midway between the umbilicus and ensiform cartilage, and the curious area of dulness made me seriously consider the possibility of acute hæmorrhagic pancreatitis being the disease from which the patient was suffering. The previous history of jaundice and abdominal pain I did not consider to be against this view, as a few months before I had seen a case of acute hæmorrhagic pancreatitis giving a similar history (Case 1). At the necropsy on this case gall-stones were found and fully accounted for the previous attack of abdominal pain and jaundice.

The most striking point of interest about Case 2 and the one I wish to draw particular attention to was the large collection of clear, bile-stained, serous, sterile fluid found in the peritoneal cavity at the time of the operation.

It puzzled us a good deal and many suggestions were made to explain its presence. No fat necrosis was found and the pancreas did not appear to be enlarged, so that the diagnosis of acute hæmorrhagic pancreatitis was given up. It was suggested that possibly the bile-stained fluid might be accounted for by a perforating ulcer of the duodenum, but against this view was the absence of peritonitis, the clear character of the fluid, which proved also to be sterile, and the fact that the duodenum was carefully examined and found to be intact. The gall-bladder at the time of the operation was shown to be full of bile and intact, so that a perforation or rupture of this organ was excluded. The cystic duct was also normal but the bile ducts and the hepatic ducts could not be satisfactorily examined. We thought that possibly one of the ducts had ruptured and that the previous attack of pain and jaundice suggested a gall-stone as being the most probable cause of the trouble. At the necropsy a biliary calculus was found, but it was small and was not obstructing the flow of bile. The tissues in the neighbourhood of the bile-passages and pancreas had a swollen and sodden appearance and were all very deeply stained with bile, but there was no abnormal opening in the gall-bladder, cystic duct, hepatic duct, or bile duct which could allow of the escape of bile. I thought that the inflammatory and sodden condition of the tissues and ducts had allowed of an escape of bile into the peritoneal cavity by means of either the lymphatics or blood-vessels, or by both. Although this peritoneal fluid and the urine both contained large quantities of bile pigment there was no general biliary pigmentation, which seemed a point in favour of a local exudation of bile. A large quantity of bile-stained serous fluid was also found in the peritoneal cavity of Case 1 at the time of the operation, and at the necropsy the tissues in the neighbourhood of the bile passages were stained with bile. Another point of interest in Case 2 was the marked pigmentation of some of the cells and of the débris in the affected areas.

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