Although, as will be seen later, I can support Dr. Slade's conclusions in advocating cholecystectomy in cases where the gall bladder is thickened and seriously altered at the time of operation, I cannot agree that any thickening of the wall of the gall bladder is presumptive evidence of a carcinomatous change, for I know that in my earlier operations on the biliary passages I found many thickened gall bladders containing gall stones, and the operation of cholecystotomy proved entirely curative, and the patients are continuing well many years later. Moreover, I only know of two cases in which cancer of the gall bladder developed subsequently to cholecystotomy, one of the cases having been under my immediate observation.

The practical conclusions which I feel confidence in urging, both from my own experience and that of others, are, that there is an undoubted relationship between cholelithiasis and cancer of the gall bladder and ducts; and as gall stones produce characteristic symptoms, and are therefore as a rule easily diagnosed, and since they can be removed in the early stages before serious complications have supervened with very little risk (in my experience, extending over some hundreds of operations, less than 1 per cent.), the preventive treatment for cancer of the gall bladder is obviously removal of the source of irritation. So impressed am I with the importance of this view, that although I know the symptoms of gall stones, which frequently depend on the associated catarrh, can often be relieved for a time by general treatment (though the gall stones producing the catarrh cannot be removed by medicine), yet I consider it wise to recommend their early removal, not only because it can be safely done, but also because the symptoms are likely to recur and lead to other complications, and, not least important, because, in a considerable percentage of such cases, malignant disease will be likely to supervene if the irritation be not removed.

[A number of specimens of gall bladders removed by cholecystectomy were shown, and others were demonstrated by photographs thrown on the screen.]

CASE OF INTRAHEPATIC CALCULI.

BY

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SINCE large intrahepatic calculi in the hepatic ducts are very rare the following case is of much interest:

R. V., a coffee-tavern keeper, aged 52, was admitted to the Cardiff Infirmary on May 2nd, 1905, complaining of "painful swelling in the stomach and jaundice."

Past History.

He had a severe attack of typhoid fever when 11 years of age and was never robust afterwards.

Since the age of 23 years he had been much troubled with constipation, and had suffered at frequent intervals from what he called "bilious attacks," the attacks being characterized by severe colicky abdominal pain, never lasting more than a day or two, and being always relieved by purging. These attacks at one time occurred almost every week. About two years ago he had a prolonged and severe attack, and after this there was an intermission of three months, and subsequently the attacks recurred every three or four weeks. He was never jaundiced during or after any of these paroxysms. His appetite was good and he seldom took stimulants of any kind.

In October, 1904, he was laid up for a few days with a rather severe attack of pain, since which time he had fewer recurrences and had expressed himself as feeling better than usual until taken ill on April 16th, 1905, when he was seized with very severe pain in the abdomen and back without any definite localization; the face was flushed, the pulse rapid, he was very restless and irritable, and the temperature was 102° F. There was marked tenderness in the epigastrium, especially just below the xiphisternum, and the liver was felt extending to three fingerbreadths below the right costal margin.

The pain and pyrexia continued till admission to the infirmary and frequent hypodermic injections of morphine

were necessary. Jaundice made its appearance for the first time on April 27th, and rapidly deepened.

State on Admission.

May 2nd. The patient complained of pain over the epigastrium and right hypochondrium, of flatulence and of insomnia. He was very weak and considerably wasted, there was deep jaundice with drowsiness, and the pain caused him to be restless and sleepless.

The appetite was much impaired; the tongue was dry, cracked and furred; nausea and vomiting were absent and the bowels constipated. The temperature was normal. Slight albuminuria was present and there was some oedema about the ankles. The abdominal muscles were rigid above the umbilicus and there was tenderness on pressure, especially marked in the epigastrium. The liver was considerably enlarged, extending downwards to within a fingerbreadth of the navel, and the organ was tender and smooth, but the gall bladder was not palpable.

Fig. 1.—Section of the liver showing numerous dilated ducts from which calculi have been removed. It also shows an enormous cavity.

Progress.

The patient rapidly became worse, with marked prostration; subnormal temperature; rapid, feeble pulse; drowsiness; partial unconsciousness; rapid, feeble breathing; deepening jaundice, and increasing hepatic enlargement.

On May 11th a marked change occurred. The jaundice became much less marked, bile appeared in the motions for the first time since admission, the hepatic enlargement diminished, and the patient's general condition was better than it had been since the beginning of his illness.

On May 13th 46 oz. of a clear, bile-stained fluid was removed from the right pleura.

On May 14th the patient became worse and rapidly sank into his former grave condition; the jaundice

deepened, the hepatic enlargement increased, the stools became colourless, and he died in a comatose state on May 16th.

Post-mortem Examination.

The liver weighed 97 oz. Between the upper surface of the right lobe of the liver and the diaphragm there was a fairly large abscess. The surface of the liver showed over the whole of its extent small projections, which were found to be caused by underlying calculi, and over the upper surface of the right lobe there were numerous white points, which on section proved to be tiny abscesses containing thick pus, none being larger than half a split pea.

The gall bladder was of normal size, there were no signs of inflammation in or around it and it contained a little mucus, but no bile nor gall stones. A probe could be passed from the gall bladder into the cystic duct for about half an inch, but there was no communication between it and the other bile ducts. The hepatic duct and upper end of the common bile duct formed a remarkable dilata-

varying sizes. The calculi were of all shapes and sizes and many were faceted.

REMARKS.

The points of interest in this case are numerous:

1. *History of Typhoid Fever.*—Since his attack of typhoid fever when 11 years of age, the patient seems never to have been robust, although no symptoms suggestive of gall stones appeared until he was 23 years of age, since which time till his death, twenty-nine years afterwards, he had suffered from frequent attacks of colicky pain attributed to "dyspepsia."

2. *Jaundice.*—This symptom never appeared until nineteen days before his death. The diminution of the jaundice associated with the appearance of bile in the motions and with the marked diminution in the size of the liver, and the subsidence of the grave "cholaemic" symptoms on May 17th, or five days before his death, was a marked feature of the case. This can only be attributed to a temporary removal of the obstruction of the common bile duct; and since no stone was found in the stools, the particular one which was causing the trouble must either have passed unobserved or have slightly shifted its position, since the sudden diminution of the jaundice could not have been due to a dilatation of the duct at the point

Fig. 2.—Section of liver showing several of the smaller softer calculi which have been cut across.

tion (resembling a dilated gall bladder) which contained mucus, bile, and a large number of calculi of various shapes and sizes, but all of firm consistence. Over one hundred calculi were counted, the largest weighing nearly 100 gr.

† The liver presented a most remarkable and interesting condition. The hepatic ducts throughout the whole organ were greatly dilated, and in many places there were large cavities with a shining internal lining. These dilated ducts and cavities contained calculi, mucus and bile, but no pus.

On making a section of the liver some of the calculi could be cut through while others were hard and no part of the liver was free. No less than 520 calculi were counted, with a total weight of 1,378 gr., the largest being 1½ in. in length and weighing 270 gr., and was contained in a large cavity with several other stones of smaller and

Fig. 3.—Section of liver showing several calculi in situ.

of impaction. The rapid diminution in the size of the liver is easily accounted for by the emptying of the bile from the innumerable hepatic cavities. It is very remarkable, with such an enormous number of gall stones, that jaundice did not appear sooner from one of the stones getting impacted. Although the calculi had probably been forming for many years, the concomitant dilatation of the ducts had permitted of the bile reaching the duodenum, and the patient's health had remained fairly good and he had continued at his work, with short intervals of rest, up till April 16th, 1905.

3. *Fever.*—There had been apparent freedom from pyrexia until within a month of his death, and while under observation in the infirmary the temperature was normal or subnormal. At the autopsy a large abscess was found between the liver and the diaphragm, and there were numerous tiny suppurating points on the upper surface of the right lobe, but there were no signs of suppurating in the dilated ducts.

4. *Gall-bladder.*—The freedom of this organ from any signs of cholelithiasis (past or present) was a feature of the case. At first sight the enormous dilatation involving

the hepatic duct and the upper end of the common bile-duct might easily have been mistaken for an enlarged gall bladder containing numerous gall stones.

5. *The Liver*.—The appearances presented by this organ are represented in the accompanying photographs.

Chemical Analysis of the Intrahepatic Calculi.

For this we are indebted to our colleague, Dr. Schölberg, who carried out a careful analysis on 20 grams of the calculi after the method described by Salkowski, with the following result:

Cholesterin	...	...	18.0 per cent.
Calcium bilirubin	...	...	38.9 "
Iron	...	...	0.01 "
Phosphates	...	...	A faint trace.
Water	...	...	43.09 per cent.

From the small abscesses on the surface of the liver Dr. Schölberg isolated the *Bacillus coli*. The typhoid bacillus was not discovered.

Fig. 4.—Calculi removed from the intrahepatic ducts.

Literature on Intrahepatic Calculi.

1. Mayo Robson, *Diseases of Gall Bladder and Bile Ducts*, p. 216: "Gall stones formed almost entirely of bile pigment may be seen. On two occasions there were found soft concretions of this nature in large numbers in the hepatic ducts within the liver."

2. Rolleston, *Diseases of the Liver, Gall Bladder, and Bile Ducts*, p. 721: "Large intrahepatic calculi occupying the hepatic ducts and distending them are very rare. I met with one such case in a man who died with diabetes from secondary chronic pancreatitis (vide Fig. 95). Murchison (*Diseases of Liver*, second edition, p. 545) refers to a plate of Cruveilhier showing large intrahepatic calculi like coral. There is a good specimen of multiple intrahepatic calculi in the Westminster Hospital Museum (No. 581). These calculi almost necessarily set up jaundice and a good deal of pericholangitis, which may be suppurative. The calculi are chiefly composed of bilirubin-calcium. Small black bilirubin-calcium calculi are not uncommon. Occasionally masses of calculous material are found embedded in the substance of the liver in dilated ampulla-like terminations of bile ducts which have lost their continuity with the bile ducts."

3. Naunyn, *Cholelithiasis* (Trans. A. E. Garrod, 1896, N. S. S.), p. 29: "Bilirubin-calcium gravel in the bile ducts within the liver are in size from finest gravel to nodular and stalked masses in thick, greasy, brownish-black bile." "They consist of calcium compounds of the bile pigments." "Contain large amounts of the higher oxidation products of bile pigments and bilirubin." "One finds in such concretions biliverdin, bilicyanin, and bilifuscin—the transition substances between bilirubin and humin." "... found ... in the large bile ducts ... calculi of cholesterin tightly enclosed by the mucous membrane of the duct." "... exceptional circumstances, calculi can even originate in the large bile ducts ... increase in size ... due to bilirubin-calcium and cholesterin."

4. Frerichs, *Clinical Treatise on Diseases of the Liver*, vol. ii, p. 512—Gall stones in the interior of the liver, in the branches of the hepatic duct: "Gall stones are rare in this locality. Morgagni, however, long since collected a series of observations from the works of Plater, Fallopius, Dodonoeus, Columbus, Paysch, and others,

showing that concretions had been found in the interior of the liver. Biliary concretions in this locality most frequently present the form of brown or black grains. Sometimes, also, we meet with larger round stones, or, more rarely, with branched, coral-like concretions which form casts of the ducts and are sometimes solid, but at other times hollow. The branches of the hepatic duct are dilated by these deposits, either uniformly or in a saccular manner. The concretions may give rise to inflammation and ulceration of the bile ducts, and also to hepatic abscesses and pylephlebitis."

OBSERVATIONS ON PANCREATIC NECROSIS, WITH A REPORT ON TWO CASES.*

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TOGETHER WITH A NOTE

By C. LOVATT EVANS

ON CAMMIDGE'S PANCREATIC REACTION IN THE URINE.

THE two following cases of pancreatic necrosis form together an interesting study. In a paper in the **BRITISH MEDICAL JOURNAL** of December 22nd, 1900, I drew attention to infection spreading up the common bile duct and setting up various inflammations of the pancreas. Probably this is the channel of infection in the majority of such, and in the second case here described it is very probable that this was the channel of infection. This is in marked contrast to the conditions found in the first case; here there was no clinical evidence of infection, and the removed fluids proved to be quite sterile. It seems probable, therefore, that the death of pancreatic tissue was due rather to deprivation of blood supply, possibly through thrombosis of some of the arterial supply to the organ. In acute infective lesions of the pancreas haemorrhages into and around the organ are common, but haemorrhages may be found altogether apart from infection, and for these there is often no adequate explanation.

In a short paper on pancreatic cysts¹ I drew attention to the presence of large quantities of blood in some of these cysts. Injury may no doubt account for some of the bleedings, but in one of my cases there was no evidence of any traumatism, and the explanation of the bleeding remains obscure. Is there any relation between these and the first case here described?

The notes by Mr. C. Lovatt Evans on Cammidge's test are of considerable interest, as Mr. Lovatt Evans is a skilled chemist, constantly engaged in physiological chemistry. The utility of this test is considerably restricted by the fact that it requires an expert to carry out the examination, and that even then the result may be vitiated if suitable precautions are not taken.

CASE I.—Pancreatic Necrosis, with Cyst Formation, but apparently without Infection. Operation.

A woman, aged 43, was admitted to the General Hospital under the care of Mr. Barling on July 1st, 1904, with a history that she was taken ill on June 12th with severe abdominal pain and vomiting, followed by diffuse tenderness over the whole abdomen; the patient was so ill that perforation of a gastric ulcer was suspected. For a week she improved, but on June 20th she had another acute attack of pain in the epigastrium, going through to the back, with incessant vomiting, which continued until the day of admission, and soon after this second attack of pain a fullness was noticed in the upper part of the abdomen. Morphine had been required on several days to subdue the pain.

State on Admission.

The patient was a well-developed woman, with a swelling in the epigastric and upper part of the umbilical region, which was firm, but rather elastic, and lay with its long axis transversely; stomach resonance appeared to be entirely above it. At this time the chief pain complained of was in the dorsal region about the level of the last dorsal vertebra, and the eleventh dorsal vertebra was very hyperaesthetic on pressure. The pulse was 124, temperature 99.6°, respirations 24; the urine was free from albumen and sugar.

* Read at a meeting of the Pathological Section of the Birmingham Branch of the British Medical Association.