Some Remarks on the Pathological Complications of Cholelithiasis with illustrative cases.

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Introduction

In considering a subject for a thesis for the degree of M. D. there presented to my mind, in addition to other possible subjects, the idea that some cases of Cholecystotitis, which came under my notice as a house-surgeon in the Victoria Infirmary, might be worth recording, and that some interest might be found in investigating the pathological complications of gall stone disease, together with the bearing which such have on the clinical history of the cases.

During the last few months the opportunity of completing this study presented itself, and I am indebted to the Physicians and Surgeons of the Victoria Infirmary for permission to record the notes of their cases; and to Dr Anderson, the Pathologist for allowing me access to the pathological records, for material for microscopic examination, for the facilities for preparing photo-micrographs, as well as for occasional valuable advice.

I trust I have presented my subject in an acceptable form for the degree, and would take this opportunity of acknowledging my indebtedness to the above named gentlemen.

Contents

Historical Resume.

Although gall stones and gall-stone disease with its many complications are familiar incidents in present day clinical medicine, it is remarkable to think how recently we are indebted for our knowledge of these conditions, and what a small share of the contributions are due to the "Fathers of Medicine". To them gall stones were evidently unknown or overlooked, and it was not till the middle of the 16th century that we find them first mentioned by Antonius Benevenius.

It may be the case that, in the earlier days of medicine, they were exceedingly rare, and their frequency at the present day is dependent on the evolution of modern civilization.

Following Benevenius came Fernelius, who, in 1554, gave a very good description of gall stones with the symptoms produced by them, and to him has been attributed the observation, that occlusion of the common bile duct occasioned a swelling of the gall bladder and clay coloured motions

Still later in 1563, we find a valuable contribution to the then literature by Paracelsus, who brought to bear on the subject the full weight of his clinical knowledge, and, independent of the researches of others, entered into the question of the origin of the disease. His observations are of special interest since they indicate the part which diet plays as an etiological factor.

Further advances were made by his immediate followers, Kentmann, Cäller, Plater, and Hildanus, who paid special attention to the various forms of stones found, and by Glisson, to whom we are indebted for various anatomical investigations in connection with the liver and bile passages. From him we have also a description of a typical attack of hepatic colic with jaundice — the outcome of the sufferings of the observer himself. The later part of the 16th century shows contributions from Blasius, Wille, Thilesius etc. relating more especially to the relation of gall stones to the formation of abscesses. Ettmüller also, at the same time, gives a most lucid description of the clinical symptoms associated with this condition, in his classical dissertation "De ictero flavo, nigro et albo." Passing now to the beginning of the 18th century, we find Morgagni, Sydenham, Vater, and others, contributing to the literature of the subject, dealing with its clinical aspect and the lines of treatment. Contributions bearing on the complications of the disease were dealt with by Friedrich Hoffmann, and Gottfried Müller, while in 1743, Petit drew attention to suppuration of the gall bladder existing in connection with gall stones, and, by the suggestion of the drainage of the pus, was the pioneer of the later Epoch of the surgery of the bile passages. The middle of the 18th century is characterized by a further development of the anatomical, pathological, and chemical, knowledge of the conditions under

discussion and the names of Haller, Morgagni, Fourcroy, Soemmering and others are associated with such descriptions, while towards the end of that century and the beginning of the 19th we have the excellent clinical accounts of Prunescau, Frerichs, and Fauconneau-Dufresne, while still later, Meckel von Hembach recognised, and pointed out, the significance of catarrh of the bile passages in the formation of concretions.

Charcot's investigations and the light which bacteriology has thrown upon the subject gave an impetus to the investigations of those following and helped to improve our knowledge of a condition which was previously but little understood. From this point it becomes almost impossible to continue the record in a chronological order, as the various additions to the literature come under the headings of the various departments of medicine, pathology and pathological chemistry being responsible for the description of the stones and the lesions which they have produced as determined by post-mortem examination. We will have occasion to refer to some of the more recent observers in discussing the origin of gall stones.

To modern surgery on the other hand, — rendered possible by the dawn of antisepsis and asepsis and by the exactitude in the technique of abdominal operations — we can ascribe still further advances in our knowledge of the subject. Since Petit first suggested the possibility of operation upon the gall bladder (after adhesions to the anterior abdominal wall had taken

place) the surgery of the bile passages has attracted the attention of many men, and after Kocher and Sims performed their first successful cholecystotomy and Langenbuch cholecystectomy, this branch of surgery has developed enormously till now the number of operations, and the variety, in that region, is very considerable.

Of the modern surgeons, who, by their operative work, have added to our knowledge and literature on the subject the names of McGill and Mayo Robson, Lawson Tait, Reidel, Kehr etc occur first to my mind.

Their operations, frequently undertaken for the condition per se, from time to time disproved the deductions from clinical observation, and were instrumental in showing, not only the variety of pathological lesions in the biliary passages, but also the important relationship which exists between gall stones and diseases in other organs in the upper abdominal segment, such as diseases of the pancreas and liver.

To them, then, as well as to the pathologist must we look in the future for a still clearer and more definite understanding of gall stones and the diseases associated with them.

Origin of Gall stones.

Many theories have been put forward from time to time regarding the origin of gall stones. Galen first formulated the idea that they were formed from

coagulation of bile. This opinion held good for a long time till Paracelsus propounded his doctrine of "Tartarus" whereby he sought to show that digestive disorders caused an acidulation of the blood, and these acids acting on the bile caused a precipitation of concretions

Other writers then came forward holding the view that there might be an excess of the natural constituents of the bile and that stone formation arose from the precipitation of this excess.

In the 18th century Haeckel von Hemsbach called attention to the part which chronic catarrh of the gall bladder and ducts played in the formation of calculi and, though various authors have since then given us other causes, this one holds its own to the present day.

Of the recent investigators who have studied the question, we are indebted most of all to Naunyn for throwing light on this subject. According to his researches, gall stones are formed primarily from the desquamated epithelial cells of the mucous membrane of the gall bladder which had undergone fatty degeneration and formed a central nucleus, around which a deposit of cholesterine from normal bile in a crystalline form takes place. Further additions to this occur giving rise to the smaller and larger stones.

Another recent view which has been brought forward is that the stone may arise from sediment present normally in human bile - namely small granular

brownish lumps composed of cholesterine, bilirubin - calcium, alkaline salts of the bile acids, inspissated with albumen and mucus. From this sediment the bile acids salts become eliminated and the remainder is covered by a thin shell of bilirubin - calcium; the cholesterine crystallizes, the bilirubin - calcium assumes a granular form and both are deposited on the inner surface of the shell.

This method of formation is the one which is supposed to account for the presence of cavities in the centre of some stones but even this does not get away from the view of Naunyn, for the central nucleus in either case may have undergone solution after it had been formed.

It is evident then that the first factor in the causation of gall stones is an unhealthy condition of the wall of the gall bladder and bile ducts and this may be aggravated by an abnormal formation of glands (which are seen in sections of the altered mucous membrane) leading up to an increased formation of cholesterine and calcium - containing mucus.

The explanation of the origin of this initial catarrh again gives rise to a diversity of opinion. The elder view was that some noxious substance reached the mucosa by way of the blood current or that some poisonous material was present in the bile itself which, by contact with the mucosa, produced the condition.

The action of bacteria (Gallippe 1886) has been brought

forward, on the other hand, as the more recent explanation and it has much to commend itself in spite of the fact that normal bile is regarded as sterile.

The experimental production of gall stones has further aided us in our conception of the condition and has thrown considerable light on the etiology The injection of virulent cultures of organisms into the gall bladder of animals produces an acute cholecystitis; attenuated cultures, on the other hand, have been followed by the formation of concretions, especially if the flow of bile be retarded and on these lines the view of clumping of organisms as a central nucleus, seen in connection with typhoid bacilli, may be an important factor in their production.

Further there can be no doubt that the diminished contractile power of the gall bladder of advancing years, the retarding effect on the elimination of bile of tight clothing and tight lacing, pregnancy and sedentary habits; and the anomalies of metabolism as seen in gout and arterio-sclerosis are all important predisposing factors.

Complications of Cholelithiasis

In discussing the complications of cholelithiasis it is proposed to take up the the pathological changes

which occur in this disease in their anatomical sequence — that is, to trace the gallstones from their origin and enumerate and describe the various changes which they may give rise to during their period of existence within the body. I have already described shortly the factors which lead up to the formation of the stones and it is at once seen that, while in exceptional cases gall stones may form within the ducts, in the vast majority of cases they are formed within the gall bladder.

It is well known that gall stones may lie within the gall bladder for years giving absolutely no clinical signs of their presence and be only discovered accidentally at post-mortem examination, while again they may give rise to a variety of conditions some of which are of a very serious nature and may even be followed by fatal results. Formerly little was known why in some cases gall stones should lie quiescent in the gall bladder, while in other cases they should be attended by such serious results: but since the era of bacteriology has dawned much has been done to advance our knowledge in this respect.

We know that normally bile is practically sterile and until recently it was generally supposed that it possessed antiseptic properties. One of the arguments of this belief was that when occlusion of the biliary passages occurs there is an increase of the putrefactions within the intestine. This theory has been questioned

by several authors who agree in the statement that bile is a culture medium in which organisms can be grown in abundance.

The changes which occurred in the gall bladder as the result of cholelithiasis were attributed to mechanical and chemical actions, but it has now been proved that it is the entrance of micro-organisms into the bile passages which leads to inflammation and its sequelae. Organisms may gain entrance into the gall bladder and give rise to no gross lesion and they have been found within gallstones and yet the bile around them was sterile (Gilbert and Fournier) In the majority of cases, however, the entrance of organisms into a gall bladder in which one or more stones is present is the initial stage in the lighting up of an acute inflammation, which in turn, may lead to one or other of the complications which I shall now describe

Acute Cholecystitis. This is the first of the complications in the order in which I propose to take them up. The organisms which are most frequently found in acute inflammation of the gall bladder are, the bacillus coli, which is almost constantly present and may or may not be accompanied by others, viz:- Staphylococcus albus or aureus, streptococcus, bacillus typhosus and very occasionally the pneumococcus. The method of entrance of these organisms into the gall bladder has long been open to discussion. Mayo Robson[2] writes " There are three possibilities

1/ by the bile ducts 2/ from the blood 3/ directly through the wall of the gall bladder. The last mentioned must be regarded as very exceptional, and entrance from the blood has been apparently disproved; hence the most probable source of infection is by way of the bile ducts."

Hoppe Seyler[3] says " Microbes as a rule enter these passages from the intestine and travel in a direction opposed to that of the current of bile: less frequently they enter the bile passages from the liver i.e. directly or indirectly from the blood stream. In the latter instance they produce a descending infection by travelling down the ducts. In exceptional instances, finally, they may enter the gall bladder by penetrating the walls of this viscus from the intestine, or from some neighbouring focus of disease."

Stanmore Bishop[4] in an article written on the subject quite recently describes and discusses the following methods of infection :- The infection may reach the biliary passages in one of four ways (1) through the duodenal opening (2) through the portal circulation (3) through the systemic circulation (4) through the lymphatic circulation. His views go to support the theory of infection through the portal circulation and, while he does not deny infection through the opening of the bile duct into the duodenum, he says that such a method is gravely discounted. Having discussed, then, the method of infection of

next follows to describe the pathological lesions which are seen in cholelithiasis complicated with cholecystitis. These may be of varying severity ranging from simple inflammation to suppuration and gangrene.

In the simple inflammatory condition we have a catarrh of the mucous membrane with swelling and congestion which may spread to the cystic duct, though this does not necessarily follow, and there may be a slight hypertrophy of the wall of the organ at this stage.

Later the inflammatory condition spreads through the entire coat of the gall bladder. The mucous membrane undergoes proliferation, it becomes thickened, swollen, and infiltrated with round cells while patches of epithelium are shed, and here and there on the surface a tendency to ulceration is seen. The muscular coat becomes oedematous and thickened, and there is great engorgement with blood. The serous coat presents a turbid appearance and contracts adhesions to neighbouring structures (pericholecystitis).

If the process continues other changes are seen; the epithelium loses its normal appearance, the cells become cubical and, according to Gilbert[5] a transition into pavement epithelium may be seen. The muscular wall is invaded by connective tissue and round cells, the former of which in due time contracts destroying the muscular tissue proper, and the last stage is that in which

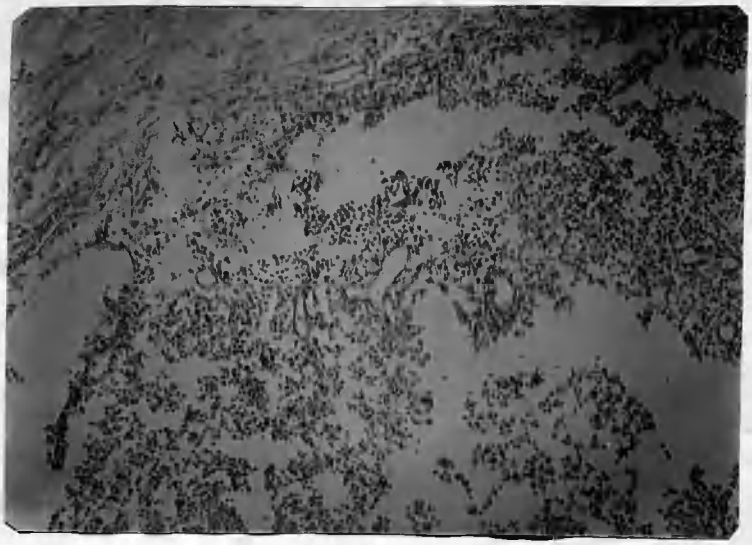

Fig. 1. — Photomicrograph of Gall bladder wall showing Cholecystitis.

Note the considerable degree of round celled infiltration which is present.

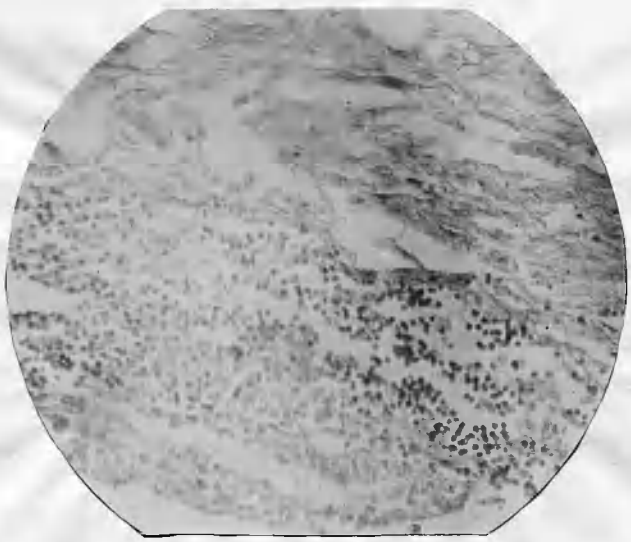

Fig. 2. — Photomicrograph of Gall bladder wall showing Cholecystitis

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it is impossible to divide the gall bladder into its separate layers - all being fused into one mass of fibrous tissue, slightly vascular, and sometimes only with difficulty recognised eg. a sclerosed gall bladder.

In other cases when the infection is, perhaps, more acute, the condition goes on to suppuration and the complication then becomes a much more serious one. The mucous membrane may be destroyed and replaced by granulation tissue, and patches of ulceration are seen here and there with perhaps a stone resting against an ulcerated portion.

The muscular coat becomes swollen with inflammatory exudation and it may also appear oedematous; while the serous coat is inflamed, adherent often to the surrounding structures by recent fibrinous exudation, and when separated it shows a reddish shaggy granular surface. Ulceration of the wall may go on until perforation occurs, and bile, with or without one or more of the gall stones, passes into the peritoneum, into a mass of adhesions, or, if a fistula be formed, into one or other of the adjacent organs.

A further stage may also take place with phlegmonous or gangrenous cholecystitis in which there is present a very acute infection with morbid changes similar in every respect to the suppurative variety but more extensive and acute. The mucous membrane shows evidence of ulceration and necrosis,

and later gangrene of a part, or the whole, of the organ may take place.

The following three cases, which were under my care as house-surgeon in the Victoria Infirmary, illustrate the condition of simple cholecystitis complicating gall stones.

Case 1. Mrs M— aged 29. Admitted into the Victoria Infirmary under care of Mr Maylard on 10th Aug. 1904. Her history was that 19 months previously, she was suddenly seized with acute pain in the right hypochondrium followed by sickness and vomiting and 24 hours later she became jaundiced. The pain, sickness, and vomiting, passed off soon, but the jaundice persisted for about a week. About 3 months later she had a second attack, similar in every way to the first one, except that, if anything, the jaundice was more intense. Following this she had an immunity from seizures for six months and even after that the seizures which she had were of a mild nature and caused her little or no trouble. In April 1904, however, she had a very severe illness somewhat similar to the first attack above described. The jaundice after this attack passed off and she remained well till three days before she came under our observation. This attack was ushered in by severe pain in the right hypochondrium, followed by sickness and vomiting, and two days later the whole body became deeply jaundiced.

On admission, she was deeply jaundiced all over the

body. The site of maximum pain was located under the lowest rib, in the parasternal line, on the right side, and on pressure over this part pain was felt and there was also rigidity, but no tumour of any kind could be detected.

The other organs presented no abnormal conditions.

She was kept for five days under observation and during that time her motions were clay coloured and the urine contained bile, but she had no more attacks of pain.

Operation was performed by Mr. Maylard on Aug. 16th.

On opening the abdomen by the oblique subcostal incision, the gall bladder was found to be slightly distended. It was opened and clear mucoid fluid escaped at first, but later this became very turbid. Several gallstones were removed from the gall bladder and one from the cystic duct. The head of the pancreas was found enlarged and indurated. The gall bladder was washed out and a fistula formed by attaching the gall bladder wall to the edges of the peritoneum

The patient made an uneventful recovery and was dismissed well.

Case 2. Mrs F.—— aged 39. Admitted into the Victoria Infirmary under care of Mr. Maylard on 6th July 1904.

Her history dates back to 6 months before admission when she began to complain of occasional

attacks of sickness and vomiting. Three months later she noticed a swelling on the right side of the abdomen which was painless and did not cause her any discomfort. Her acute symptoms came on 10 days before admission. On that date she was suddenly seized with cramp-like pains over the epigastrium and a feeling of fulness over the stomach. This passed off within a short time, leaving only a soreness of the parts behind. Two days later she had the same symptoms again which subsided within 24 hours, to reappear again in two days time, that is, she had three attacks during the week with an interval of two days between them. The last of these attacks was accompanied by sickness and vomiting, which lasted for 48 hours, and the pain was more severe than formerly.

Her previous history showed that she had always suffered from a weak stomach but was otherwise healthy.

Examination revealed a visible swelling on the right side of the abdomen, tender to touch and situated midway between the iliac crest and the last rib. It was freely movable and seemed about 2½ inches long. There was nothing abnormal found in any of the other organs.

Operation was performed by Mr. Andrew on July 13th.

On opening the abdomen a sausage shaped swelling presented itself, which, when traced upwards under the ribs, proved to be an elongated and thickened gall bladder. It was not adherent in any way and

was easily isolated. On incising it, the walls were found thickened and hypertrophied, and a gallstone was present at the opening of, and blocking, the cystic duct. On removal, the stone was found to be about the size of a pigeons egg. A drainage tube was put in and the wound closed.

Recovery was uneventful and she was discharged well 6 weeks after the operation.

The temperature throughout the illness was normal.

Case 3 Mrs B——. aged 57 was admitted to the Victoria Infirmary under care of Mr Maylard on 14th April 1904.

Her history was that 10 months previously she had severe pain in the right hypochondrium which radiated round to the back. The attack was very severe, and was accompanied by sickness and vomiting, but it only lasted for about 6 hours. Next night she had an attack similar to the previous one, and again, two days after, she had two others in every respect the same. All these attacks were characterised by pain in the right hypochondrium, sickness and vomiting, and passed off after a few hours illness. For a period of 6 months she remained perfectly well, had no trouble whatever, but at the end of that time she was suddenly seized with acute pain over the region of the liver, sickness, vomiting and diarrhoea, and when the pain went away the skin was found to be jaundiced. The jaundice

persisted for about a month and then the skin cleared up considerably, but not entirely. In February 1904. she caught a chill, and, as the result of this, the jaundice became again pronounced. There was no biliary colic accompanying it and when she recovered from the chill a fortnight later, the jaundice disappeared. Her next seizures were in April of the same year when she had another attack of acute colicy pain in the right hypochondrium, radiating upwards to the lower ribs, and posteriorly to the spine. She had also sickness and vomiting but no accompanying jaundice. Up till the time of her admission she has always had pain over the right hypochondriac region, varying in severity from time to time, but constantly present.

Her previous health was good

Examination showed jaundice to be present all over the body. Tow area of Tenderness on pressure, about an inch to the right of, and one and a half inches above, the umbilicus was present, and there was also rigidity on palpation over this area but no distinct swelling could be felt. Nothing else abnormal coved be detected in the abdomen.

The urine was of a dark olive green colour, specific gravity 1030. There was a thick deposit of urates but neither albumen or sugar was present.

Cammidge's test for associated pancreatitis was done by me with the following result:- The test

showed the presence of crystals by reaction A. which re-dissolved in 1½ minutes in 33% H_2SO_4. The complete reaction with the Sulphuric Acid took 6 minutes or fully that. With reaction B there were no crystals. According to the basis of the reaction, chronic pancreatitis was indicated but the time limit was exceeded.

Operation was performed by Mr. Maylard on April 20th.

The gall bladder was found to be of normal size and contained a calculus together with some viscid turbed bile. The bile ducts seemed fairly healthy but the head of the pancreas was enlarged, nodulated and indurated.

A drainage tube was inserted and the wound closed.

The after treatment was complicated by sickness which was only got rid of by the adoption of rectal feeding. After that she improved rapidly and was discharged well, 6 weeks after operation

Remarks. The history and course of this last case suggests clearly the descending infection which has already been commented upon. The gall bladder wall weakened by the presence of a stone becomes infected by micro-organisms and a cholecystitis is set up. This inflammation gives rise to pain sickness and vomiting but there was no jaundice present till 6 months after the first attack. The jaundice was then an indication that the catarrh of the gall bladder had extended from the cystic duct to the common duct.

Even after this had subsided a chill, caught some four months later, was sufficient to light it up again

The condition of the pancreas suggests that the infection spread down the whole length of the common bile duct to the pancreatic duct and along it, causing a chronic interstitial pancreatitis. It also bears out to a certain extent the value of Cammidge's test in the diagnosis of cases of supposed chronic pancreatitis - which will be referred to later.
The cases of cholecystitis one meets with are generally found at operations, and, as it is not a very fatal condition per se, few come to the post-mortem table. It may happen, however, that cholecystitis exists in association with other conditions which give rise to a fatal result. As examples cholecystitis was present in the case of Mrs G— (case No 11) where there was an abscess of the liver as well and also in that of Mrs D— (case No 7) where in addition to the cholecystitis the entire bile duct was buried in adhesions

<u>Pericholecystitis</u> is the name given to inflammation of the serous surface of the gall bladder and is secondary to an acute cholecystitis, the infection spreading from the mucous coat through the muscular-fibrous layer to the serous coat, with the result that fibrin is deposited on its surface and adhesions form between the gall bladder and adjacent organs. These adhesions take place more rapidly, and are not so numerous or firm, as in chronic cholecystitis. The disease itself is closely allied to, and dependent on, acute cholecystitis

Hydrops and Empyema of the gall bladder must demand our attention as complications of cholelithiasis Hydrops of the gall bladder is the term used to denote distension of that organ by mucus. It results from the accumulation of the natural secretion of the mucous membrane due to obstruction of the cystic duct by gallstones, stricture or growth. Naturally it can only occur if the gall bladder has not atrophied as the result of previous gall stone irritation.

The pathological condition of the wall varies, it may be atrophied and excessively thin or there may be considerable hyperbiophy present. Microscopically the epithelium shows transitional stages between the normal columnar shaped cell and the spheroidal or short columnar cell while it may sometimes present an almost squamous celled appearance. The epithelium may also be atrophied and in parts, absent.

Such a state of affairs, while in itself harmless, is of very serious import, as the gallbladder may become infected with organisms so ulcerate or rupture When organisms gain entrance into, and multiply in, an organ altered in the manner already described, an empyema of the gall bladder results. It differs from suppurative cholecystitis in three ways 1/ pus is formed much more slowly 2/ it resembles hydrops in its principal features 3/ and in these cases the infection is probably much less virulent than in suppurative cholecystitis. Rolleston[6] describes

empyema of the gall bladder " as bearing the same relation to suppurative cholecystitis as a chronic abscess does to an acute one. The condition of the walls of the gall bladder is similar to that described above and the fluid contains albumen, mucin, cylindric and squamous epithelial cells in a state of fatty degeneration, and bacteria

Two factors must be considered in the etiology of hydrops. These are (a) direct obstruction to the flow of bile (b) previous inflammation in the gall bladder wall with possible paresis of the musculature. It has not yet been decided whether paresis alone can give rise to this condition without a stone being present. Kehr[7] believes that dropsy of the gall bladder may result from an acute infectious cholecystitis of mild grade and is rarely due to obstruction of the cystic duct by a stone alone.

In a few recorded cases no obstruction has been found after death and in these cases the probability is, that there has been a sharp kink in the duct which was undone in the removal of the specimen. The only case of hydrops occurring in my series of cases is that of Mrs. T— case 5 but, as there was present perforation of the gall bladder in addition, it will be described under that heading.

<u>Chronic Cholecystitis</u> is the next complication which is met with in connection with cholelithiasis. As its name implies, it consists in a chronic inflammatory thickening of the gall bladder which, as we have

seen, may result from a previous acute inflammation. It may, however, be chronic from the outset and occasionally light up in the form of sub-acute attacks.

The pathological condition here found is usually some distension of the gall bladder which is filled with mucus. The walls are thickened and thrown into folds and there are usually some adhesions to neighbouring organs. Microscopically there is an increase of connective tissue between the muscular bundles. The mucous membrane and connective tissue show round celled infiltration or perhaps some oedema and swelling of the fibrous tissue has taken place.

The following is a case of chronic cholecystitis complicated with cholangitis and the clinical features presented are chiefly related to the latter condition.

Case 4. Mrs M. C— aged 52. Admitted into the Victoria Infirmary under care of Dr Parry on 31st July 1906.

Her history was, that for the last 18 years she was subject to severe attacks of abdominal pain with nausea vomiting and rigors. A fortnight before admission, she was seized with a severe attack of pain followed by collapse, and since then she has had 3 attacks of lesser severity — the last on the day previous to admission. The pain was sudden in its onset, sharp and lancinating in character, was situated in the epigastrium, and radiated round to the right hypochondrium and lumbar regions. It was associated with excessive tenderness in the

hepatic region. The onset of pain was usually followed by a rigor, and later great nausea and vomiting. This again was followed at a varying interval by jaundice. Her previous history showed that for several years she was subject to attacks of a somewhat similar nature which were attributed to indigestion

Examination. The skin was jaundiced. There was marked tenderness on palpation in the epigastric region and rigidity was present. The lower edge of the liver could be felt extending just below the costal margin. No enlarged gall bladder could be made out. The other organs presented no abnormal features.

Operation was performed on August 6th.

The gall bladder was found contracted and contained a single stone. Exploration showed a large stone impacted in the common duct and it was removed by incising the duct. A drainage tube was put into the gall bladder & the wound closed as usual.

Following the operation the temperature — which had since admission been of the "steeple" chart variety — remained high and two days later a bilateral parotitis developed. This eventually suppurated and though it was incised her condition gradually got worse and she died on 13th August 1906.

A post-mortem examination was made, and the condition of the organs found at the autopsy was as follows :—

Heart. Valves and chambers of normal size. Heart muscle is soft in consistence and bile stained.

Lungs. Are adherent at apices, show well marked oedema, slight passive hyperaemia and chronic bronchitis.

Abdomen. Liver is of normal size, soft in consistence and bile stained. A few portal radicles are thrombosed. The bile ducts throughout the organ are dilated - the main ducts containing bile-stained pus but without abscess cavity. The smaller ducts contain inspissated pus. The liver is adherent to the diaphragm and on its under surface to the pylorus and duodenum.

Gall bladder. is puckered up and adherent to the anterior abdominal wall. It is much smaller than normal, the walls are greatly thickened, and the mucosa shows proliferation.

The Common Bile Duct is dilated down to the diverticulum of Vater + shows a pressure atrophy of its walls with discoloration viz: evidence of the former presence of gall stones.

Pancreas is flabby but otherwise healthy.

all the other organs were fairly healthy.

Another complication of cholelithiasis or rather a further development of the previous one is that of Cholecystitis Obliterans. It is rarely found unless in association with gallstones, and usually only when these are of long duration. The connective tissue formed within the walls as the result of chronic cholecystitis contracts (often around a stone) and, in addition to this, there may be a deposit of calcium salts within

the wall. The gall bladder, too, may be buried in adhesions and may only be found with great difficulty at operations. Finally the lumen may be altogether obliterated and the gall bladder represented merely by a mass of fibrous tissue.

A further complication in the gall bladder of cholelithiasis is the formation of Diverticulae.

In the conditions above described, it was noted that there ensued, as a frequent occurrence, a loss of the epithelium of the mucous membrane in patches, and, when there is added to this weakening of the wall and the mechanical action of a gall stone in its immediate vicinity, pressure atrophy and dilatation ensues.

As the mucous membrane becomes ulcerated and gives way, the stone pushes the outer wall of the gall bladder before it, and when resolution occurs and the tissues begin to contract, it may happen that the stone is cut off and lies in a compartment entirely separate from the rest of the organ, or may communicate with it by a narrow channel.

If the process does not resolve, and ulceration ensues, the stone may find its way through the wall of the gall bladder, with one of the following three results:-

1/ It may find its way into the general peritoneal cavity

2/ It may lie in a mass of adhesions which have formed between the gall bladder and one or other of the adjacent organs 3/ It may ulcerate its way into the organ with which the gallbladder lies in contact

The first variety is fortunately rare. In it, the inflammation and ulceration progress so rapidly, that

rupture occurs before protective adhesions can be formed. According to Moynihan[8] there are two forms of this acute perforations met with " in the one the whole peritoneal cavity is at once invaded and a general peritonitis follows; in the other, which is more common in traumatic than in calculous cases, the peritonitis, though almost equally severe, seems to be limited by the meso-colon and adherent omentum, to the lesser right hypochondrium: the bacilli in such cases have no doubt a lesser virulence."

The following is a case of perforation of the gall bladder, with more or less localized peritonitis. Though not strictly belonging to my series of cases, since no gall stone was found at the post-mortem examination, still I have introduced it, as I am unable to find any other suitable explanation of the conditions found.

Case 5. Mrs T— aged 73. Admitted into the Victoria Infirmary under care of Mr Maylard on 23rd September 1904.

This patient was admitted suffering from some obscure injury to her hip, caused by falling. She was apparently progressing quite satisfactorily, though presenting some mental symptoms, when on October 8th she complained of pain over the abdomen, and her temperature rose to 102 2/5 F. On examination a tumour was seen on the right side of the abdomen which was very tender to pressure. It was firm to the touch and appeared to be continuous with the liver, and could be pushed

forward by the hand in the right flank.
Owing to her mental derangement no history or facts could be gleaned concerning this swelling, but certainly no tumour or swelling was present at the time of her admission.
The following day the tumour was still present, but the temperature fell to 100°F and was soon back again to normal.
On October 13th, i.e. five days after it was first noticed, the swelling suddenly disappeared, causing great pain and symptoms of peritonitis. There was sudden collapse and the pulse got much weaker. From that time she never rallied & died on 18th October 1904.
The following was the condition found at the post-mortem examination :-
Heart. Hypertrophy of the left ventricle. Right ventricle and both auricles slightly dilated. Aortic cusps and commencing aorta showed slight atheroma. The organ was otherwise quite healthy.
Lungs showed well marked emphysema and on section passive hyperaemia as well. Bronchi were congested
Abdomen. The upper part of the abdomen showed bile staining on the surface of the liver stomach diaphragm and colon, and on the surface of these organs there was a small quantity of fibrous exudate, binding stomach and liver to diaphragm, and forming adhesions of gall bladder to stomach, duodenum, and colon. These adhesions were more marked around the gall bladder, which

was in a state of distension. On examination of the gall bladder, oozing of bile into the peritoneum was seen, and, on stripping the exudate, an aperture of the size of a split pea was found. No trace of a gall stone could be discovered.
When opened up the gall bladder was much distended with an extremely thin wall but no evidence of cholecystitis.
Liver on section showed slight cirrhosis of its free edges but was otherwise normal.
Kidneys showed chronic interstitial nephritis with cysts in the cortex.
Intestine. Small intestine was collapsed, serous coat congested with areas of fibrous exudation at various parts & the mucosa was also congested. The caecum was much distended and so also was the ascending colon. The transverse colon was normal, the descending colon collapsed. The caecum descending & transverse colon had very thin walls.

The second variety is found when, as the result of the irritation and inflammation set up by the stones, the serous coat of the gall bladder becomes inflammed, and pours out protective lymph on its surface, binding it to adjacent organs. This lymph later becomes organized, and, in a cavity of newly formed tissue, the gall stone may lodge, often surrounded by pus and granular debris; or if the gall bladder becomes adherent to the omentum, the gall stone may lie in omental adhesions.

The third and last variety, the one most commonly met with, is that in which an ulcerating gallstone forms a fistula between the gall bladder and one or other of the adjacent viscera. If we study the anatomy of this region we find that the organs most likely to be involved are the stomach, liver, duodenum, colon, other parts of the biliary tract, such as the hepatic and common ducts, diaphragm (through which fistulæ may form into the pleuræ + bronchi) and in exceptional instances the urinary tract and female genital organs. Lastly adhesions may form between the gall bladder and anterior abdominal wall, and, a gall stone having ulcerated its way through, a fistula may result leading from the anterior abdominal wall close to the umbilicus. That it should form here is due in part to the proximity of this region of the abdomen, and in part to the guiding influence of the falciform ligament.

This last form, called 'external fistula' in contradistinction to the others, is perhaps the one most commonly recognised, and if traced inwards will be found often communicating directly with an abscess cavity formed just outside of the gall bladder and this, in turn, may communicate with the interior of that organ.

Fistulæ between the gall bladder and stomach are not common. They are usually preceded by adhesions of the gall bladder to the pylorus, or may be due to an abscess arising in connection with

a gall bladder in which stones are present, opening into the stomach. Very often, in these latter cases, an opening will be found in addition into the duodenum, or colon, or both. During the formation of such a fistula, there may be erosion of some of the vessels of the stomach, giving rise to fatal haemorrhage.
Fistulae between the gall bladder and the intestine are frequently met with, and the part of the intestine most commonly involved is the duodenum. They may, however, be formed between the gall bladder and colon, but this is an uncommon complication and according to Mawchison[9] "the exemption of the colon, as compared with the duodenum in this respect is probably due to the former bowel being more movable." Such an explanation would also serve in the case of the the small intestine as a whole, because with the exception of the duodenum, fistulae from the gall bladder rarely enter it. Fistulae between the gall bladder and duodenum are probably much more common than is usually supposed. Such a fistula may form, and give exit to a gall stone, and, if there be only one present, or if the gall bladder be emptied of all its contains, the whole process may quieten down; healing of the fistula occurs, and, at the post mortem, no opening between the two organs may be detected
In such a way, only, can these cases be explained, in which a large stone is passed per rectum and

after death no evidence of distension of the common duct is present.

Fistula between the gall bladder and colon is by no means common and when it occurs it is usually cancerous in its nature. In 9 cases collected by Murchison[10] 6 were cancerous. As he remarks, however, it is probable that while the fistula is of a cancerous nature, the ulcerative process leading to its formation is determined by gall stones. According to Rolleston[11] "while gall stones most commonly give rise to fistulae between the gall bladder and duodenum, malignant disease of the gall bladder is much more prone to set up a fistula between the colon and gallbladder than between the duodenum and gall bladder." The case of Mrs. McN— case 22 is an instance of fistula occurring between the gall bladder and duodenum but as it exemplifies intestinal obstruction it is described under that heading. Case 7 is also illustrative of this condition.

The following case illustrates the pathological lesion of a stone ulcerating its way from the commencement of the cystic duct into the duodenum :-

Case No 6 Mrs S— aged 46. Admitted into the Victoria Infirmary under care of Dr Parry on 7th July 1903.

History. She was admitted as an urgent case complaining of pain over the liver and jaundice. This pain had lasted for 3 days and her Dr diagnosed the case as one of gall stones and gave her morphia. At the onset of her illness she had an attack of vomiting,

the vomit being dark green coloured material, like bile. The pain which then followed, was stabbing in character and somewhat intermittent. She stated that she had been subject to similar attacks for the past two years, lasting as a rule for about two days.

Previous Health. She had an attack of rheumatic fever in 1892, lasting for 9 weeks, but had otherwise always enjoyed good health.

Examination. Temperature 103·2°F. Pulse 100 per min. Pain is complained of on palpating the liver. The liver dulness is not increased but a feeling of fulness is conveyed to the hand when palpating antero-posteriorly. Her right kidney is movable.

Heart. A soft blowing systolic murmur is heard over the mitral area, and the 2nd aortic sound is accentuated.

Lungs. A few coarse râles are heard over both lungs

Urine contains a trace of albumen.

Two days after admission, patient had a rigor, her temperature rising to 104·8°F her pulse to 106 per min, and with it the pain in the liver became more severe. Another rigor occurred 6 days later, and the following day a Widals test was tried, and gave a positive reaction.

Just about this time she began to be troubled with breathlessness and palpitation, and on examination of the heart, a loud A.S. and V.S. mitral, and a soft V.S. aortic, murmurs were heard. The temperature also began to oscillate, reaching as high as 103°F, while the pulse became weak and the complexion dusky. From this time on, she began gradually

to sink. Cardiac distress become very pronounced, and the features assumed a livid hue. The pulse got weaker and weaker, finally becoming imperceptible, and she died on 26th July 1903.

The following was the condition of the organs found at the post-mortem examination :-

Heart. was enlarged soft and flabby. The left ventricle was dilated - the right ventricle auricles slightly so. The aortic valve was incompetent, and was found to be the seat of a recent acute endocarditis. A large polypoidal vegitation. 3/4" in diameter, sprang from one of the aortic cusps. On the other cusp, on the ventricular aspect, there was present a thick fibrous exudate but not of the character of a vegitation. The appearance of the vegitation and of the exudate suggested an ulcerative endocarditis. The mitral valve was of normal size, and along the line of contact of this valve, similar acute warty vegitations were present. The anterior curtain was slightly affected and the chordae tendineae, leading from it to its fleshy column, were ulcerated through and separated. The tricuspid valve admitted an extra ~~curtain~~ finger but its curtains were healthy. The pulmonic valve was also healthy.

Lungs. showed emphysema of their free margins, and passive congestion, but were otherwise healthy.

Abdomen. The liver was of large size and on section showed a spongy appearance from gas production. It was slightly fatty in character, and the bile ducts throughout the organ were dilated

The Gall bladder was non-functional, and a small gall stone was found ulcerating its way from the commencement of the cystic duct into the duodenum close to the pylorus - the duodenum at this part being adherent to the gall bladder. The common bile duct was dilated with its walls corrugated, and, at the diverticulum of Vater, a congested area was present. Two medium sized stones were removed from the common duct. The Pancreas was congested and the duct dilated, but otherwise normal.

No pathological lesions were found in any of the other organs. Microscopic sections of the vegitations on the heart valves, and of the pancreas were made & examined by myself. Sections through the valve showed a fibrinous exudate on the surface - laminated in character with few nuclei - a few groups of inflammatory cells being interspersed through some. On one surface inflammatory cells were more numerous, and, in addition, areas composed almost completely of red blood cells and fibrin were apparent. The muscular tissue in the section showed hyaline degeneration. The pancreas, examined microscopically, showed the lobules to be of large size, with slight increase of fibrous tissue between them. The wall of the duct was thickened, and there was desquamation of epithelium.

The gland tissue proper showed auto-digestion.

I have described the heart condition in this case in full, as I shall refer to it later on, in another part of the test.

Other forms of fistulae which occur, are those forming

between the gall bladder and liver, and between the gall bladder and other parts of the biliary passages. The former is not a very uncommon complication and as it usually gives rise to hepatic abscess it will be considered under that heading.

A fistula which forms between the gall bladder and one or other of the bile ducts, is only of anatomical and pathological interest as it rarely gives rise to distinctive clinical symptoms.

Communications may be found existing between the gall bladder and hepatic ducts or between the gall bladder and the common duct formed in the manner already described. In my list of cases I have no examples of this interesting though not very common complication

Rarer forms of fistulae are sometimes found, such as those between the gall bladder and portal vein (of which Naunyn[12] has collected 3 cases), between the gall bladder and kidneys (Elsner[13] found gall stones in the pelvis of the right kidney) and between the gallbladder and urinary passages and vagina.

The next complication of cholelithiasis which we shall consider is that of <u>Tumours of the Gall bladder.</u>

The tumours of the gall bladder associated with gall stones, are divided into two classes, innocent and malignant of the innocent tumours, two only need be mentioned, viz. papilloma and fibroma. As papilloma of the gall bladder is very seldom met with, and when it occurs, it has been generally supposed to be secondary to gall stone

irritation. This however, does not always hold good, as in many of the recorded cases no calculi were present, nor were there any traces of their former presence.

Many authors are of opinion that papillomata form the early stage of cancer, and if a microscopic examination of the tissue of a supposed papilloma be made from a section removed during life, it would be extremely difficult to say whether the tumour is a simple papilloma, or the superficial part of a villous cancer. Post-mortem sections of these tumours give very unsatisfactory results due to the presence of intense bile staining and subsequent degeneration of the tissues.

Fibromata of the gall bladder associated with gall stones have been described. Such a condition, however, is rare and must not be confounded with fibrous thickening due to cholecystitis, or with the early stage of a primary carcinoma, the latter of which on section looks like a firm fibroma.

The really important tumours of the gall bladder complicating cholelithiasis are the cancers. The relationship between gall stones and cancer has been long noted, and various suggestions have been put forward to explain the connection between the two. Mayo Robson[14] says " The two theories which have been put forward to explain the co-existence of gall stones with cancer of the gall bladder are :- 1/ the "irritation" theory — that gall stones are formed first, and by acting as foreign bodies, set up irritation which leads to malignant growth 2/ the "concentration" theory.

that gallstones arise from stagnation of bile in the ducts, ensuing on their obstruction from malignant growth".

In support of the first or irritation theory, we have the fact, that irritation plays an important part in the etiology of carcinoma of other parts of the body, such as the lip, breast, scrotum, etc; whereas in regard to the concentration theory, there is no evidence to prove that — provided the gall bladder is aseptic — stagnation of bile leads to crystallization and separation of its component parts. Hence at present, the consensus of opinion is in favour of the irritation theory, but until the true cause of cancer is discovered it will be impossible, and unwise, to make a definite statement on the subject.

The percentage of cases of primary carcinoma of the gall bladder in which gall stones are found varies according to different writers. Some of these, such as Siegert[10], have found them present in practically every case (95%), while others have named the figure as low as 50%. In four cases which I have investigated, gallstones were present in three giving a percentage of 75.

It will thus be seen that, whether by irritation or otherwise the presence of gall stones must be taken into consideration when discussing the etiology of carcinoma of the gall bladder.

As a rule the disease begins in the fundus, probably because this is the most dependent part, and therefore most liable to irritation. From this it may

spread to the neck of the gall bladder and give rise to obstruction, or it may form a uniform thickening of the wall of the organ. In not a few cases, again, the starting point of the disease is at the neck, where a stone has become impacted. As the disease progresses it may involve the whole of the gall bladder, and it then becomes impossible to say definitely in which part the process began.

Two distinct varieties of carcinoma are met with in the gall bladder, the columnar celled, and the spheroidal celled, and there are in addition transitional forms, as we shall see later. The columnar celled carcinoma may present a villous appearance, or papillomatous arrangement, or may be found as a dense hard tumour allied to the scirrhous type. As a rule this last type is of very slow growth - slower even than the spheroidal celled cancer.

Squamous celled carcinomata, or at least carcinomata, indistinguishable in structure from squamous celled carcinomata, are met with in connection with the gall bladder. The existence of this type has long been doubted and has been, and still is, the subject of a good deal of controversy.

Mayo Robson[16] records a case on which he operated and the microscopic appearances of the tumour removed were those of an epithelioma of squamous celled type. Rolleston[17] explains this condition by affirming - That frequently a change of type of the carcinoma is visible, parts of the growth may be columnar celled, others cubical,

and other parts spheroidal celled. In transitional parts the large epithelial cells may be so far modified as to appear flattened, and have then been described as squamous cells." Hoppe Seyler[15] says. "The effect of gall stones on the epithelium of the mucous membrane is to convert it into a horny epithelium, and as this is the same tissue as that seen in carcinomata, we have an argument in favour of the role of gall stones in the formation of carcinoma". If then the effect of gall stones is to convert the mucous membrane into horny epithelium we can readily understand how a malignant growth taking its origin at the site of an impacted calculus should present the characters of the epithelium from which it takes origin. An example of this squamous celled carcinoma will be found in case 7 described below. Extension of the growth is usually by continuity of tissue, hence as we would expect metastatic growths are most commonly found in the adjacent liver and bile ducts. This was found to be the case in two, out of three, cases which I investigated.

If the fundus be affected then the colon may also be involved and, less commonly, the disease spreads to the duodenum. I have already referred to the close connection which Hutchison proved to exist between the fistulae of the gall bladder and colon, and cancer, proved by the fact that out of 9 cases of such fistulae, 6 were cancerous.

The method of spread of malignant disease, from the

gall bladder to the common hepatic ducts, may be by direct continuity of tissue, or by the lymph channels leading from the cystic duct, and this latter method of spreading is the most likely one in those cases where the peritoneum is involved in addition.

The following is a case of primary carcinoma of the gall bladder associated with cholelithiasis, showing the transitional or squamous celled variety of the tumour:-

Case 7 Mrs D— aged 70. Admitted into the Victoria Infirmary under care of Dr Parry on 23rd September 1903.

History. She was admitted in a dying condition, and no history of her illness could be got.

On examination, she was deeply jaundiced and much emaciated, and a large mass could be felt in the region of her gall bladder. The urine was bile stained. Soon after admission she became comatose and died on 25th September 1903.

The following is the post mortem report:-

Heart is small in size. There is slight calcareous deposit on the aortic valves. The heart muscle is soft and the endocardium shows bile staining.

Lungs. The right lung is adherent by old pleurisy. The left lung is non-adherent. Both show slight oedema passive congestion and chronic bronchitis.

Abdomen. There is a slight degree of ascites present and, in addition to the bile stained fluid in the pelvis, there are flakes of fibrinous exudate. The liver capsule shows

well marked signs of perihepatitis

Liver is of normal size and on section shows a slight degree of passive congestion. The parenchyma of the organ is bile stained, and the ducts throughout the organ are somewhat dilated. There are no malegnant nodules present.

Gall bladder is dilated, and around the organ are firm fibrous adhesions uniting it to the hepatic flexure of the colon, so that on removing the colon this part of the wall had to be cut through. On incising the gall bladder, a gall stone is found in its interior, and an aperture through which a gall stone could pass is found leading into the duodenum — as if a gall stone had ulcerated its way through. The wall of the gall bladder is thickened in parts, and the appearance presented on section is that of dense fibrous tissue. The cystic duct is dilated.

The common bile duct shows dilatation also at its first part, while the middle portion is stenosed by a scirrhous like mass, resembling inflammatory tissue, fully 2" in diameter and extending for a distance of over an inch in the direction of the duct. Beyond this the calibre of the duct is normal, and no lesion can be detected in that part which lies in contact with the head of the pancreas.

No abnormal features are found in the pancreas or spleen.

Kidneys. Capsules are adherent, and on removal the surface presents a granular appearance with numerous small cysts in the cortex. On section they show

well marked interstitial nephritis and are bile stained.
Stomach & Intestines present healthy appearances.
Sections of the liver, gall bladder, duct tumour and pancreas were made and examined by me and the following microscopic characters were noted :-
Liver. The liver tissue shows well defined lobulation from the presence of fibrous tissue in the portal zone, and, throughout the sections, the same areas are demarcated by excess of bile pigment. The hepatic cells are loosely arranged with congestion and dilatation of the capillaries. The larger ducts show fibrous tissue in their walls with irregularly distributed and desquamated epithelium. Around the free margins of some of the sections are areas of fibrous-like tissue with poor nuclear staining and containing a few vessels and ducts.
With the high power lens the hepatic cells show a cloudy and granular appearance with well stained nuclei but no fatty degeneration. The portal areas show pigment in considerable quantity in the hepatic cells while pigment is also present between the cells. The cellular condition in the portal zones is of the nature of a slight degree of portal cirrhosis and an occasional new formed bile duct is present. (See Fig 3)
Gall bladder. The section goes through the wall of a fibro-muscular organ in which there is an excess of fibrous tissue. Scattered through this tissue are islands of irregular shape and varying much in size. In parts of the section there is a suggestion of

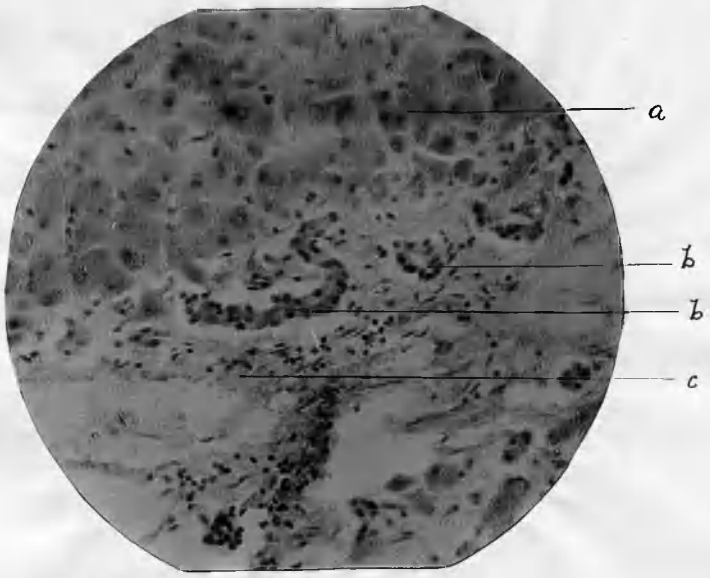

Fig. 3.— Photomicrograph of Liver in Biliary cirrhosis

a., liver cells. b., new formed bile ducts. c., increased connective tissue around portal zone.

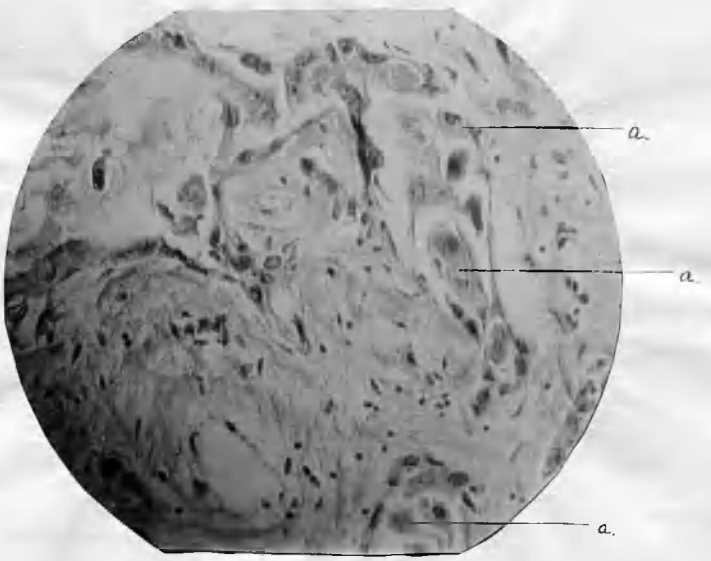

Fig. 4.— Photomicrograph of Carcinoma of Gall bladder. (Transitional type)

a., Squamous epithelial cells.

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dilated tubules, while in others the clustering of the cells approaches to the character of the laminated capsules of epithelioma. (See Fig 4)

In the inner aspect of the section the tumour cells stain very poorly and are merely represented by a failure of staining. Under the high power lens, the character of the cells forming the tumour area is shown to be very varied - the columnar arrangement being but slightly apparent. The appearances are rather those of a cancer arising from a transitional or squamous epithelium. Spheroidal cells with large round nuclei, or flattened cells with elongated nuclei, are the predominant features. In several places the cells are aggregated together and within them can be seen multiplication of the nuclei but without cell division.

Duct tumour. Sections through this area show dense fibrous tissue traversed by a number of muscular bundles. These are bounded externally by the duct wall, and here and there throughout these, are irregularly shaped islands of columnar epithelium presenting the appearance of dilated tubules. The bile duct has lost its mucous coat entirely and is only represented by the muscular wall. The fibrous tissue is somewhat chronic in character, but new formed connective tissue cells can be identified. The nature of the epithelial cells in the fibrous tissue above noted, varies both as regards size and outline. Though no definite muscular walls are present to suggest duct-like

character, the epithelium, nevertheless, is distinctly columnar in type, and both cell and nuclei resemble the bile duct character. The cells in places are coiled up, with a tendency to proliferation of the individual cells.

Pancreas. In sections prepared of this organ, the acini show a healthy appearance, though there is a tendency for the cells to be closely packed together. The islands of Langerhans are few in number, and the contents of each are small, as well as few in number. The pancreatic tissue throughout the entire gland is well demarcated by coarse strands of fibrous tissue passing along the line of the ducts, and giving the appearance of a well marked hypertrophy of their walls. The character of this fibrous tissue is distinctly chronic - loosely cellular, with fibrous characters of these cells, and only occasionally are evidences found of a more recent formation of connective tissue, with a few inflammatory cells.

Remarks. There is no doubt, I think, that in this case the primary lesion was in the gall bladder, and that the tumour mass in the common duct was either a secondary ~~gra~~ involvement, or an independent growth. The changes in the pancreas in this case were those of chronic interstitial pancreatitis, and to these I shall refer later.

Another case of primary carcinoma of the gall bladder associated with gallstones, in which a secondary involvement of the liver occurred is the following:-

Case 8. Mrs McB— aged 50. Admitted into

the Victoria Infirmary under care of Mr. Maylard on 13th September 1906.

History. Four months ago she began to be troubled with pain in the right side of the abdomen and in the small of the back. It was an aching pain, present continually, and had no relation to the taking of food. Two months later she developed a pain just under the zipheid cartilage, which came on immediately after taking food, was made worse by it, and has confined her to bed ever since. The pain was always present at night and prevented her from sleeping. She has had no vomiting or diarrhoea.

Since the onset of this last pain she has lost flesh to a considerable extent.

Her previous health, with the exception of an attack of rheumatism 3 years ago, has always been good.

Examination. She is of a sallow colour, lips and conjunctival pale.

Heart is normal, pulse irregular + weak, numbers 112 per min.

Lungs normal.

Abdomen. On palpation a smooth swelling is detected in the region of the stomach, which is limited by a groove extending across from the 9th costal cartilage on the one side to the corresponding point on the other, and about 1½ inches above the umbilicus. There is also marked tenderness over the epigastric region and over the inferior edge of the liver, and at this same area a resistance is met with extending down towards the caecum. The abdomen is tympanitic to light percussion except over the stomach, where a dull note is

obtained. The area of gastric resonance corresponds to the groove already mentioned.

On September 16th 1906 the case was transferred to the medical wards as the condition was deemed inoperable

From that time the pain became much worse and she required 1/4 gr morphia, at first once per day, later twice.

On October 12th the abdominal tumour is noted as having increased in size though she slept very much better at nights.

On Nov. 18th the following note was made:- The abdominal swelling is much larger, and the tumour much harder and firmer, than formerly while the nodules on the surface of the liver are felt more easily. There is marked oedema of both legs but very little fluid in the abdomen. The pulse is also failing.

On Nov. 25th the pulse is noted as becoming very weak and thready and she died on Nov. 26th 1906.

Her Temperature from Sept 18th till Sept 29th ranged from 98° to 99.2° F. From then till Oct 6th, each morning the temp. was 97.6° & each evening 100°. From Oct 7th till Nov 10th, there was an evening rise and morning fall, the variation being about 1½° and from Nov 11th, the temperature became subnormal and continued so till she died.

The following was the result of the post-mortem examination (at which I assisted):-

Heart. Small in size, slightly atrophied and with slight excess of fat. Chambers and valves are healthy.

Lungs. are slightly adherent by a few fibrous bands. They show emphysema of the free margins, and on

section, a slight degree of congestion. The bronchi show evidences of chronic bronchitis.

Abdomen. Liver is greatly enlarged, measuring 12" from side to side 10" from above downwards and 5" from before backwards. Externally it shows the presence of numerous malignant nodules with umbilication, and conglomerate appearance of the surface. On median section shows the presence of a large central tumour mass, which extends backwards into contact with the gall bladder. The mass is somewhat fibrous in character, of a pale yellow colour, with slight indication of softening but no haemorrhage. Smaller nodules throughout the liver have similar characters. On separating the liver a gall stone is detached from the commencement of the bile duct.

Gall bladder and cystic duct are completely filled by a mass of gall stones. On opening the organ it shows a rugged honeycombed character of the wall from the impression of the gall stones and, at its upper part, is apparently in continuity with the tumour nodule of the liver, already described. The bile duct, from where the stone lodges, to its termination, is slightly dilated but has healthy walls.

Spleen and pancreas healthy.

Right kidney has a dilated pelvis containing a calculus of the size & shape of a kidney bean. Left kidney healthy.

Stomach intestines and pelvic organs all present normal appearances.

Microscopic sections of the liver, gall-bladder, and

pancreas were made examined by me the following appearances found :-

Liver. The liver cells throughout the organ are slightly swollen and cloudy in appearance, but the nuclei are sharply stained. The cells are divided into columns by congested vessels, the result of a passive hyperaemia. There is an increase of fibrous tissue around the portal zones, scarcely amounting, however, to a definite cirrhosis

Sections made through the tumour ~~in~~ the the liver show that the greater part of the liver substance included in it has undergone atrophy and change, and that there are very few properly staining liver cells. In their place are areas of ill-defined staining which, under the high power lens, show occasional nuclei and necrotic cells. The fibrous stroma of the tumour area proper, is well formed and in parts presents a scirrhus appearance. The tumour cells are arranged in small alveolar masses with round character of the cell, and oval vesicular nuclei which occupy the greater part of their interior. Some islands of cells, columnar in character, and duct like in arrangement are visible throughout the section. (See Fig 5)

The main character of the cancer cell is that of a spheroid, and the nuclei are for the most part oval in shape but in the larger swollen cells they are spherical.

Gall bladder. Sections through the wall of the gall bladder with the tumour, show a fibrous tissue stroma infiltrated throughout with groups of cells – these being arranged in parts in small clusters, while in others, a definite duct like character is maintained. In one part of the

section there is a loss of cell staining, and in the vicinity of this area dense fibrous tissue with large spaces is seen. These spaces have a cyst like character, and are lined by columnar epithelial cells, arranged in rows, and free from the margin. In other parts of the tumour the cells are arranged in clusters, & in these regions large numbers of mono nuclear inflammatory cells are present.

Pancreas. The cells of the parenchyma and of the Islands of Langerhans are normal. There is an increase of the fibrous tissue between the acini and accompanying the ducts; the latter show thickened walls with desquamation of the epithelium. There is a slight degree of fatty infiltration in the organ.

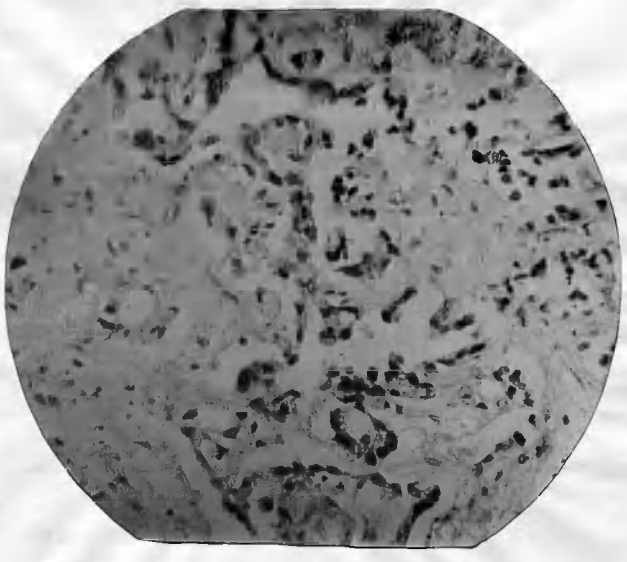

Fig. 5.— Photomicrographs of Secondary cancer of Liver. - Spheroidal celled type.

The next series of complications of cholelithiasis which we have to deal with are those affecting the <u>Cystic Duct</u> and they are practically the same as those we have already considered in connection with stones in the gall bladder. If a stone becomes impacted in the cystic duct, there will be hydrops or empyema of the gall bladder resulting. Or such a stone may give rise to acute cholecystitis in its various forms:- catarrhal, suppurative and gangrenous, or to sclerosis of the gall bladder. Again if ulceration occurs in connection with a stone in the cystic duct, fistulae may result, opening into the various surrounding organs, just as we have seen in connection with the gall bladder itself. The case of Mrs D— case 7 already described, shows an aperture leading from the commencement of the cystic duct into the duodenum, as if a gall stone had ulcerated its way through. For example of a stone ulcerating its way from the cystic duct into the liver will be found referred to in case 11.

In a few cases perforation of the cystic duct occurs, but not as a rule until adhesions have formed around the area, through which the stone is eroding. In the case of John M— case 10, on separating some dense adhesions, a gall stone was found perforating the cystic duct.

Lastly should a gallstone become localized in the cystic duct, the chronic irritation set up thereby may be the starting point of a carcinoma, which may

involve the gall bladder above or the bile duct below.
The following case exemplifies the condition referred to :-

Case 9. Mrs Sarah P— aged 44. Admitted into the Victoria Infirmary under care of Dr Parry on 3rd Sept. 1906.

History. Her health was fairly satisfactory till May 1906, when she complained of pain in the epigastrium, accompanied by nausea and vomiting. The pain lasted for 4 months and then jaundice appeared, after which the pain disappeared. There was no vomiting to any marked extent till about a week before the jaundice set in, but since, it has been most persistent till latterly rectal feeding had to be resorted to. She is very definite about the order of her symptoms - pain at first, gradual, of a dull aching character, felt in the epigastrium and back; then the vomiting, and a week later, jaundice, with disappearance of the pain. Since the jaundice occurred the stools have been light in colour but not 'clayey', and the urine has been almost black.

Previous Health. For 12 years last she has been subject to so called bilious attacks, coming on about once a month, but unaccompanied by pain. A year before her present illness began, she had severe pain in the epigastrium and vomiting, lasting for one day, with less acute pain for a week, but no jaundice.

Examination. She is deeply jaundiced both in skin and conjunctivae. Heart and Lungs are normal.

Abdomen. Some tenderness on pressure is detected

over the area of the gall bladder but no tumour, swelling, or resistance can be made out.

The urine is tinged with bile but otherwise is normal.

Operation was performed by Dr Parry on September 6th.

On opening the abdomen a hard mass was felt in the transverse fissure of the liver - rather high up to be connected with the pancreas. A secondary small nodule was found near the anterior margin of the liver and another small nodule was also found in the omentum, which was excised for examination

The condition was considered inoperable & the wound closed.

After the operation the patient continued very weak, and about 10 hours later collapse set in. Stimulation was resorted to, but without avail, and she died an hour and a half later.

A post mortem examination was made the following report made

Heart. There is slight increase in the sub epicardial fat, and a soldiers spot is found on the anterior aspect of the left ventricle. The muscular tissue is weakly bile stained and soft in consistence. There is some thinning and dilatation of the ventricles but the valves are healthy.

Lungs. Both are slightly adherent to the chest wall. They are small in size with some emphysema of the free margins and on section they show a moderate degree of passive congestion and oedema.

Abdomen. There is some blood stained fluid in the abdominal cavity, and there is some blood clot present in the retro peritoneal tissue in the region of the

liver and kidneys

Gall bladder. is adherent to the operation wound and is dilated. When opened into, it is seen to contain dark coloured bile with 2 large and 3or4 small gall stones. The larger stones are about the size of a hazel nut; the smaller ones are the size of ordinary cholesterine stones. At the neck of the gall bladder, involving the cystic duct, and origin of the bile duct, is a tumour nodule of the size of a pigeons egg, which is scirrhous like in character. The common bile duct is traced through its entire extent, & shows a gall stone impacted at the diverticulum of Vater. The pancreas is soft in consistence and bile stained but otherwise normal.

The liver, on section, shows deep bile staining, general soft character of the organ, and dilated bile ducts. The Omentum is thickened, pulled up, and indurated, with fibrous change and slight haemorrhage in its interior The spleen shows perisplenitis with fibrous tissue increase. The kidneys show slight interstitial nephritis. All the other organs are apparently healthy

The nodule in the omentum, which was sent down for microscopic examination was proved to be malignant. It consisted of a fibrous stroma with a few dilated glands distributed through it These glands were lined with columnar epithelium resembling the character of that of the cystic and bile ducts. (See Fig 6)

The tumour which was situated at the neck of the gall bladder, already described, is undoubtedly

the primary malignant growth but I regret that a portion of this area was not preserved for examination

Fig. 6.- Photomicrograph of Secondary Cancer of Omentum

a., Scirrhus connective tissue

b., Epithelial cells arranged in duct like manner.

Our next consideration is that of the complications of cholelithiasis which are related to the Liver

In describing these it will be necessary for us to consider, not only the changes which are found in the liver cells, but also those occurring in the biliary passages leading from the liver; hence it is proposed to include under this section the complications affecting the right and left hepatic duct, the

bile ducts within the liver, the biliary canaliculi, and the liver tissue proper.

Though gall stones in the great majority of cases, as we have already seen, take their origin from the gall bladder, there is no reason why they should be limited to that one part of the biliary system. As a matter of fact, all the necessary ingredients for their formation are present in other parts as well, and hence it is not surprising that, in a few exceptional cases, the origin of the stones is undoubtedly from the bile ducts themselves. Stones formed within the intra hepatic ducts are rare, being less frequently found here than in any other part, and when such are present, there are usually others to be found in the gall bladder or common duct as well. These concretions are usually small in size, and are composed of bilirubin calcium. Murchison[19] says in regard to this condition " These concretions may be very numerous, but small, constituting what has been called 'biliary gravel'; at other times they are large and branched, like a piece of coral as in a drawing in one of Cruveilhiers Pathological Plates."

These intra hepatic calculi, after they are formed, usually pass down the biliary tract, just as gall bladder stones do, giving rise to the same symptoms, but, in a few cases, they remain stationary and gradually become larger by deposits received from the bile stream.

It must not be assumed that all calculi found

within the intra hepatic ducts are formed there, for it may happen that stones from the gall bladder, after passing through the cystic duct, may turn into the wider hepatic duct and be found there, either at operation or post mortem examination. Similarly, a fistula may form between the gall bladder and hepatic duct, & a stone pass from the former to the latter.

The mechanical effect of such stones in the hepatic duct, if small, might be nil, but if of large size, they would be liable to cause a stasis of bile within the liver.

The effect of this biliary stasis is first seen in dilatation of the bile ducts within the liver. These may dilate to a considerable esctent and relieve the pressure, but, if the obstruction be not removed, the effect of the back pressure comes to be seen on the liver cells themselves. When this occurs we have a double factor to consider, first a mechanical action resulting from direct pressure, and secondly a chemical ~~actin~~ change from the action of the pent up bile upon the liver cells.

The effect of such a condition is that the liver cells become reduced in size, irregular in outline, and contain more granules than normal. Bilirubin is also seen within the cells, either produced there, or pressed in from outside. Later the nuclei become indistinct, fatty degeneration occurs, with finally necrosis of the cells.

In addition we find changes in the finer interlobular bile capillaries. Here the epithelial cells become detached filling the lumen, and at the same time

proliferalis, diverticulae are formed, and these communicate with each other. There may also be a considerable degree of proliferation of the connective tissue. This proliferation of the connective tissue, and the changes in the bile capillaries, when present generally go hand in hand, leading to a true biliary cirrhosis such as we have seen illustrated in case 7. (See Fig 3)

Such, then, is the picture seen when a simple mechanical stasis of bile occurs. If infection by micro-organisms now takes place, a new complexion is put upon the appearances presented. The organisms most likely to invade the ducts are the bacillus coli, streptococci, staphylococcus albus and aureus & typhoid bacilli. Of all these, perhaps the most virulent infection arises from the bacillus coli. The result of the entrance of these organisms, is to produce within the liver a suppurative cholangitis with destructive changes in the liver cells. The intra hepatic bile capillaries show ulceration of the mucous membrane, softening, and later dilatation, of their walls. There is a proliferation of the epithelial cells with increased desquamation, diffuse infiltration with round cells, and ducts filled with purulent debris mixed with bilirubin. The dilatation which results in this way may be considerable. the ducts reaching to 3 or 4 times their natural size.

When these suppurative changes extend to the liver, it gives rise to what L. Rogers[20] terms "biliary abscess" or hepatic abscess. The liver cells around

the portal spaces undergo necrosis, and a small abscess is formed. This may coalesce with another, formed in a similar way, by enlarging and destroying the intervening tissues, and so form one large abscess which may, or may not, have a fibrous septum stretching across it. When these small abscesses do not run together, they form little dilatations at the end of the ducts, often near the surface of the liver.

In addition to the purulent disintegration, there is also seen, at the margin of the necrotic area, an increase in the peripheral connective tissue, with liver cells lying around in various stages of degeneration. Should these abscesses be situated near the surface of the liver, the bacteria may penetrate into the surrounding peritoneum and set up a localized peritonitis, or one of these small abscesses may leak into the peritoneum, giving rise to a general peritonitis or a localized peritoneal abscess. In the substance of the liver, abscesses may form in the lymphatics, suppuration extend into the branches of the portal vein, setting up pylephlebitis with thrombosis. The following is a case of purulent localized peritonitis with an abscess cavity in the centre of the right lobe of the liver:-

Case 10 John M— aged 5 y. Admitted into the Victoria Infirmary under care of Dr Parry on 11th September 1906.

History. He has suffered from slight attacks of pain in the right iliac region for 3 years previous to admission, but these were never sufficiently severe

to make him discontinue his work.

About 6 weeks ago he was suddenly seized with acute pain in the epigastrium, followed next day by sickness and vomiting – the vomited material being bilious in colour. This continued for three days, and then the pain disappeared, except that he felt slight discomfort in the right iliac region. For the next two weeks he had acute attacks of pain in the right iliac region on alternate days, without any sickness.

A fortnight before admission he became very ill, having a rigor, followed by acute pain in the part previously affected. Later the pain became less, but never disappeared entirely. His bowels during all the attacks were very costive.

Examination. He is very ill – pulse almost imperceptible, and there is profuse perspiration. Abdomen is much distended, and, though there is no acute pain, he complains of slight pain in the right hypochondrium on movement. There is no distinct rigidity unless just under the right costal margin, where there is decided tenderness. The percussion note over this area is dull, and is continuous with the liver dulness. There is no marked tenderness over the liver.

The following note is added :- Patient was moribund on admission, his state not permitting operative interference. He gradually sank during the night, and died the following morning.

At the post-mortem examination, which was made next day, the condition of the organs was

found to be as follows :-

Heart. Slightly enlarged, with hypertrophy and dilatation of left ventricle, and a lesser degree of same in the other chambers. The aortic valves show slight atheromatous Thickening, and there is atheroma of the commencing aorta.

Lungs. Congested, but otherwise healthy.

Abdomen. The liver and stomach are adherent to diaphragm by a fairly thick purulent exudate, and on separating this, a pocket of pus is opened into at the lower edge of the liver about the middle of the right lobe. There is a localized peritonitis at the neck of the gall bladder, and, on separating the exudate, a perforation of the cystic duct, close to the gall bladder, is noted, and a stone is seen protruding from it. On incising the Gallbladder its walls are found to be contracted, and in addition to the perforation above noted, three superficial ulcers of the mucous membrane are seen. Two large soft stones are present lying free in the cavity of the organ.

The Liver is enlarged and congested, and on section a large abscess cavity is met with, situated in the central part of the right lobe, and containing about 2 pints of foul thick pus. The walls of this abscess are sloughing in character, irregular in outline, and with no delimiting capsule from the hepatic substance. There is no portal Thrombosis.

The common bile duct is dilated, but shows no evidences of gall stones.

Spleen is enlarged, dark in colour, soft and diffluent. It presented the appearances of the septic spleen.

The pancreas is healthy. the kidneys are congested but otherwise healthy, & all the other organs present normal appearances.

In connection with this same condition I might call attention to the case of Mrs McC — case 4, where, at the post mortem examination, the bile ducts throughout the organ were dilated, and contained bile stained pus, but without abscess cavity. Hepatic abscess, or at least abscess in the liver, may occur in another way. When the gall bladder is inflamed and there is pericholecystitis present, adhesions may form between the gall bladder and the liver, and if there are stones present in the former, they may ulcerate their way through the parenchyma of the latter, and finally come to rest in an abscess cavity within the substance of the liver. This form of abscess, which is in reality a fistula, will, however, be more conveniently described here than elsewhere, and the example of the condition occurring in my series of cases is appended. In it, a stone was found blocking the cystic duct and communicating with a cavity in the left lobe of the liver, which contained purulent debris, and 3 or 4 small stones.

Case 11 Mrs G— aged 44. Admitted into the Victoria Infirmary under care of Dr Parry on 8th May 1906.

History. She has been liable to attacks of abdominal pain for nearly a year, coming on about once in 6 weeks, but of late more frequently. These attacks were characterised by sudden onset of pain in the right hypochondrium, and epigastrium, with nausea, and vomiting of yellow bilious fluid. For 10 days previous to admission

she had daily spasms of pain in the area above mentioned, and shooting through to the right shoulder. Between the paroxysms, she suffers from a burning sensation and a feeling of discomfort over the stomach, which is ascribed to indigestion. Today she had another severe attack, with the passage of some blood per rectum, and in consequence was removed to hospital.

Previous Health. She had an attack of cholera many years ago, but otherwise has always enjoyed good health.

Examination. Countenance is pallid, pulse weak, numbers 144 per min. temperature 105° F. She is in a drowsy condition and does not seem to have much pain, save when she moves in bed, and then she suffers from pain in the upper quadrant of the abdomen.

Abdomen. There is extreme Tenderness on pressure over the region of the liver, which can be felt extending a little below the costal margin. In the region of the gall bladder there is a large tense rounded swelling extending down almost to the umbilicus. It is tender to ~~percussion~~ pressure, and on percussion its dulness is continuous with the liver dulness.

Heart and Lungs. No marked departure from normal is detected

Rectal examination reveals some internal haemorrhoids present.

After admission she gradually got weaker, and although saline infusion was given, it only gave temporary benefit, and she gradually sank and died at 9 am on May 9th 1906.

The post-mortem examination revealed the following state of the organs :-

Heart. Is enlarged, there is well marked hypertrophy of the left ventricle of the concentric type. The right ventricle and both auricles show slight hypertrophy and dilatation. There is slight atheroma of the commencing aorta, and the anterior mitral cusp also shows atheromatous patches at its insertion.

Lungs show slight congestion.

Abdomen. There is an increased amount of fat in the abdominal walls, mesentery, and omentum.

The Liver is enlarged, and on section shows congestion, slight fatty change, with dilatation of the portal vessels and bile ducts. Gall bladder is distended and is adherent to the omental fat, to the structures in the portal fissure, and to the under surface of the liver. On separating these adhesions some purulent, and blood stained, fluid is seen exuding into the peritoneal cavity. In the cavity of the gall bladder, three or four small mulberry shaped calculi are present, surrounded by blood clot and desquamated products; and a larger stone of the size of a hazel nut is found blocking the cystic duct. On further examination a communication is found with the lower part of the left lobe of the liver, and a small cavity in it being opened into, shows the presence of purulent debris with 3 or 4 small stones.

The common bile duct is in a normal condition.

Kidneys show slight parenchymatous nephritis.

Stomach is normal. Duodenum shows presence of bile staining, and the mucous coat of the bowel is congested.

The other organs present healthy appearances.

The next series of complications with which we have to deal, are those related to stones in the <u>Common Bile Duct</u>.

In the vast majority of cases of gall stones, once a stone has left the gall bladder, and is through the cystic duct, it passes without much difficulty along the common duct till it reaches the opening into the duodenum, where it is gripped by the contraction of the muscular wall. In not a few cases, however, the stone being either larger, or the lumen narrower, than usual, the arrest takes place much higher up than this, and stones have been found impacted in the common duct at all parts, from the junction of the cystic duct right down to the ampulla of Vater. The effect of this impaction is to produce a stemming back of the bile. The bile ducts become dilated above the seat of obstruction, and, as a general rule, the longer the stasis of bile lasts, the greater the dilatation.

It thus happens that, in long standing cases, some of the main bile ducts may be sufficiently enlarged to admit a finger. Later, if the obstruction continues, changes are seen further back in the smallest bile ducts of the liver, these become dilated. The dilatation of the duct walls, as a rule, is of the cylindrical variety, but sometimes it is saccular, forming little cysts on the surface of the liver. The effects are last of all seen in the substance of the liver itself, and this has already been described

The fluid which is contained in the dilated bile ducts is at first exclusively bile, but as we have seen in

the case of the gall bladder. the colour soon disappears, and the fluid becomes colourless, and of a serous, or mucous, character. There is no doubt also, that, under the altered condition of affairs within the liver, the production of bile is decreased, and the bile which is formed, does not mix with this secretion, but is absorbed directly into the general circulation.

What I have described above, is the condition found when a calculus blocks up entirely the lumen of the duct, so that no bile can get past. Such an occurrence, though found in a few cases, is not common and a complete obstruction of the duct when it does occur, is more likely to be due to a tumour of the duct, or of the head of the pancreas, than to a stone. Even if a calculus should become impacted, and completely occlude the lumen, it will in all probability soon become loose from the following sequence of events:- the obstruction causes dilatation of the duct behind the stone at the point of impaction, while the constant pressure of the calculus produces atrophy of the walls, with which it is in contact, and softening and ulceration are extremely liable to occur. Thus, in cases where there is a clear history of chronic obstruction, the calculus is found lying loose in the duct. Even if this be the case, it must be remembered that loose stones, by a ball-valve action, may give rise to intermittent obstruction. as when it lies in certain positions it may block the duct, and in other

positions the bile passes practically unimpeded.

As a general rule, the lower down the duct a stone is found, the smaller it is. Stones the size of a marble have been found in the common duct high up, whereas at the ampulla of Vater the average size is that of a split pea. Taken all over, the commonest site of impaction of a stone in the duct is at, or near, the ampulla. Courvoisier[21] found them in the upper part in 14 %, middle in 15 %, and in over 50 % at, or near, the duodenal orifice. Mayo Robson[32] found calculi in the upper part in 15 %, middle in 18 %, and the remaining 67 % in the lower part. Of the four cases in my series in which calculi were found in the common duct at the post-mortem examination, one was in the upper part, and three near the diverticulum.

Wherever there is a stasis of bile, it is likely that sooner or later invasion of microorganisms will take place, giving rise to a clinical and pathological picture, which differs markedly from the original condition. In this, the common bile duct is no exception to the rule.

As we have already discussed the methods of infection in regard to the gall bladder, and the organisms usually found, it will be unnecessary to recapitulate, as the same principles apply here. It may, however, be stated, that, whereas the infection may be primary in the common duct, and from thence spread back to the gall bladder causing a cholecystitis, it may, on the other hand, be primary in the gall bladder,

and descend as a secondary infection to the duct, or both infections may occur simultaneously.

The first pathological complication of cholelithiasis in connection with the common duct which demands our attention is that of catarrh of the duct. I have previously stated that catarrh of the biliary passages is due to bacterial infection, but this is not accepted by all writers on the subject, nor is this to be wondered at, when we consider how difficult it is to determine the rôle which bacterial infection plays. There is always the possibility, in making examinations, of post mortem change, and bacterial invasion after death, as well as accidental contamination while making cultures.

The pathological changes seen in this condition, are practically identical with catarrhal changes in a mucous membrane, in any other part of the body, namely, swelling of the mucous membrane, proliferation and desquamation of epithelial cells, and excessive secretion of mucus along with a varying number of leucocytes. This swelling of the mucous membrane may progress till the lumen behind the stone is closed up, or a plug of mucus form & give rise to the same condition.

The next complication to be dealt with is that termed suppurative Cholangitis. It is, perhaps, less frequently met with than the simple catarrh, but it is a much more serious condition, and may end fatally. I have emphasized the important part which microbic invasion plays in the diseases of the biliary

system already, especially if it be associated with cholelithiasis, and in no part is this exemplified more clearly than in the condition which we are now discussing. Of all the causes of suppurative cholangitis, cholelithiasis is the most common, as was proved by L. Rogers,[23] who found it to be so in 18 out of 20 cases which he investigated. The factors which go to its causation are first of all the calculus, impacted on its way down the duct, stemming back the bile, and leading to stasis. Then the duct becomes dilated, with consequent weakening of its walls, and they are rendered less able to resist the intrusion of organisms. There is also very often an associated gastro-intestinal catarrh, which may spread up from the duodenum, and lastly, there is the possibility of a descending infection from the liver, through the portal system.

The organism usually found in this condition is the Bacillus Coli communis, and, if cultures be made, it is very often the only one present, but this may perhaps be accounted for by the fact, that from the prolific growth which this bacillus possesses other organisms are crowded out & do not get a chance to develop.

If smears be made directly from the ducts in cases of suppurative cholangitis, we may find in them, streptococci, staphylococci, pneumococci, or typhoid bacilli.

To the course of a suppurative cholangitis is sometimes added a more or less general septicaemia, usually developing slowly and insidiously, and manifesting itself by an

endocarditis, pleurisy, pneumonia, or other septic lesion. In a few cases it takes the form of an acute ulcerative endocarditis. To this latter category belongs the case of Mrs S— case 6, already described. It will be seen, on referring to the description given, that 6 or 7 days after admission the heart condition, which had been previously quiescent, became lighted up and was probably the cause of death. At the Section there was present acute ulcerative endocarditis.

That, in such cases, the acute endocarditis and cholangitis are directly related to one another, and not merely a coincidence, is proved by the fact that often the same organisms can be isolated from both lesions.

In Mrs S— 's case the isolation of the organisms was not carried out, but the clinical history shows that there was a latent affection of both parts, and the lighting up of the one was synchronous with the development of the other. The positive reaction to the Widal test, which was got in this case, suggests the possibility of a typhoidal infection.

The following case, I think, should also be included under the same heading. In it there was a development of a septicaemic condition soon after an operation for gallstones, the symptoms being mainly referable to the chest, and the post mortem examination showed an acute ulcerative laryngitis to be present. Such a complication seems to be extremely rare, so I can find no mention of it in any of the text books.

Case 12. Philip McD— aged 52. Admitted into the

Victoria Infirmary, under care of Dr Parry, on 26th June 1903.

History. He had an attack of gallstone colic 4 years ago, with acute pain in the upper abdominal, and thoracic, regions, lasting about 12 hours, nausea, vomiting and rise of temperature. Similar attacks occurred regularly after this, at intervals of 2 or 3 months. After these attacks he was often jaundiced. He had a very severe one in Dec. 1902 but got better, and since then has had 4 seizures in all. He never noticed any swelling in the region of the gall bladder during any of these times he was ill, but there was always great tenderness in that region. He has lost flesh during the last 6 months.

Previous Health. Is liable to slight bronchial attacks in winter.

Examination. No swelling could be detected in the region of the gall bladder, but there is tenderness and slight resistance. The heart is normal, while over the lungs, the respiratory murmur is harsh, more especially over the right apex. The urine is normal.

Operation was performed by Dr Parry on July 2nd.

Cholecystotomy was done, but no stones were found. A drainage tube was inserted the wound closed as usual.

A fortnight later, when convalescence was apparently progressing satisfactorily, he complained of breakiness, and a feeling of choking. Later, pain was complained of over the base of the right lung, + on examination, dulness to percussion, diminution of the respiratory murmur, and of the vocal fremitus, were discovered. The sputum was examined and pneumococci were present. Had some

evening he died.

Post mortem examination revealed the following condition of the organs:-

Heart. Is enlarged, left ventricle hypertrophied, other chambers normal. All the valves are competent, and the chambers healthy.

Lungs. The left lung is firmly adherent at the apex. On section it is found indurated. At the apex, there is a large area of fibroid induration of the nature of stone masons phthisis, while there are other smaller nodules scattered throughout the lung. The free edges are emphysematous, and the lung is deeply pigmented.

The right lung is adherent from apex to base by a recent fibrinous pleurisy, and sero fibrinous fluid is present at the base. On section, it shows appearances similar to that of the left. There are evidences of acute and chronic bronchitis in both lungs.

Abdomen. The Liver is enlarged, indurated, and with areas of hepatitis in the centre of the organ.

Gall bladder has a thickened wall, and granular congested surface as if from gall stones. The common duct is dilated, and, at the opening into the duodenum, there is the same congested granular surface.

The pancreas is congested, and the kidneys show parenchymatous, and interstitial, nephritis.

Trachea & Larynx. are congested. At the position of the arytenoid cartilage on each side, there is found a sloughing ulcer, with firmly adherent membrane, and congested periphery. The ulcers measure about 1/4" diameter.

Bacteriological examination. Films prepared from the ulcer show the presence of a diplococcus very abundant,

broad shaped bacilli somewhat larger than, but not unlike, true diphtheria, and numerous elongated filaments similar in appearance to the long bacilli.

Microscopic examination of the larynx. A section was taken through the laryngeal mucosa. It showed a stratified columnar epithelium lining the greater part, with its central area detached. Beneath the epithelium a highly cellular area was present, composed of polymorpho-nuclear leucocytes, fibroblast proliferation, and areas of fibrin with entangled leucocytes.

Remarks. Though no gallstones were actually found present in this case, I have included it in the series, as the clinical history, and the congested granular appearance found at the P.M. indicate their former presence.

The pathological condition of the duct in cases of suppurative cholangitis is of considerable interest. The mucous membrane becomes swollen with inflammatory exudation; the epithelium proliferates, and there is a casting off of epithelial cells. The secretion contains more cells than in the catarrhal form, and resembles more or less the appearance of pus. The connective tissue of the walls of the duct show a well marked round celled infiltration. This inflammation may extend through the walls of the duct and set up a local peritonitis, giving rise to what is called a pericholangitis. When this occurs there is, as a direct result, considerable matting around the duct, causing perhaps its obliteration as in the following case:-

Case 13. Mrs Mary S— aged 32. Admitted into the Victoria Infirmary, under care of Dr Parry, on Feby 7th 1904.

History. Her illness began 3 days before admission, with sickness and vomiting, followed 20 minutes later by pain in the upper part of the abdomen. Next morning there was pain over the entire abdomen, but in a few hours the pain located itself to the right iliac fossa and the vomiting still persisted. That evening, the pain again spread over the entire abdomen. On Feby 6th the abdomen began to distend and the vomiting became less, but increased again the next day. The bowels never moved since the onset of her illness.

Examination. Abdomen is distended and there is tenderness all over, but no marked rigidity, and no resistance.

Previous Health. Six months previously had inflammation of the bowels. The pain, then, was very severe, and was confined to the upper part of the abdomen.

Operation was performed on the day of admission.

When the abdomen was opened. The intestines were seen to be distended, but there was no general peritonitis. A mass was felt in the region of the right kidney, so this was exposed, and a simple cyst was found on its convex border. There was great congestion of the retro-peritoneal tissue below the kidney, and a considerable amount of lymph was present, but no pus.

She died the following day.

At the post mortem examination, the gall-bladder was found to be small in size, and shrunken, but its walls intact.

It contained about 30 stones of varying size and shape, and, in addition, a small quantity of grumous, but not distinctly purulent, fluid. The cystic and hepatic ducts were patent. The common bile duct lay completely buried in adhesions, and could not be traced. The diaphragm was adherent to the upper surface of the liver, by a thick layer of plastic lymph.

The stomach & intestines were moderately distended, and a few loops of small intestine were gently glued together. All the other organs presented fairly healthy appearances.

In addition to the burying of the common bile duct as a result of the pericholangitis, there may follow obliteration of the foramen of Winslow, or the local peritonitis may spread to the portal vein and give rise to a hylephlebitis. Then, too, adhesions may form between the duct and various organs round about, such as the colon, duodenum, and gall bladder, etc with fistulae forming later.

These infective changes spread back sooner or later into the liver, giving rise to intrahepatic cholangitis, with, perhaps, abscess. The part which the lymphatics play in this spread is not quite fully understood. Should they be the means of infection, it would be against the lymph stream, yet, in these cases, there is enlargement of the glands in the portal fissure, and perhaps softening. As the disease progresses, the mucous membrane of the duct becomes destroyed in parts, and little patches of ulceration are seen, and this is most liable to occur where the stone is lying. Gradually the various

coats of the duct give way, and one or other of the following conditions result ;- the stone may push the outer wall of the duct before it and come to rest in a diverticulum which it has made for itself, or it may lie in a cavity formed within new connective tissue, which resulted from a previous peritonitis.

A not uncommon result is the formation of fistulae from adhesions previously formed, and lastly, in a few exceptional cases, the ulceration goes on so rapidly that adhesions have not had time to form, and the stone, perforating the duct, finds its way into the general peritoneal cavity.

First of all we shall take up biliary fistulae occurring between the common duct and adjacent organs, as the stomach, duodenum, and colon. The choledocho - duodenal fistula usually takes place at the 1st part of the duodenum. It is a condition which we would expect to find more frequently than is actually the case, but this may be due to the fact that the condition is not recognised at the post mortem examination, and the artificial opening is mistaken for the natural one. This explanation would also hold good for those cases in which a gallstone has been found impacted in an opening into the duodenum, and no symptoms of back pressure on the pancreas found. Again, it is only by supposing that ulceration and fistula between the common duct and duodenum, and between the gall bladder and duodenum, has formed, that we can explain the finding of large gallstones in the intestine. While it is true that, in some cases,

these openings have been found, in others no sign of their presence can be detected, and the question naturally arises as to how far the bile duct is capable of distension in order to allow a calculus to pass. The point has been raised especially in connection with intestinal obstruction as a result of cholelithiasis. Most authors are agreed in stating that a concretion, which has found its way through the bile duct, is not likely to become arrested in the bowel. Stolpe Seyler[24] remarks "that only by the formation of fistulous connections between the biliary passages and the duodenum, can the passage through the intestine of stones, larger than a hagel nut, be explained."

On the other hand Rokitansky[25] observes that "owing to the extreme distension which the biliary passages are capable of, calculi of the size of a hens egg may be enabled to pass through".

It is probable, however, that the more recent view is correct, viz. that if large gall stones are found in the intestine a fistulous channel must be sought for.

Even with these cases included, it is very doubtful if fistulae between the common duct and duodenum are as common as fistulae between the gall bladder and duodenum.

Choledocho-gastric fistulae — those between the duct and the stomach — are rare, and when found, are usually due to an abscess having formed in connection with the duct, which, by reason of adhesions contracted, bursts into the stomach. In such a case, if there

were any stones present in the abscess, they would probably be vomited from the stomach. Some writers have affirmed that when gall stones are vomited up during life, it is a sign that biliary-gastric fistula exists. Though this may be the case when large stones are ejected, it does not necessarily follow in the case of small ones. Just as bile may regurgitate through the pylorus into the stomach, so too may small stones. This undoubtedly happened in the case of Mrs A— case 18, where a stone, which was impacted at the diverticulum of Vater, escaped shortly before death into the duodenum, and was vomited from the stomach.

Fistulae between the common duct and the colon are not common, those between the gall bladder and colon being much more frequently met with.

Regarding the remote results of suppurative cholangitis one would expect that stricture of the duct would be one of the commonest, partly from the compression of the duct by contraction of the connective tissue around it, and partly owing to the cicatricial healing of ulcerated mucous membrane. As a matter of fact the reverse is actually the case, and simple strictures are extremely rare, while even in the cases recorded, microscopic examination does not seem to have been carried out, and it is questionable whether they may not have been carcinomata, although to outward appearances they looked non-malignant.

A form of <u>chronic cholangitis</u> is met with associated with gall stones in the common duct, and in it the ball-

valve action of the calculus, already described, is an important factor. It usually occurs when the calculus is at, or near, the ampulla of Vater. The mucous membrane of the duct shows inflammatory change, but there is little or no tendency to ulceration. The duct walls are dilated, and there is an increased amount of fibrous tissue in the fibro muscular wall, causing considerable thickening. The changes in the liver in these cases are much less marked than in the acute form. The chief of these is an increase in the fibrous tissue around the portal zone which, by subsequent contraction, compresses, and causes atrophy of, the liver cells. The intra hepatic bile ducts are also dilated, with thickening of their walls.

This condition, in addition to the local disturbance, causes changes in the other organs to which it is related.

The gall bladder is usually found thickened contracted from previous cholecystitis, is very often adherent to the tissues around. The infection is also liable to travel along the pancreatic duct & give rise to a chronic interstitial pancreatitis, with enlargement of the head of that gland. These changes will, however, be dealt with in full in the section relating to that organ.

The next complication of cholelithiasis demanding our consideration is <u>Tumours of the Bile Duct</u> associated with calculi.

These are, naturally divided into two groups, non-malignant, and malignant, tumours, and of these the former class are rare. Papillomata, however, have been described as arising in the inside of the common duct.

Such a case is described by Rolleston[26], who found a papilloma arising above to a gall stone, which had been impacted for 2 months + which he removed by operation. It was described as a branching papilloma, composed of a basis of fibrous tissue covered over by columnar epithelium. He adds, however, that the subsequent history of the patient suggested that she had malignant disease. The same difficulty exists here as in the gall bladder, namely, the differentiation between a villous carcinoma in the early stage and a simple papilloma, and this same difficulty applies in the unique cases of fibromata that have been reported.

Malignant disease of the bile ducts, while not nearly so commonly met with as malignant disease of the gall bladder, is nevertheless of very great importance. In the majority of cases in which carcinoma is found in the bile ducts, it is a primary growth. The disease is now oftener described than formerly, probably owing to the fact that it was overlooked, and the value of microscopic examination in determining the incidence of the disease cannot be too strongly emphasized.

A carcinoma of the lesser omentum, to outward appearances a primary growth, may, by careful examination, prove to be secondary to a small calculous mass - in reality a cancer - in the duct. This was what actually occurred in the case of Mrs P— case 9, where the microscopic examination showed the primary growth to be at the junction of the cystic and hepatic ducts

The relationship of gallstones to carcinoma of the bile ducts is not so clearly defined as it is in the case of the gall bladder. Some authors have found stones present in 94% of cases of primary carcinoma of the latter, while in the former the percentage is only about 37. It must be taken into account however, that gall stones may give rise to serious irritation, and then pass out of the body, unnoticed, before death — the effect remaining, though the cause cannot be discovered.

If we assume, as in cancer of the gallbladder, that the irritant factor of gallstones plays an important part in cancer of the common duct, then we would expect to find the seat of election of the cancer at the point, or points, of the duct where calculi are usually impacted, and this is exactly what is found. In the statistics quoted by Rolleston[27], we find that the growth was present in 31% of cases at the junction of the common, cystic + hepatic ducts, and in 26% at the lower end of the common duct near the duodenum.

On account of this, at least apparent, connection between gallstones and cancer of the duct, I have included in the series two cases of malignant disease of the duct, in which no stone was discovered post mortem; nevertheless, there is every reason to suppose that gall stones may have played an important part in the etiology of the condition.

As a rule the growths which occur are small, about the size of a Barcelona nut, and anything larger than this is exceptional. In rarer varieties they take a

diffuse infiltrating form. When examined with the naked eye, they may show a villous appearance projecting from the mucous surface, and this is of special interest in connection with the view, that the growth starts as a simple papilloma which later becomes malignant. The type usually met with is a firm whitish tumour which may project at one part into the lumen or may surround it forming an annular stricture. It usually arises in the wall of the duct at a point where a gall stone causes, or has caused, irritation of the mucous membrane and proliferation of the epithelium, with resulting cicatricial tissue and it may happen that a gall stone is found in the centre of the growth.

The differentiation of carcinomata in the common duct from those arising round about, is sometimes rather difficult. The typical cancer of the common duct is, as we would expect, a columnar celled one. Spheroidal celled varieties are also met with, and it has been suggested that these take origin from the mucous glands in the walls of the duct. In addition other forms are met with and these have been called atypical cancers. They show transitional changes between columnar celled, and spheroidal celled, tumours and, if there be present mucoid degeneration of the cells with alteration in shape, a flat swollen appearance is presented almost identical with squamous epithelioma. The possibility of there being a true

squamous-celled carcinoma of the bile duct raises the same question as that already referred to in connection with the gall bladder and need not be discussed here.

The nature of the tumour cells is of considerable interest. As already stated the columnar or short cylindrical cell with oval, vesicular, nucleus is the predominant feature, and these tend to form a duct like arrangement. Then there is the spheroidal cell, with its more or less round nucleus staining deeply. Between these two are various transitional cells. Some of these are ovoid, tailing off at the extremities, and with an oval nucleus which is often vacuolated. Some are polygonal cells with large nuclei, situated often where there is inflammatory change going on. The nuclei of these cells may show mitotic division, and in some of the cells 3 or 4 nuclei may be present.

It is possible that these transitional cells represent a retrograde development in the life history of the tumour, as they are found often in the interior where degeneration is going on.

When carcinoma of the bile duct occurs, changes result in the other component parts of the biliary system. Below the tumour, the lumen of the duct is of normal calibre while above, it is often much dilated. The gall bladder, as a rule, is distended unless when it is found bound down and contracted, as the result of a former cholecystitis. The ducts of the liver are dilated, with atrophy of the liver cells around the portal area, and perhaps necrosis.

This atrophy of the liver substance brings the fibrous tissue into prominence, but there is, in addition, an increase in the connective tissue, producing cirrhosis and an attempt at the formation of new ducts. The following cases illustrate the conditions usually found :-

Case 14. Wm G — aged 80. Admitted into the Victoria Infirmary, under care of Dr Napier, on 6th Nov. 1906.

History. His illness commenced three months before admission, with a severe attack of pain in the abdomen, followed by vomiting, and soon after this he became jaundiced. The pain disappeared after a short time, so did also the vomiting, but the jaundice persisted, and he became troubled with dyspeptic symptoms. He has lost flesh, and has been confined to bed for over 6 weeks. He has been troubled with bronchitis lately.

Previous Health was good.

Examination. Jaundice is noted all over the body. The abdomen is slightly distended, and the liver is found to extend considerably below the costal margin. Its upper surface feels rough, and over the site of the gall bladder there seems to be a tumour. There is considerable tenderness on pressure over the liver, and especially over the region of the gallbladder.

A fortnight after admission he became much worse, showed signs of heart failure, and died on 23rd November 1906

At the post-mortem examination, at which I assisted, there was found the following condition of the organs:-

Heart. There is hypertrophy and dilatation of both ventricles, slight atheroma of the aorta + aortic cusps. The endocardium is deeply bile stained.

Lungs. are adherent to the chest by old adhesions. They show slight emphysema of the free margins and on section passive congestion. The bronchi show evidence of marked chronic bronchitis.

Abdomen. There is a marked increase in the abdominal fat. The Liver is of normal size, flattened from before backwards, and from above downwards. It is deeply bile stained and on section shows dilatation and undue prominence of the bile ducts, from which muco-purulent bile can be expressed. The consistence of the organ is very soft.

Gall bladder. is distended, resembling in size that of a large pear. It is thin walled and when opened shows bile, with desquamated catarrhal products. The wall is congested, but otherwise healthy.

Cystic, hepatic, and common bile ducts, are all dilated but contain no stones. Close to the papilla, an area of the mucous coat of the common bile duct, 3/4" in length, is found raised and congested, and presents the appearance of chronic inflammation, as if from the passage of a gall stone; but there is very little thickening of the wall itself and no obvious stenosis.

Pancreas is of soft appearance + congested but otherwise healthy.

The condition of the other organs does not call for special comment.

Microscopic sections of the liver, gall bladder, tumour

tissue, heart + kidneys, were prepared and examined by me, with the following result:-

Liver. The microscopic examination of the liver shows the soft character of the organ to be due to a toxic change with cell necrosis, fatty degeneration, and deposit of pigment. Some of the hepatic cells are small in size and atrophied, while others are swollen and irregular in outline. Throughout the sections fibrous tissue increase is apparent, following the line of the bile ducts.

Gall bladder. Microscopic examination shows slight increase in the fibrous tissue of the wall, while the epithelial layer shows a well marked cholecystitis to be present.

Tumour. A section of the growth shows it to be confined to the mucous and submucous coats of the duct, though infiltration of the muscular coat to a considerable depth is apparent at one part. The tumour area is of small dimensions, and causes a heaping up of the surface. It is composed of a well marked stroma containing malignant cells, which in places line the wall, but, for the greater part, are desquamated in bunches, and mixed up with inflammatory cells.

Under the high power the cells are seen to be of short cylindrical, or columnar, type (See Fig 7) In parts there is an irregular heaping up of these cells, with large and deeply staining character of their nuclei. Cell division is apparent in a number of the cells. In the part where the muscle is infiltrated, there is an out-planting of the cells,

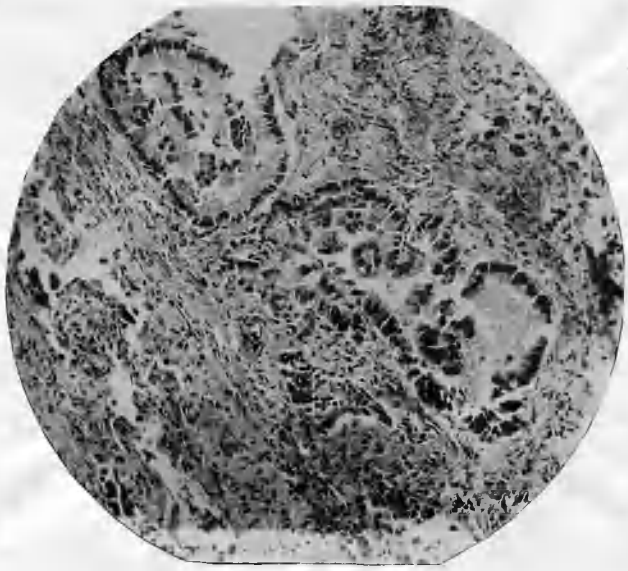

Fig. 7. — Photomicrograph of Carcinoma of the Common Bile Duct — Columnar celled.

Fig. 8. — Photomicrograph of Cancer of the Common Bile Duct.
(Transitional type.)

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with an attempt at duct like arrangement.

Around the tumour area, the duct wall shows inflammatory reaction and desquamation of catarrhal products. There are also aggregations of cells at different parts of the muscular wall.

Heart. Microscopic examination shows a fibrosis - the interstitial connective tissue is increased, and the muscular bundles show a degree of atrophy.

Under the high power a loss of striation is apparent, while brown atrophy granules are present in some of the cells.

Another case, presenting features of a slightly different type of tumour, is the following :-

Case 15 Adam G— aged 77. Admitted into the Victoria Infirmary on 13th September 1903, under care of Dr Duncan.

History. Very little history could be obtained, but it seems he had been ill for about 5 weeks. At that time he began to suffer from jaundice and pains in the back. About 3 weeks ago he began to wander in his mind, but seems to have had no complaint apart from the jaundice.

Previous Health. Always enjoyed good health.

Examination. He is jaundiced all over the body. The liver is slightly enlarged to percussion, but is not tender to pressure. There is present, however, a considerable degree of resistance over the right hypochondrium

Heart is normal. Lungs show chronic bronchitis to the

present.

Mental condition. Dazed and rambling in his speech.

After admission he became gradually worse, lapsed into a condition of semi-coma, died on 29th September 1903.

A post-mortem examination revealed the following:-

Heart. Is slightly enlarged, with hypertrophy of the left ventricle, and a lesser degree of hypertrophy and dilatation of the right. Valves are healthy. The heart muscle is slightly fibroid in character, endocardium shows bile-staining.

Lungs. Show emphysema, and on section passive congestion, and oedema. The bronchi show chronic bronchitis, with a recent acute exacerbation.

Abdomen. The Liver is slightly enlarged, the enlargement being a lateral one. On section it shows deep bile staining of the organ, with well marked dilatation of the veins and bile ducts. There is a moderate degree of cirrhosis, and the surface of the organ is granular.

Gall bladder. Is attached at its top, by a fibrous adhesion, to the duodenum. Its walls are healthy, and it contains a small quantity of fluid bile of thick consistence. An area of stenosis of the common bile duct is met with, shortly after the junction of the cystic duct, but the chief obstruction is evidently due to another area of cicatricial fibrous tissue, fully 1" in extent, which is found situated at the junction of the two hepatic ducts. The rest of the duct is normal.

Pancreas is of normal size, pale in colour, and firm in consistence. It shows a considerable amount of bile staining, and, on section, an atrophy of the

glandular tissue, with extensive fatty change.

Spleen is enlarged and congested, soft + diffluent in consistence, and shows bile staining

Kidneys show slight interstitial nephritis, and arterio-sclerosis.

Microscopic sections of the areas of supposed cicatricial tissue, of the pancreas, of the liver, made, + examined by me, showed the following pathological features:-

Areas of cicatricial tissue? These were seen to be composed for the most part of firm fibrous tissue, with some recent connective tissue, and numerous areas of tumour cells scattered through it. The fibrous tissue in parts appeared fairly healthy, but, in other parts, had the appearance of a scirrhus-like tumour. The cells in the fibrous tissue were present in small groups and presented varied characters - the size and shape of the cell showing the appearances met with in transitional epithelium (See Fig 8) + number of the cells were definitely columnar in shape. Tailed transitional cells, of the type which I have already described, were even more abundant, while a large proportion were either sphenoidal or squamous, in character. The larger cells in many places showed the presence of dividing, and even of several, nuclei.

The fatty tissue in the sections was infiltrated with inflammatory cells and a number of recent connective tissue cells, while the lymph nodules showed an invasion in places by tumour cells.

Pancreas. Sections made showed atrophy of the gland to a marked extent, whole acini in places being lost. These

that persisted were small in size, and showed fibrous tissue infiltration. The islands of Langerhans were few in number, but had healthy appearances.

Liver. Sections showed the hepatic tissue to be divided into ill-defined lobules. There was an increase of connective tissue around the cells, while in the portal zones the cells stained very poorly & were laden with pigment. The hepatic cells, generally, showed fatty change.

The next series of complications of cholelithiasis which merits our attention is that occurring with calculi at the Ampulla of Vater. The important difference which exists between calculi at this particular part of the common duct and calculi in other parts, is due to the anatomical relationship which exists between the common duct and the pancreatic duct, and hence I have given this portion special consideration.
The common bile duct and the duct of Wirsung, in their passage towards the intestine, penetrate side by side the coats of the duodenum for a distance of fully ½ an inch, forming, at their entrance, a papilla like elevation on the mucous membrane of the bowel.
Within this papilla they unite to form a short common cavity called the diverticulum of Vater. This is a somewhat conical cavity, into the base of which enter the two ducts, while the apex is their common orifice into the duodenum. It may be, however, that the ducts have no common orifice, but open separately on the lip of this papilla

At the point of entrance of the common duct into the wall of the intestine there is a slight constriction and its walls, at this place, have very little elasticity so that gall stones are frequently impacted here.

The common bile duct also bears a distinct relation to the head of the pancreas. The lower part of the duct, for a distance of from 1 to 2 inches, is in contact with the head of the pancreas, in some cases being completely surrounded by pancreatic tissue, and in others lying in a groove on the surface of the gland. These relationships have a very distinct bearing on the subject under discussion. If a calculus enters the diverticulum and becomes caught there, it may, or may not, obstruct the flow of pancreatic juice from the duct of Wirsung, depending to a considerable extent on the size of the calculus. If the calculus be impacted just at the entrance into the diverticulum, the effects are seen, not upon the pancreas, but on the liver. The following is a case in point:-

Case 16. Mrs F — aged 64. Admitted into the Victoria Infirmary, under care of Dr Parry, on 29th December 1904.

History. She was operated on 4 years previously for appendicitis & was admitted with a large ventral hernia at the site of the old scar. This was operated upon, & convalescence was satisfactory, till 11 days after the operation, when she complained of severe pain in the epigastrium & had a rise of temperature. The following day she was distinctly,

Though not markedly, jaundiced and the urine contained a fair amount of bile. For the next week she remained fairly well, then another attack came on, with pain in the abdomen, over the site of the gall bladder, and a rise of temperature to 103°F. The jaundice, which had been absent for a few days, reappeared on the morning after this second attack. Two days later she had a rigor, and another on the two successive days, and she lapsed into a semi-comatose condition with occasional attacks of delirium. The pulse began to fail and, though she rallied a little under the effect of stimulation, it did not last long; she gradually sank into deep coma (cholaemia) and died on July 13th 1903.

The post mortem examination showed:-

Heart. Is of normal size. Ventricles are somewhat dilated but there is no hypertrophy. The muscle wall is soft and flabby, with bile staining of its wall, and of the endocardium. Lungs. are non-adherent. They show a moderate degree of emphysema, and, on section, passive congestion and oedema. Abdomen. The Liver is slightly enlarged, soft, and friable and is bile stained. On section it shows fatty change, and dilatation of the ducts throughout the organ. Gall bladder is dilated, with thin walls, and contains about 6 ozs of fluid bile. There is an excess of mucus on the surface, and in it are two cholesterine stones about the size of small peas. The common bile duct is dilated throughout its entire length, and, at a spot just outside the duodenum of Vater a gall stone, of the size of a green pea, is found

blocking the duct.

Pancreas is of normal size, very soft in consistence and, on section, shows passive congestion; but there is no indication of haemorrhagic or chronic pancreatitis.

There were some petechial haemorrhages in the fat of the abdominal wall, but no fat necrosis.

A point of considerable interest in connection with the subject under discussion, is the fact that a gall stone may lodge in the diverticulum of Vater without giving rise to any severe symptoms or gross pathological lesion. This is shown in the following case:-

Case 17. Robert C — aged 76 was admitted to the Victoria Infirmary, under care of Mr Maylard, on September 29th 1902.

History. He was admitted, and treated, for strangulated femoral hernia the only point of interest to us in his history is the fact that he had been treated for gall stones at various times, being once treated in the Royal Infirmary for this complaint.

From our point of view the progress of the case is unimportant; for, as the result of gangrene of the bowel, he died on October 26th 1902.

At the post mortem examination, however, the common bile duct was found dilated, and there was a gall stone of the size of a small hazel nut lodged in it, just at the point of its opening into the duodenum. The stone had acted more as an obstructive agent to the common duct than the pancreatic duct, as

the latter was but slightly dilated.

The Liver was slightly enlarged, with fibrous induration, and the head of the Pancreas was firm, but no evidence of interstitial pancreatitis was noted.

Perhaps in this case the absence of any changes in the pancreas was due to the fact, that the accessory duct of the pancreas, the duct of Santorini, was patent and was able to relieve any obstruction of pancreatic juice which was liable to occur. This accessory duct however, cannot be relied upon, as it is only present, according to Skriner[39] in about one-fifth of all cases examined.

Chronic Interstitial Pancreatitis That this disease is a frequent complication of, and is closely related to, cholelithiasis, is a statement which all surgeons operating upon the biliary tract will readily bear out. In a large number of cases, after calculi have been removed, the pancreas is found hard indurated, the head, as a rule, being affected more than the other parts of the gland.

The pathological changes resulting from the blocking of the pancreatic duct by a calculus in the diverticulum are somewhat akin to those produced in the liver by the blocking of the hepatic, or common bile duct. The pent up secretion, partly by its mechanical backward pressure, + partly from its auto-digestive faculty, causes a degeneration + partial necrotic change in the secreting cells. These become diminished in size, the protoplasm becomes more homogeneous, + the nuclei are lost. In the walls of the dilated ducts an increase of connective tissue is seen, spreading

from there, and causing an increase in the interlobular and interacinar tissue, and, by penetrating between the acini, separate these from each other.

Two types of chronic interstitial pancreatitis have been described, depending on whether the interlobular or interacinar tissue is primarily affected, but as a general rule the type met with in that complicating cholelithiasis is the interlobular form - at least that is my experience.

In addition to the fibrous tissue increase, there is also an increase in the fatty tissue present, denoting a fatty degeneration of the parenchyma.

With this progressive sclerosis and fatty degeneration, the gland tissue proper becomes compressed and gradually atrophies, till finally it may almost disappear.

One important point in the pathology of this lesion is the condition of the islands of Langerhans.

That they do not show alterations corresponding to those which occur in the tissues around, is apparent at once on microscopic examination; in fact the adjacent parenchyma may be almost destroyed, and they themselves be but little implicated. One explanation of this, which has been given, is that the cells which form these islands are shut off from the ducts, and do not secrete pancreatic juice, + hence the stasis of that secretion does not influence them.

The changes in the secreting cells in this condition consist in a gradual diminution in size of the cell, which later becomes ill-defined, the nuclei

lose their staining power, and the whole presents a somewhat homogeneous appearance. The blood vessels, too, show some thickening of their walls similar to that which occurs in the ducts.

While very often in these cases the whole head of the gland is affected, with perhaps other parts as well, in not a few it is only a small part of the head which becomes involved, forming a small nodular tumour. This may persist for years and yet, after a gall stone is removed, may utterly disappear. Such cases would be very difficult to distinguish from commencing carcinomata, except by microscopic examination.

In addition to these, what one might term, mechanical changes in the pancreas, as the result of blocking of the duct by a biliary calculus, we have changes brought about by the invasion of the stagnant secretion by micro-organisms, which may enter from one of three sources - the blood stream, lymph channels, or directly by the duct.

This last method may be derived indirectly from catarrh of the bile ducts or be due to a spread upwards from the intestine.

The effect of this infection is to produce a general or localized pancreatitis. If we examine a section of the organ in this condition we find a proliferation of the epithelium lining the tubules - later spreading to that lining the acini. There is a round celled leucocytic infiltration, with inflammatory exudation, and invasion of red blood

corpuscles, causing a heaping up of the cells, which are seen lying crowded together. If the infection now subsides the whole condition may resolve, or go on to the chronic form already described but, if it persists, suppuration results, with its consequent destruction of gland tissue, and the formation of minute pancreatic abscesses, which may or may not coalesce to form large abscesses.

The next complication which I wish to discuss is Acute Haemorrhagic Pancreatitis. It is only within a comparatively recent period that haemorrhagic pancreatitis has had a claim to be ranked with the complications of cholelithiasis, and even at the present time there still remains a great deal that requires to be cleared up, before the definite relationship of the two conditions can be clearly established.

The term, haemorrhagic pancreatitis, is used to denote a condition, in which a haemorrhage, affecting usually a considerable area of gland tissue, is present, and gives rise to more or less characteristic symptoms. In practically every case there is present, in addition to the haemorrhage, a certain amount of inflammation, and this has given rise to a difference of opinion, as to whether the haemorrhage precedes the inflammation, or is preceded by it, and this question is not yet definitely settled.

There is one form of the disease which has no relationship to gall stones, namely, that due to traumatism or rupture of a vessel — the damage in such a case is due mainly to the acute inflammation which is set

to perseverance.

In the class to which we are giving our attention both of these causes can be eliminated, and the disease is found in those who have been previously healthy, or with perhaps some antecedent history of gastric catarrh, or biliary colic. The pathological lesion found after death is predominantly a haemorrhage, and although inflammation is present in addition, it is easy to understand how infection could take place, since the pancreas is in direct communication with the intestine, and is in close proximity to the peritoneum; and moreover it has a peculiar innate liability to decomposition and has a secretion unique in chemical composition.

The cases are recognised clinically, by sudden onset of pain over the epigastrium, with vomiting and collapse - the symptoms of acute abdominal mischief. Sometimes after the lapse of 24 hours a tumour mass may be felt in the epigastrium but in most cases the abdominal wall is too rigid for anything to be palpated. These cases usually run a very rapid course - the patient dying of shock within 24 to 48 hours. On the other hand, if they survive the initial stage, they may die from gangrene or necrosis of the organ.

The post mortem appearance of the pancreas in this acute form shows it to be of a uniform chocolate colour, or perhaps mottled red or yellow, with, or without, adhesions to the surrounding tissues. There may also be a considerable area of haemorrhage in the peripancreatic tissue. On section, areas of necrosis are seen, with congested

vessels and widespread extravasation of blood. If the case be an early one, the pancreas may be hard to the touch, but later it becomes pulpy, and soft, and of a uniform pale colour.

Microscopic examination shows the haemorrhagic areas to be made up of necrotic tissue, round about which are areas of demarcation, separating them from the adjacent pancreatic tissue. In the necrotic area the cells are destroyed, the nuclei no longer stain distinctly, and a homogeneous mass results, in which only the structure of the gland can be recognized. The connective tissue presents a darker colour from the presence in it of altered blood.

In the apparently healthy pancreatic tissue round about certain changes may be recognized. There are places where an early stage of degeneration, and even of necrosis, can be seen. In these, the cells are more granular than usual, and, if anything, somewhat smaller in size. Their nuclei are no longer oval, but take on an irregular outline, and do not stain satisfactorily. Numerous red corpuscles can be seen present, as well as polymorphonuclear leucocytes while the delimiting zone is composed of fragments of pancreatic cells and nuclei, and areas of leucocytic infiltration. In addition to these changes there is present an alteration in the tissues to which special attention has been given, namely the presence of fat necrosis. This presents itself as small opaque white or yellowish white patches, found in the

fat of the omentum, mesentery, subperitoneal and retro-peritoneal tissues, as well as in, and around, the pancreas itself. In rare instances it has been found in the pericardial and mediastinal fat (Bryant[29]).

The essential nature of the condition consists in a splitting up of the fat into fatty acids and glycerine. The fatty acids being insoluble are deposited within the cell, (which has lost its nucleus) and unite with the calcium present to form calcium salts, while the glycerine is absorbed. Some writers have attributed the presence of fat necrosis to bacterial infection, but I think it is generally agreed that the primary factor is an interference with the discharge of the pancreatic juice, thereby causing it to escape into the tissues around: from which it may be taken up by the lymphatics, or blood vessels, and distributed to other parts of the body.

It is almost invariably present in cases of haemorrhagic and gangrenous pancreatitis, but may be found in other cases as well (see base 19).

Having discussed then, as briefly as possible, the essential changes found in haemorrhagic pancreatitis, it only remains for me, in a few sentences, to explain its relationship to cholelithiasis.

Until lately there were two theories to account for the disease, namely the microbic, and the chemical, theories. The former sought to prove that haemorrhagic pancreatitis was due to an invasion of the pancreas by organisms, either backwards along the ducts of Wirsung and Santorini,

or by the blood stream and lymphatics. Extensive bacteriological investigations of the blood, and tissues of the gland, were made, but the results of these have not proved satisfactory, in so much as no organism was found constantly present to account for the condition. The organism which was most commonly found, and often the only one that could be isolated, was the Bacillus coli communis but even then post-mortem invasion from the intestine could not be excluded - so this theory has been rather discounted.

The chemical theory sought to prove that the condition originated from certain chemical substances getting into the pancreatic duct and thereby caused the disease. For example, it was suggested that gastric juice might be forced into the duct of Wirsung from the duodenum, and it has been proved that, if gastric juice be injected into the duct of Wirsung, experimentially, haemorrhagic pancreatitis results.

Recently much support has been given to a third theory - the one in which we are interested - which we might term the mechanical theory, though, in reality, it is closely related to the chemical theory. This theory has been advanced chiefly by the researches of Dr Opie of America, who has recorded a number of cases, and conducted many experiments, bearing on it. It seeks to prove that the disease arises from the presence of a biliary calculus at the ampulla of Vater, which prevents either bile or pancreatic juice from entering the intestine, and at the same time converts the common bile duct and the duct of Wirsung

into one continuous channel. In order that the disease may be produced certain conditions, according to Halstead[30], have to be fulfilled. These are "I. In order that bile may be retrogected into the pancreatic duct the calculus must be 1/ too small to occlude the pancreatic duct, or to interfere with the force of the jet 2/ too large to pass the ampulla. II. One calculus would be more likely to cause the pancreatitis than several, for other stones in the common duct would weaken the force of the shurt of bile which drives the ball valve against the papillary orifice III The gall bladder must be normal, or nearly so, and not thickened, shrunken, or weakened by inflammation." Granted then, that we have a calculus at the ampulla, not sufficiently large to block either duct, and at the same time converting the two into one continuous channel, it follows that bile will be forced along the duct of Wirsung. Both the biliary and pancreatic juices are secreted at a relatively low pressure, but as Opie[31] mentions," any slight difference that might exist would be overcome by the gall bladder, - a muscular organ which at intervals forces bile in considerable quantity along the common duct." The effect of bile, thus thrown into the duct of Wirsung, has been experimentially tried on animals, and the results are invariably the same, namely the production of acute haemorrhagic pancreatitis. It is not unnatural, then, to infer that in human beings the same cause would give rise to the same effect, and, therefore, the theory is a practical one.

Exactly how many of the cases on record would conform with this method of production, and how many would not, is rather difficult to determine. Even in the cases where no gall stones have been found, there is always the possibility of the lesion being due to a single stone, which passed, just before death, into the intestine and was lost, and so no mention is made of it in the post mortem record. From the statistics gathered, it would seem that gall stones are present in nearly 75% of all cases of acute haemorrhagic pancreatitis, and we can infer that in quite a number more they have been present, but were not found.

The following case illustrates the condition of acute haemorrhagic pancreatitis very well. A point of considerable interest in this case, and one which I think I have referred to previously, is the fact that just before death, the stone, which was obviously impacted in the diverticulum, passed into the duodenum, was regurgitated into the stomach, and vomited up.

Case 18. Mrs A— aged 25. Admitted into the Victoria Infirmary, under care of Mr Maylard, on November 19th 1906.

History. Her attack started on Sunday evening 18th Nov., when she was seized with severe pain in the region of the gall bladder. The pain was sharp in character, and continuous — not paroxysmal. It was so severe that it prevented her from sleeping and kept her moving about and crying out. Soon after this she became

sick and vomited, and the sickness and vomiting have continued up to the time of admission. Her bowels have been opened regularly. As she became worse she was sent to hospital.

Her condition on admission was as follows:-

Pulse was regular, full, and numbered 100 per minute, while the temperature was normal. She complained of intense pain over the abdomen and felt tired and exhausted, but had no appearance of collapse. Her colour was fairly good and there was no jaundice. Pupils were somewhat contracted but reacted to light. Tongue was moist and furred.

Examination Abdomen showed no marked fulness in the upper part or regularly, but over an area extending from the ensiform cartilage to the umbilicus, there was very marked tenderness on pressure.

Patient continued in much the same condition as on admission till 6 am. next morning, when she became suddenly collapsed and pulse. There was no sign of peritonitis though there was a considerable degree of rigidity present over the abdomen

Operation. Mr Maryland. Nov 20th.

An incision was made in the middle line of the abdomen above the umbilicus, and a quantity of dark coloured fluid was found in the abdominal cavity. The omentum showed signs of fat necrosis - a delicate lace like appearance, with large white particles scattered through. The abdomen was washed out with warm saline

solution and a tube put into the pelvis for drainage – no further operative procedure being deemed advisable, as the pulse was barely perceptible & patient was becoming exhausted She was put back to bed, but immediately started vomiting dark, greenish, fluid Two hours after the operation she vomited ~~it~~, ~~in~~ about 10 ozs of greenish fluid, a faceted gall stone of the size of a green pea. Though conscious she never recovered from the shock, so at 2 pm she had 15 ozs saline solution given by the vein. She rallied somewhat at the time, but later collapsed again, and died.

Post-mortem examination.

The necropsy, at which I assisted, was performed 20 hours after death.

The external appearances were those of a well developed, and well nourished, body with slight excess of fat. Rigor mortis was pronounced, pupils were equal & medium. There was an operation wound present, 5½ inches in length, in the right linea semilunaris, and above the symphysis there was a drainage wound 1" long. There was no jaundice present.

THORAX. Heart. weighed 9 ozs. The pericardium was healthy, and the heart was of normal size. All the chambers presented healthy appearances, the muscular tissue was of good colour and consistence. The Aortic, & Pulmonic, valves were competent. The Mitral admitted 2 fingers. the Tricuspid Three, all the valves had healthy cusps.

Lungs. The right lung was adherent at the apex, the left was non-adherent. Both lungs, on section, showed

intense engorgement - passive hyperaemia with slight oedema, emphysema of the free margins, and congestion of the bronchi.

The right lung weighed 1 lb 4 ozs. the left 13/4 ozs.

Abdomen. There was some free fluid in the abdominal cavity, blood stained and bile-stained. The parietal peritoneum, the omentum, and serous coat of bowel and mesentery, showed a disseminated fat necrosis. Loops of intestine were congested and there was slight adhesion by means of a recent deposit of fibrin, but non purulent in character

The Liver weighed 3 lbs 4½ ozs. It was of normal size, pale in colour, and somewhat soft in character. A fibrinous exudate was present on the upper surface of the right lobe. The organ was not congested or bile stained, but the appearance resembled somewhat, cloudy swelling

The Gall bladder was slightly enlarged and there was some hypertrophy of its walls. It contained a considerable number of small gall stones. A few were present at the neck and origin of the cystic duct. The common bile duct was traced to its termination and there was no evidence of gallstones. The diverticulum and papilla of Vater were patent

The Pancreas was deeply congested, almost purplish in colour, and infiltration of blood was general throughout the gland. The entire organ was firm in consistence and was firmer at its head than elsewhere, while on its surface were small areas of fat necrosis. The duct

and are regular in outline. The greater part of the section shows only an ill-defined appearance of acini, with occasional nuclear staining. Islands of Langerhans cannot be recognised, and the ducts are only recognisable by the fibrous tissue of their walls. The extravasated blood already referred to, is recognised by the fibrinous meshwork, ill defined outline of red cells, and presence of white ones.

Sections through the body of the gland show changes similar to those in the head.

Sections through the tail of the gland show fairly well stained acini, with an increase of the inter-acinous connective tissue. In other parts there is marked auto-digestion. The fat cells show an occasional area of fat necrosis. In the periphery of the gland the connective tissue is raised up and infiltrated with recent haemorrhages, having the usual characters of fibrinous meshwork, with the presence of red and white cells. In places the leucocytes are increased forming actual clusters, and this is apparent between the meshes of peripheral fat. (See Figs 10 and 9)

Liver. Sections through the liver show it to be the seat of a uniform, but slight, degree of cloudy swelling. There is no actual fibrosis, but the connective tissue along the line of the medium sized ducts shows slight proliferation

Kidneys. These show a moderate degree of cloudy swelling and slight interstitial fibrosis.

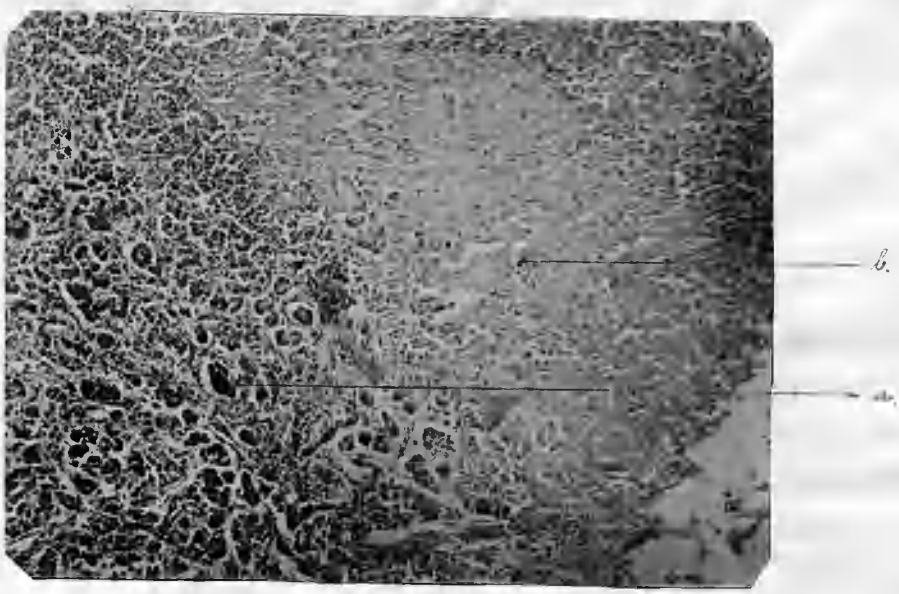

Fig. 9.— Photomicrograph of Pancreas in Acute Haemorrhagic Pancreatitis

a. necrosed glandular tissue

b. Haemorrhagic + leucocytic infiltration

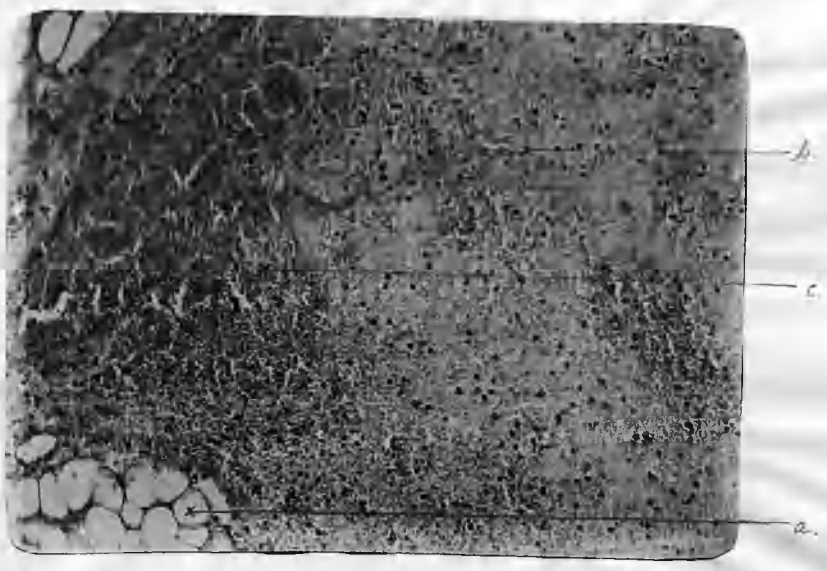

Fig 10. — Photomicrograph of Pancreas in Acute Haemorrhagic Pancreatitis.

a. Fat necrosis

b. Fibrinous meshwork with entangled leucocytes.

c. Aggregated red corpuscles

There is some desquamation of the epithelium into the lumen of the tubules and the tubules at the periphery show slight dilatation

Spleen. Microscopic examination shows capsule and trabeculae well formed and prominent. The Malpighian bodies are rather small in size. The pulp shows slight excess of blood as evidenced by increased proportion of red cells. There is a considerable amount of pigment deposit in the form of small granules throughout the organ.

Bacteriological Examination:

Cultures were made, at the autopsy, from the duct and substance of the pancreas, on agar, glycerine-agar, and bouillon, and subcultures made at a later stage from the latter, on agar. Growths were got on all the cultures within 24 hours, and of these film preparations were made. It was then found that they were almost pure cultures of Bacillus Coli communis. These bacilli were, in some of the cultures, somewhat smaller than usual and had a tendency to run in pairs, thus resembling diplococci

No other organisms were found.

Fresh smears were also taken from the body of the gland and examined bacteriologically but no organism, other than the Bacillus Coli, could be identified

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In connection with these changes in the pancreas associated with gall-stones, and more especially the presence of fat necrosis, the following case is of

considerable interest.

Case 19. Mrs S—— aged 63. Admitted into The Victoria Infirmary, under care of Dr Parry, on 4th April 1904.

History. Has suffered from periodic pain in the abdomen for the last 3 or 4 years. The pain is situated just about the middle of the right costal margin and extends round the right side, occasionally down towards the umbilicus. She has also been liable to attacks of biliousness, with sickness and vomiting, for many years. She never had jaundice, however, till after an attack three ~~years~~ weeks ago and it remained for 3 days. During her attacks the urine is very dark in colour and the stools inclined to be clay coloured. She has lost flesh recently.

Examination. There is no undue projection of the liver below the costal margin. About the centre of the right infra costal margin a swelling is felt, rounded in shape, firm, and circumscribed, except below where the lower edge cannot be differentiated from the taut muscles - over which pain is felt on pressure. The swelling has the character, and is in the situation of the gall bladder.

A month after admission she had a rigor with sickness and vomiting (the usual herald of her attacks) and about 2 hours later developed a typical attack of biliary colic, which was relieved by morphia.

Operation was performed by Dr Parry on May 16th.

The gall bladder was exposed and opened in the usual way. It was found to be very much atrophied but no stone could be found, either here, or in the ducts.

Cholecystectomy was done and a rubber tube inserted for drainage, also a glass tube was put into the right loin for the same purpose.

The patient was in a very weak state and collapsed, so a saline infusion was given into the basilic vein, but it only acted with temporary benefit, and she died next day.

At the post-mortem examination, the following condition of the organs was found :-

The body was well developed and corpulent. Both legs, especially the left, were pigmented.

Heart. The chambers showed slight hypertrophy and there was some fibroid change in the endocardium, otherwise the organ was healthy.

Lungs. The left lung was adherent throughout by firm fibrous adhesions. On section, both lungs showed a moderate degree of congestion. The bronchi were also congested.

Abdomen. In addition to the marked fatty increase in the parietes, there was also a great increase in the mesenteric, and omental, fat.

Liver was of small size and showed well marked stag-deformity. On section, it showed a slight fatty infiltration with dilatation of the bile ducts, and bile staining.

The Gall bladder was excised & obliterated by sutures.

The common bile duct was traced down to the duodenum and, just before it the duct of Wirsung, there was found in it a gallstone of the size of a small kidney bean. This stone, although filling the duct, was not impacted and could be easily moved.

There was slight haemorrhage in the omentum and mesentery and a slight extravasation and passive congestion around the pancreas

Pancreas showed a marked fatty infiltration and in the head of the organ there was present well marked atrophy of the glandular tissue and small areas of fat necrosis. The duct of Wirsung was somewhat dilated throughout its length and narrowed again just before its termination in the diverticulum of Vater. Santorini's duct was present and well marked, but narrowed as it reached the duodenum its opening into the latter could not be detected. The lesser biliary papilla was not well marked

Spleen showed perisplenitic adhesions. It was enlarged and, on section, showed passive congestion

Kidneys. Both kidneys were embedded in fat and their capsules were adherent. On section, they showed fatty infiltration with atrophy of the cortex and interstitial nephritis

The other organs presented no abnormal characters

Remarks

The post-mortem changes recorded here are of very great interest and not very easily accounted for. As we have already seen, the primary factor in the causation of fat necrosis is supposed to be a retention of pancreatic secretion and this has probably been present in this case since the duct of Wirsung was found dilated. Yet the duct of Santorini was well marked and one would have expected that it would have carried off the pent up secretion

and so saved the pancreas from injury. The cause of the obstruction was probably a gallstone lodging in the diverticulum, which had, before death, passed into the intestine and been lost, since the one which was found at the post mortem was too high up in the duct to cause the changes noted.

The next complication of cholelithiasis to which I wish to draw attention is <u>Carcinoma of the ampulla of Vater</u>. That it is a complication of cholelithiasis, or at least that there is any direct connection between the two, is by no means universally allowed. One would naturally expect that, as gallstones play such an important rôle in the etiology of carcinoma of the gall bladder, and to a less extent in carcinoma of the ducts, ~~that~~ the same relationship would be found in the condition under discussion. Statistics however do not favour this view and Rolleston[32], who only found gall stones in 2 out of 16 cases, feels himself justified in saying that "there is no relationship between gallstones and this form of malignant disease of the biliary system". It cannot, however, be denied that in this disease, as in the case of malignant disease higher up in the duct, the gallstones which have been the initial cause, or may have been the initial cause, of the lesion may have been passed into the bowel + lost, while their effect remains to be seen in the post mortem room, and it is for this reason that I feel quite in order in including this lesion under the heading adopted.

The differentiation of carcinoma (primary) of the ampulla of Vater from other allied conditions is not an easy one, as the area from which it arises is so small. It has to be distinguished from carcinomata arising from the lower end of the common duct, from that arising at the termination of the duct of Wirsung, from carcinomata of the duodenal surface of the papilla, and perhaps from carcinoma of the head of the pancreas. From this latter it can usually be distinguished histologically; carcinoma of the pancreas is spheroidal celled, whereas that of the ampulla is columnar celled. Carcinoma of the termination of Wirsungs duct is very uncommon, as also is that arising from the duodenum at the site of the papilla, and hence the one which gives the most trouble in differentiation is that arising from the lower end of the common duct

According to Graven Moore[33], the differential features appear to consist in the presence of neoplastic change in the mucous lining of the ampulla, with the absence of such change from the lower end of the common bile duct; and a dilatation present of the duct of Wirsung in addition to that of the common bile duct.

I need not enter into details of the structure of the growth, suffice it to say that it is usually a very small one and begins with a thickening of the mucous membrane of the papilla. This induration gradually spreads deeper till it infiltrates the sub-mucous and fibro-muscular coats. The growth may project

from the surface in a polypoidal form causing the biliary papilla to be mainly prominent, but rarely shows any sign of ulceration. Microscopically the growth is found to be a columnar celled carcinoma similar to that found in the bile ducts but from its position it tends to obstruct the opening of the duct of Wirsung into the ampulla; hence we find dilatation of that duct and of its branches and generally this leads to infection with organisms with resulting chronic interstitial pancreatitis. The following case, which I have included in my series, is of special interest as it is probably an example of this rather rare condition.

Case 20 A. McG — aged 54. Admitted into the Victoria Infirmary, under care of Dr Parry, on 11th November 1905.

History. For the last 6 months he has felt himself getting gradually weaker, with loss of appetite and growing lassitude. This continued for a month and then Jaundice set in, beginning slowly and insidiously and without pain. It began in the eyeballs, spread over the face trunk and extremities in turn, and at the end of a fortnight he was quite chrome coloured. In addition, he had intense pruritis all over the body due to the jaundice and this was sometimes so severe that he could not sleep at nights. The Jaundice lessened somewhat after it had been present for about a month but never entirely disappeared. Since then he has got gradually weaker, till it was deemed advisable to have him removed to hospital

Previous History. He had typhus, or typhoid, fever at 10 years of age but has otherwise always been healthy. There is no history of alcoholic excess or syphilis.

Examination. He is a thin spare man with flabby muscles. There is an intense condition of jaundice over his whole body, which is well seen in the conjunctivae and mucous membranes. Pulse is slow but regular. Heart is normal.

Lungs. A few rales can be detected over the left lung and the respiratory murmur is diminished in places.

Urine contains bile but no albumen, sugar or blood.

The faeces are clay coloured.

Abdomen. There is a slight fulness present in the right hypochondriac region and also in the right half of the epigastrium. There is no abdominal pain but tenderness on pressure can be elicited over the region of the gall bladder. There is a feeling of resistance over the right hypochondrium but no swelling can be made out owing to the tense abdominal wall.

On Nov. 16th Operation was performed by Dr. Parry.

The gall bladder was exposed and found to be considerably distended. It was accordingly punctured and the bile drawn off. On further examination the head of the pancreas was found hard, + the obstruction to the duct was located to that region. The gall bladder was therefore stitched to the hepatic flexure of the colon and an opening made between the two. A drainage tube was also inserted into the gall bladder leading to the surface and the wound closed.

After the operation the patient was very collapsed and the temperature became subnormal nor could it be got to rise to normal; and he developed acute gastric catarrh with sickness and vomiting – blood being occasionally present in the vomit. Four days after operation he began to show signs of respiratory difficulty, with mucous rales all over his chest, and he died on November 21st 1905.

The following was the result of the post-mortem examination which was performed the following day:–

The body is well developed but emaciated, with pronounced jaundice all over. Rigor mortis is present.

Thorax. The pericardium is healthy but has bile-stained walls. The heart is of normal size and all its valves and chambers present normal characters, except that the latter are bilestained

Lungs. Both lungs are adherent by a few firm fibrous bands, anteriorly and at the apex. There is slight emphysema of the free margins and, on section, they show passive congestion with slight oedema and congestion of the bronchi.

Abdomen. There is a considerable amount of haemorrhage noted between the layers of the omentum, on the under surface of the stomach & behind the liver and gall-bladder, and some free blood clot in the pelvis. Liver is considerably enlarged, deeply bile stained and on section it shows an increase of the fibrous tissue with a hypertrophy of the walls of the bile ducts, and some dilatation. The common bile duct is dilated

but otherwise normal.

Gall bladder is found implanted into the transverse colon towards the hepatic flexure and the loops of intestine are matted together by chronic peritonitic bands.

Stomach presents normal appearances.

Intestine. The duodenum is healthy but the diverticulum of Vater projects for about 1/4" into its lumen – it is enlarged and very dense in character. The small intestine, from the jejunum downwards, is partially collapsed and slightly congested, the large intestine is somewhat distended and the faecal material contained in it is deficient in bile though not absolutely clay coloured

Spleen is enlarged and shows evidence of a former perisplenitis. On section the organ shows a deep purple colour with moderately firm consistence, and want of definition of the Malpighian bodies, trabeculae, and pulp.

Kidneys are slightly enlarged and on section show pronounced bile staining with a fatty condition of the epithelium, the yellow fatty areas being quite apparent.

Pancreas is of normal size. The duct of Wirsung throughout the entire length of the gland is greatly dilated and knotted. At the head of the gland, where it joins the common bile duct, it is slightly stenosed and surrounded by firm fibrous like tissue which is most pronounced at the diverticulum of Vater itself. There is, in addition, a small area of induration in the head of the pancreas at the part which is behind the duodenum. The rest of

the pancreas, on section, shows healthy pancreatic tissue.

Microscopic sections of the Liver, Heart, Spleen, Kidneys, Pancreas, and Ampulla, made and examined by me, showed the following:-

Liver. The low power shows a spacing out of the hepatic cells due to an increase of connective tissue around the portal radicals, and following the line of the ducts, corresponding more to the monolobular than multilobular cirrhosis. The high power lens reveals a fatty change in a number of the hepatic cells, the fat globules being of small size. The cells are slightly swollen and somewhat cloudy in appearance, many of them containing yellow pigment, while there is also pigment present between the cells. The connective tissue above noted is loosely cellular, for the most part of the elongated spindle type, with very slight indication of new formed bile ducts.

Heart. There is a slight degree of interstitial fibrosis in the wall of the left ventricle, and slight brown atrophy is present in the cells which are otherwise normal.

Kidneys. The glomeruli are regular and uniform and some of them show slight congestion. The convoluted tubules are slightly dilated and contain products of desquamation, with a considerable amount of yellow pigment, and, in some, a little blood. The capillaries are engorged and the interstitial fibrous tissue increased in amount. In the medullary portion of the organ the connective tissue increase is more apparent and a few of the tubules show dilatation amounting almost to cystic change.

Spleen. The stroma is very richly infiltrated with red blood corpuscles, leucocytes, & there is much yellow pigment in the sections

Pancreas. Sections through this organ show an interstitial fibrosis present throughout but the gland cells are fairly healthy, though somewhat diminished in size. There are few islands of Langerhans & these present normal characters.

Ampulla. A section was made through the fibrous area in the head of the pancreas in order to include the passage of the common bile duct, and the duodenal wall. The ampulla was found to consist for the most part of firm fibrous tissue of a somewhat chronic character, with very few nuclei present and even these staining badly. Here and there in this fibrous tissue are groups of epithelial cells of the small columnar variety and arranged in duct-like formation. (See Fig 11) There is also an attempt at cyst formation — large spaces being recognised in which mucoid secretion is present. In addition, there are epithelial clusters irregularly distributed through the muscular wall of the duodenum.

Another section of the head of the pancreas, in the indurated area already described, shows an invasion of new formed tissue, and epithelial cells similar to those found in the ampulla. (See Fig 12) These same cancerous cells are present in the fibrous, and fat, areas beyond the gland tissue.

Remarks.

At first sight one might be inclined to group this case as a cancer of the pancreas spreading to the ampulla, but there are some points which negative this view. In this case the lesion was manifested chiefly in the ampulla, it caused obstruction of both the duct of Wirsung and the common bile

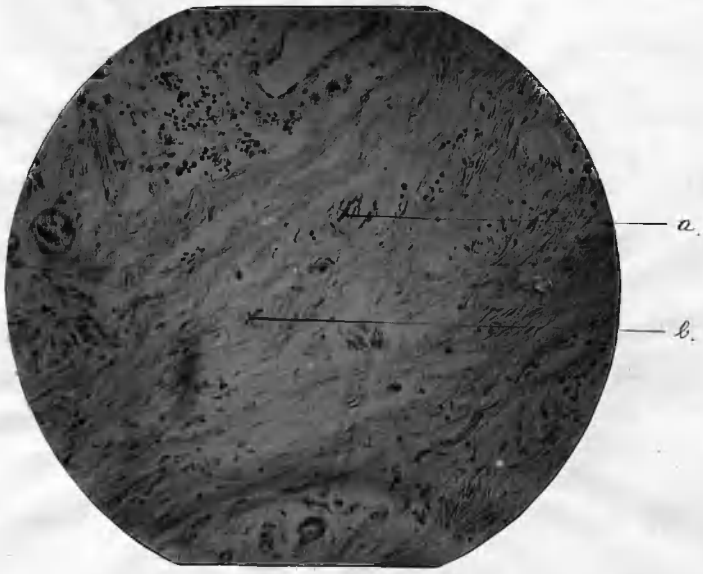

Fig. 11. — Photomicrograph of cancer of the Ampulla of Vater.

a., columnar epithelial cells.

b., connective tissue increase.

Fig. 12. — Photomicro-graph of Secondary cancer in the Pancreas.

a. a. Transitional epithelium approaching ½ spheroidal type.

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duct, and it was subsequently called on microscopic examination; it is, therefore, more than likely that the lesion in the head of the pancreas was secondary to the ampullary cancer.

The next complication of cholelithiasis to which I wish to draw attention is that of Carcinoma of the Pancreas. One notes, as a matter of common observation, the frequent occurrence of these two diseases together but whether there is any direct relationship between the two is quite another matter. Most of the authors whom I have consulted make no mention of cholelithiasis in the etiology of the disease, though gallstones are frequently mentioned as being present in the cases recorded. When we consider how close a relation the head of the pancreas has to the termination of the common bile duct, that the head of the gland is the part most frequently affected in cancer of the organ, and the important relationship which evil have proved to exist between such pancreatic diseases, as chronic interstitial pancreatitis and acute haemorrhagic pancreatitis, and cholelithiasis, a doubt arises in ones mind as to whether the presence of these two diseases is merely a coincidence. The disease itself is so well known and has been so extensively described that I shall not enter into a description of the conditions found, but will content myself with giving an illustrative case where the presence of calculi was complicated by a pancreatic carcinoma.

Case 21 Mrs B — aged 56. Admitted into the Victoria Infirmary, under care of Mr Mayland, on 1st May 1905.

History — She has suffered from pain under the right

costal margin and in the shoulders, for the last 9½ months. This pain was sharp and cutting in character and when it eased a little, it assumed a gnawing character. In addition she has had vague pains in her right breast, shooting through to her back and up to her arm. Later she began to be troubled with nausea and vomiting with a good deal of retching, and this has continued for the last 3 months. The appetite then became affected and she has hardly been able to take any food for the last 3 weeks.

She has always been constipated, though since the sickness and vomiting came on she has been liable to occasional attacks of diarrhoea alternating with the chronic ~~diarrhoea~~ constipation. She has lost flesh rapidly during the last 3 months

Previous Health. She has been liable to attacks of indigestion with vomiting for nearly 10 years — these attacks coming on at intervals of one or two months.

Examination. Her body is thin and emaciated, complexion is sallow and the teeth are bad.

Lungs. There is slight dulness over the lower half of the right lung, and on auscultation here, prolonged expiration is heard and some creaking râles.

Heart. Normal.

Abdomen Over the liver region the slightest touch on the skin causes the patient to cry out with pain. This pain appears to be nervous in its origin as it differs from an apparently real pain which is got on pressure over this region. On percussion

the liver is found much enlarged, particularly the left lobe. The other organs appear normal.

After admission she gradually became weaker, the area of liver dulness increased, while the dulness at the base of the right lung spread upwards. Her breathing became worse and she lapsed into a comatose condition from which she never recovered.

She died on 21st May 1905.

The post-mortem examination was made on the following day. A description of the condition of the organs is herewith related:-

External appearances. A well developed but emaciated body, showing deep jaundice especially in the conjunctivae

Thorax. Heart is rather small in size. All the valves are competent and, with the exception of a small warty vegetation on one of the cusps of the mitral, are healthy.

Lungs. These are rather small in size. The left lung shows emphysema of its free margin and congestion of the bronchi. The right lung is fairly healthy.

Abdomen. The Liver is enlarged, weighing about double that of a normal organ (6 lbs 10 ozs) The left lobe is slightly enlarged and can be felt below the edge of the sternum, but the right lobe is chiefly enlarged, it does not extend so much below the level of the rib margin but the diaphragm is vaulted upwards and the thoracic area encroached upon, so that anteriorly it reaches the level of the 3rd rib. It is studded throughout with tumour nodules which have a typical umbilicated appearance, while on median section the organ has a conglomerate

appearance. The nodules vary in size from a hazel nut to a Victoria plum - central necrosis and haemorrhage can be seen in some.

The Gall-bladder is the seat of a chronic cholecystitis, contains muco-purulent material and two large gall stones. Its wall is much thickened. The common bile duct, where it tunnels the head of the pancreas, is found to be stenosed by a scirrhus mass in that organ around the duct, about 1" in diameter. Wirsungs duct is similarly implicated.

Pancreas is of normal size, pale and indurated, and with the tumour nodule in its head already described

Spleen is of normal size in its substance is a small pale infarct.

Stomach showed evidences of chronic gastric catarrh, and the loops of intestine supplied by the superior mesenteric artery, are in a condition of marked stasis, deep congestion being present and effusion of blood into the lumen.

The other organs presented no unusual appearances.

Sections of the liver, spleen, and pancreas, made and examined by me, gave the following results:-

Liver. The section shows the liver tissue to be infiltrated by dense fibrous tissue with intervening fat spaces, and supporting in its meshwork loose cellular aggregations. The tendancy of these cellular areas is to be distributed in gland-like spaces but the epithelium lining the walls has become detached and free cells are seen in the spaces. These cells present the appearance of spheroidal or flattened epithelium. The connective tissue is denser

in some parts of the section than in others. but on the whole is well formed.

Spleen. The external capsule is thickened and beneath this the superficial layer of the hilus shows congestion and marked increase in pegment. The trabeculae show a considerable degree of thickening. The Malpighian bodies vary in size and show, on minute examination, a degree of hyaline change.

Pancreas. The section, which includes the mucosa of the duodenum, shows the gland tissue of the pancreas to be replaced by a fibrous stroma, irregular in its meshwork, and varying in density. There are numerous fat spaces towards the duodenal aspect. The character of the fibrous tissue is of a chronic nature with very few nuclei. The cells in the meshwork are present in small bundles but are few in number and an attempt at glandular arrangement is evident. The appearances are those of a scirrhus cancer of the head of the pancreas of the alveolar epithelial type.

The last complication of cholelithiasis to which I wish to draw attention is that of <u>Intestinal Obstruction</u>. When a gallstone ulcerates its way from the gall bladder or ducts into the duodenum or colon and comes to lie in the bowel, it may be of sufficient size to cause mechanical obstruction to the onward passage of the intestinal contents. This, however, as one would expect, is not a very common occurrence and hence intestinal obstruction may be classed among the

rarer complications of cholelithiasis. In spite of its rarity quite a number of cases have been recorded, perhaps owing to the fact that being an unusual condition, special attention has been paid to it.

The commonest method of entrance of a gallstone into the intestine is by ulceration from the gallbladder into the duodenum and it is questioned by many, whether it can happen in any other way, since a gallstone which has found its way through the bile passages is not likely to become arrested in the bowel. On the other hand we have the statement of Rokitansky[25] already quoted in which he says that the bile ducts can dilate sufficiently to allow a calculus the size of a hens egg to pass through. Numerous writers have laid emphasis on the fact that a calculus which has passed into the bowel may lie there for a very long time, adding to its bulk by the deposit of phosphates and faecal material, and when finally dislodged may then cause mechanical obstruction. This is probably true but there is an equal chance that if the calculus lies for a time in the bowel it will become disintegrated and finally disappear.

When a calculus in the bowel gives rise to intestinal obstruction it is generally situated at, or near, the ileo-caecal valve, though it may occur anywhere in the small intestine, or even in the large intestine in these rare cases where the stone ulcerates directly into the colon. When this is the case, obstruction is most likely to occur either at the sigmoid flexure, [illegible] to the

ones. Sometimes intestinal obstruction is met with in connection with gallstones which, in themselves, are not sufficiently large to occlude the lumen and we have then other factors which come into play and therefore require consideration. One of these is the irritation in the bowel which an irregular faceted stone may set up. These cases are very liable to be misinterpreted since at the post-mortem examination the stone lies free in the bowel and consequently may be thought to have no connection with the obstruction.

Again if the stone lies for some time in contact with the mucous membrane of the bowel it may set up irritation, with inflammatory swelling and oedema, of the wall of the bowel and this, together with the calculus, produce a complete blockage.

In addition to these — what one might call direct — methods, there are other indirect methods by which gall stones may give rise to intestinal obstruction. As examples of these we might take 1/ paralysis of the bowel due to a local peritonitis in the neighbourhood of the gall bladder — this peritonitis being the direct result of a cholecystitis set up by gallstones. 2/ a violent attack of gall stone colic may give rise to a volvulus of the small intestine 3/ stricture of the intestine may result from bands of peritonitic exudate, the result of a previous peritonitis set up by gall stones.

These conditions are less important than direct occlusion.

Finally gallstones in the intestine, whether impacted or not, may, by their mechanical action, give rise to

irritation, ulceration, and perhaps gangrene, of the wall of the bowel and may then escape by perforation either into the peritoneum or externally The following case of intestinal obstruction as the result of gall stones, contains some points of considerable interest :-

Case 22 Mrs Mc N——. aged 54. Admitted into the Victoria Infirmary, under care of Mr Mayland, on 14th January 1901.

History. Eight days ago she began to suffer from severe pain over the abdomen specially marked over the Epigastrium, with a constant tendency to retching and with a burning pain in the throat. She also had a sense of pain and fulness over the stomach after taking food. On the day previous to admission she began to vomit some very offensive material and on the morning of her admission the vomiting became stercoraceous. The bowels were constipated for 5 days but on 13th Jany an enema was given which brought away faeces and flatus.

Previous History. Has been troubled with indigestion for many years and 12 months ago she had some 'liver' trouble, with pain in the right hypochondrium.

Examination. She looks very ill and exceedingly weak Breath is very foul, tongue is dry and coated with a brown fur. The rectal temperature is 100·4° F and the pulse numbers 128 per minute.

The heart and lungs appear normal.

The abdomen is uniformly distended, markedly

resistant and tender all over, the tenderness being most marked over the epigastrium

Before operation the stomach was washed out and some faeculent material brought away.

Operation was performed by Mr Mayland on 14th Jany 1901.

A median supra-umbilical laparotomy was done and the transverse colon, which presented, was found contracted and empty. On exploration the upper part of the jejunum was noted to be greatly distended, so enterotomy was done here and the distended portion of the gut emptied On tracing the bowel downwards for a short distance a gall stone was found impacted in the gut, being prevented from passing downwards owing to a small projection having caught in the mucous membrane. This stone was removed.

A few inches higher up a small circular sloughing patch was noted in the wall of the bowel, evidently due to pressure from the projection which was on the calculus. The serous coat of the bowel was stitched over this area.

The rest of the intestine was examined there was no sign of any peritonitis, so the operation was finished in the usual manner. During the operation the patient was very collapsed and continually vomiting mouthfuls of fluid, so when it was finished the stomach was washed out. The pulse now became very feeble the heart's action weak, the patient died immediately after reaching the ward.

Actual size of gall stone removed by operation, with its projection.

The post mortem examination was performed next day and gave the following results -

External Appearances. It is a well developed + corpulent body.

Thorax. The heart is slightly enlarged and the subpericardial fat is increased in amount. The left ventricle wall is hypertrophied but there are no valvular lesions.

Lungs. The left lung is adherent to the chest wall and shows slight emphysema of its edges while the bronchi are congested.

Abdomen. The Liver is slightly enlarged and on section it presents a fatty appearance, with dilatation of the bile ducts. The gallbladder is found to be non-functional and is filled by a large stone which blocks the duct. It opens into the duodenum, ½" from the pylorus, by a large opening which admits the tip of the little finger and the finger passes only a short distance (⅛") from duodenum into gall bladder. Around the opening, the duodenum is congested and slightly ulcerated.

Intestines. The duodenum, jejunum, and ileum, are distended and intensely congested. In the upper part of the ileum there is found an ulcerated condition of the mucous coat of the bowel and a small perforation of the wall has been closed by sutures. At the site of the perforation there has evidently been the lodging of a gallstone and for a distance of 6-8 inches from this site there are, at intervals, small ragged ulcers of the mucous coat, with congestion around the ulcers, evidently caused by the passage of the gall stone. For a distance of about 2½ feet at the upper part of the ileum the bowel

presents congestion both on its serous and mucous surfaces, and there is slight ruffling of the serous coat and adhesion of loops together, but no evident peritonitis. Below the obstruction the lower part of the ileum is much collapsed — the collapse extending to the ileo-caecal valve. The caecum and colon contain well formed faecal matter and the walls are healthy. The other organs presented no abnormal features.

Table of cases.

	Name and Age	Under care of	Clinical Summary	Pathological Summary
1.	Mrs M— . 29.	Mr Maylard	Several attacks of biliary colic with jaundice	Cholecystetis. Numerous gallstones in gall bladder. Head of pancreas enlarged + indurated
2.	Mrs F— . 39.	Mr Maylard	Three attacks of biliary colic. The last accompanied by sickness + vomiting	Cholecystitis. Enlarged and thickened gall bladder. Gallstone blocking cystic duct.
3.	Mrs B— 51.	Mr Maylard	attacks of biliary colic, with jaundice coming on after 4th attack	Cholecystitis. Single stone present. Head of pancreas enlarged and indurated.
4.	Mrs McC— 52.	Dr Parry.	attacks of typical biliary colic for 15 years. Operation - cholecystotomy Stone present in gall bladder + common duct.	Chronic cholecystitis. Hepatic ducts contain bile stained pus. Mucous coat of common duct shows pressure atrophy.
5.	Mrs T— . 75.	Mr Maylard	While under treatment for an accident developed acute abdominal symptoms.	Perforation of gall bladder - which was thin walled and distended
6	Mrs S — . 46	Dr Parry	Acute abdominal symptoms with rigors. Later heart condition supervened	Gall stone ulcerating it way into duodenum.
7.	Mrs D — . 70	Dr Parry	Deeply jaundiced and emaciated. Large mass felt in region of gall bladder.	Common duct contains 2 stones. Acute cholecystitis Carcinoma of gall bladder and fistula into duodenum. Secondary cancer of liver
8.	Mrs McB — 50.	Mr Maylard	Pain over right side of abdomen and stomach, with swelling and tenderness.	Carcinoma of gall bladder with secondary involvement of liver.
9.	Mrs P— . 44	Dr Parry	Pain vomiting and jaundice becoming gradually worse	Carcinoma of cystic duct at its junction with common duct. Secondary nodule in omentum.
10	J. M— . 57.	Dr Parry.	Acute abdominal symptoms	Perforation of cystic duct, abscess cavity in right lobe of liver
11.	Mrs G— . 44.	Dr Parry	Abdominal pain becoming acute, with sickness and vomiting.	Large stone blocking cystic duct. Abscess cavity in left lobe of liver containing 4 stones

Table of cases - cont^{d}

Name and Age.	Under care of	Clinical Summary	Pathological Summary
12. F. McD— . 52	Dr Parry.	Seizures of biliary colic on several occasions. Operation cholecystotomy - no stones	Granular congested surface on gall bladder and diverticulum. Acute laryngitis (ulcerative).
13. Mrs S— . 32	Dr Parry	Acute abdominal symptoms	Common bile duct buried in adhesions. Gall bladder filled with stones.
14. W. G— . 80	Dr Napier	Pain in abdomen and vomiting. Later jaundice which progressively deepens.	Carcinoma of common bile duct.
15. A. G— 49.	Dr Duncan.	Obstructive jaundice which becomes gradually more pronounced.	Carcinoma of hepatic and common bile ducts.
16. Mrs F— 64.	Dr Parry	During convalescence from operation for hernia took biliary colic with rigors.	Gall stone impacted near diverticulum of Vater.
17. R. C— . 46.	Mr Maylard.	Operation for ventral hernia No clinical symptoms	Impacted stone at diverticulum of Vater. Pancreas congested.
18. Mrs A— . 25	Mr Maylard	Acute abdominal symptoms.	Acute haemorrhagic pancreatitis.
19. Mrs S— . 63.	Dr Parry	Symptoms of biliary colic for many years.	Gallstone near diverticulum of Vater. Parapancreatic fat necrosis.
20. A. McG— . 54.	Dr Parry.	Progressive loss of flesh and strength with gradually deepening jaundice	Carcinoma of Ampulla of Vater. Secondary growth in pancreas.
21. Mrs H— . 56	Mr Maylard.	Pain over abdomen, progressive loss of weight and increasing weakness	Carcinoma of Head of Pancreas with secondary nodules in liver.
22. Mrs McN— . 54.	Mr Maylard.	Symptoms of acute intestinal obstruction	Acute intestinal obstruction from gall stone in intestine

Conclusion.

The table of cases, which has just been given, illustrates the complications which befall the gall stone, in an anatomical order. Examples of certain complications have not been demonstrated on account of a lack of illustrative cases.
From those dealt with, however, there emerges two features, namely the possibility of grouping according to the prognosis involved, or as to the nature of the lesion, whether simple or malignant.
Three of the cases were examples of a cholecystitis accompanying gall stones and were operated on with a successful issue. In such cases the operation of cholecystotomy is usually attended by a brilliant result and the prognosis is a favourable one.
Twelve cases were of a non-malignant but fatal character and these showed the variety of complications which might be met with in simple gall stone disease. The first group of such were due to profound septic conditions, e.g. hepatic abscess, suppurative cholangitis, acute ulcerative endocarditis etc. The second group were those in which the lesion was dependent more on the mechanical factor e.g acute intestinal obstruction, obliteration of the common bile duct by adhesions, acute haemorrhagic pancreatitis following blockage of the diverticulum of Vater etc. In these cases the question of treatment was an important one and depended entirely on the nature

of the lesion in each instance. Whether surgical interference was resorted to, or not — and it is evident that such was the only possible course - it is quite apparent from the last of the cases that they would still have been followed by the same fatal result.
The seven cases of a malignant nature were examples of cancer in the gall bladder, cystic duct, common duct, ampulla of Vater, + head of pancreas, and presented the features of greater chronicity of the disease, an absence of any localizing character, and a history of chronic biliary obstruction. The malignant cases, especially, presented a most hopeless class as far as prognosis and treatment was concerned.
Into the details of operative treatment in any of the cases I have made no attempt to enter as such presented large and complex issues.
In connection with the malignant cases, however, there was shown an interesting feature in the histology of the cancers, namely a tendency to a metaplasia of epithelium (the departure of the columnar celled cancer in the direction of transitional and squamous celled types).
There remains to be demonstrated the value of recent research in connection with this subject. The case of acute haemorrhagic pancreatitis is one of a lesion which formerly presented an obscure etiology, but now, in the light of Opie's work, a more feasible interpretation arises, and if his conclusions can be demonstrated as correct, it affords a reasonable solution of the origin of this disease.

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In addition to the above, a number of text-books and articles, bearing on this subject, were consulted, but no attempt has been made to supply a full bibliography further than the above references which are quoted in the text.