A CASE OF MULTILOCULAR CYSTIC DISEASE (CYSTADENOMA) OF THE PANCREAS:

[WITH SPECIAL PLATE.]

By ERNEST C. HADLEY, M.D., B.S.LOND., F.R.C.S.E.,

RESIDENT SURGEON TO THE BIRMINGHAM GENERAL DISPENSARY;
LATE HOUSE-SURGEON TO THE GENERAL HOSPITAL, BIRMINGHAM;
HAM; RESIDENT MEDICAL AND SURGICAL OFFICER TO THE
GUEST HOSPITAL, DUDLEY; SENIOR HOUSE-SURGEON TO
THE STAFFORDSHIRE GENERAL INFIRMARY, ETC.

THE first part of this remarkable case was published thirteen years ago in this JOURNAL (1901, vol. ii, p. 1160). The patient was completely lost sight of until July 19th, 1910, when quite by chance I was called in to attend her at her own home. The attendance lasted until her death on March 30th, 1911.

I am much indebted to Mr. George Heaton for his kindness in allowing me to make use of the notes which I made upon this case when acting as his house-surgeon; and to Dr. Mackey and Mr. B. J. Ward for their assistance in cutting the sections. My thanks are also due to Professor Leith for granting me permission to photograph the tumour, which is preserved in the pathological museum of the Birmingham University (Spec. 200), and for the photomicrographs which were taken by him in the pathological laboratory of the university:

I. D., aged 27, single, was admitted to the General Hospital, Birmingham, on October 20th, 1900, with an abdominal tumour situated above and to the left side of the umbilicus, but below the stomach. The patient had noticed the lump for five or six months only; her attention was drawn to it by a little pain she had experienced on exertion during this time. As a child she was never active as other children, owing to pain in the back, which any extra exercise invariably brought on.

Since leaving school she had been a nursemaid, and later and up to the time of her admission worked at a pen factory. Upon admission her general health was good, and with the exception of a little habitual constipation the digestive organs were performing their functions normally. The stools were normal. The urine, with the exception of a faint haze of albumin, was always normal and free from sugar.

The bladder and ureteral orifices were found to be normal on cystoscopic examination, and urine was seen to spurt normally from both orifices. The abdominal tumour was globular, freely movable, and gave the examining hand the impression that it was a tense cyst. It did not move with the respiratory movements. The spleen could be mapped out and was found to be in its normal position and to be unconnected with the tumour. Examined bimanually from the left loin to the abdominal wall, the tumour could be felt projecting backwards into the loin. It could be felt to fill the abdominal cavity between the two hands and ballottement could be obtained. A provisional diagnosis of hydronephrosis was made after several consultations.

On November 8th, 1900, Mr. Heaton operated by first exposing the left kidney through the usual lumbar incision. With the exception of a few small cysts on the surface of the kidney, such as are seen in cases of chronic interstitial nephritis, the kidney, its pelvis, and the upper end of the ureter were normal. The tumour, however, could now be felt to be in front of the kidney and quite distinct from it and to pass to the right across the abdomen; the kidney was replaced and the lumbar wound sutured. Mr. Heaton then opened the abdomen in the left linea semilunaris over the most prominent part of the tumour, the great omentum was pressed forward by the tumour, which projected between the stomach and the transverse colon. A large cyst first came into view. It was approached through the great omentum and tapped. One and a half pints of dark reddish-brown fluid were withdrawn. It was intended to stitch the edges of the opened cyst to the abdominal wound, but, on further examination, the tumour was found to be much more extensive and to be composed of a multitude of smaller cysts congregated to form a large lobulated tumour extending to the right. It shelled out quite easily until the duodenum was

reached. The pancreas was therefore ligated at its neck; the head, although very cystic, was left behind for various reasons.

After the operation the patient was rather collapsed—but, with the exception of a delay in convalescence caused by a portion of the abdominal wound bursting open ten days after the operation, which necessitated the patient being again anaesthetized for the wound to be resutured—recovery was uninterrupted. After the operation digestion remained good, and food was well assimilated. The urine remained free from sugar. On January 5th, 1901, she was sent to a convalescent home.

The tumour (Figs. 1 and 2) removed consisted of the whole of the body and tail of the pancreas, and measured 10 in. by 7 in. It consisted in the main of a large number of cysts varying in size, separated from one another by septa of fibrous tissue and a varying amount of apparently normal pancreatic tissue. The cysts were larger at the tail end than at the head end of the organ. The large cyst, which gave rise to most of the physical signs, was at the extreme tail end. It occupied the whole thickness of the tumour in this situation. The fluid from this large cyst contained altered blood and a large quantity of albumin. It had no amylolytic or proteolytic properties. It was alkaline in reaction. The fluid contained in the smaller cysts was colourless and watery.

From January, 1901, until June 6th, 1910, this patient was able to work continuously at her trade as overlooker in a large steel pen factory in Birmingham. During that time she had needed practically no medical attendance.

In July, 1910, when she again came under my care, she

was almost completely confined to bed. She complained chiefly of gradual loss of power in her hands and arms, with numbness and tingling of the fingers. It was on account of these symptoms that she had been compelled to leave her work, as she was unable to pick up the pen nibs. The muscles of the body generally, and especially of the hands and arms, were much wasted. She had a large tumour in the abdomen situated immediately above and extending to the right of the umbilicus. The tumour was recognized as the head and a portion of the neck of the pancreas in a state of cystic degeneration. It formed a prominent mass and displaced the intestines downwards and into the left iliac

region of the abdomen. The tumour, according to the patient, had been getting gradually larger for the last two or three years, but much more rapidly during the last two or three months. It was painless, well defined, and slightly movable. A large cyst could be recognized to the left of the tumour, and numerous small tense cysts studded all over the rest of it.

The skin of the chest, abdomen, and thighs was curiously pigmented in irregular patches of a dark brown colour, producing a piebald appearance. Except that every two or three weeks she had what she called "bilious attacks," the digestive functions were good. These attacks were "bouts" of uncontrollable vomiting; they were unaccompanied by pain or jaundice, and tended to recur more frequently towards the last. The urine, frequently tested, invariably contained a faint haze of albumin, a few granular and hyaline casts, but never any blood or sugar (Fehling and phenyl-hydrazine tests were used for sugar). The Cammidge reaction was positive throughout this part of her illness.

The course of her illness was, at first, one of rapidly advancing peripheral neuritis, with rapid wasting of the muscles, most marked in the upper extremities. One month later she had very little sensation in her arms or legs. The deep and superficial reflexes were abolished. Soon after this rigidity followed by contractures commenced in her hands. The fingers became flexed at the interphalangeal joints, and over-extended at the metacarpo-phalangeal joints. The wrist joints also became over-extended.

DESCRIPTION OF SPECIAL PLATE.

Fig. 1.—The body and tail of the pancreas removed by operation, front view.

Fig. 2.—The same, viewed from behind, showing, A, the large cyst and some of the smaller ones laid open.

Fig. 3.—The head and neck of the pancreas, anterior view. A, Duodenum; B, gall bladder; C, large cyst at the neck end.

Fig. 4.—The same, posterior view. A, Duodenum; B, gall bladder; C, the large cyst which represents the stump of the neck; D, the superior mesenteric artery and vein.

Fig. 5.—The right kidney bisected, showing hypernephroma. Note the cystic appearance of the tumour; the probe passes from the pelvis of the kidney into the ureter.

Fig. 6.—Photomicrograph of pancreatic tumour, showing the proliferation of cysts to form larger multilocular ones.

Fig. 7.—Section of pancreatic tumour showing a portion of a large cyst with its epithelial lining. The section also gives some idea of the great thickness of fibrous tissue which surrounds the larger cysts. In the centre of the field is a portion of zymogenous tissue undergoing atrophy, followed by hyperplasia of the fibrous tissue between its lobules. Note that there is no sign of inflammation. The pancreatic tissue in the lower part of the field is normal.

Fig. 8.—Section of same, high power, showing the large columnar cells which line the glandular tubules in commencing cyst formation.

ERNEST C. HADLEY: MULTILOCULAR CYSTIC DISEASE (CYSTADENOMA)
OF THE PANCREAS.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

FIG. 7.

FIG. 8.

Towards the end of November, 1910, her condition resembled an advanced case of progressive muscular atrophy with contractures. The right leg was flexed at the hip and knee joints, and could not be voluntarily or forcibly straightened; any attempt to do so caused intense pain. A month later the left leg also became contracted; the knee and hip joints became flexed. There was no period of relaxation from these contractures. A bed sore formed over the sacrum in spite of diligent and careful nursing.

In the beginning of 1911 the muscular wasting had become extreme. Both legs were immovably contracted, and both hands clawed (*main en griffe*). There was still a little voluntary movement possible in the arms, but complete loss of co-ordination. She had been quite unable to feed herself or move herself in bed for some time. There was never any jaundice. Sahli's sign was present. The bowels only moved with aperients, and later, as all drugs were vomited, only after enemata.

During the last two months of life mucous casts were passed in the stools, which were otherwise normal. Liquid food appeared to be well digested; at all events, no undigested fat or other material were seen in the dejecta. During the last few weeks of her illness there was incontinence of urine and faeces.

At the time of her death, on March 30th, 1911, no musculature could be felt; she had literally wasted to a skeleton. There was only partial relaxation of the contractures at death. Her mental condition remained clear until the end.

Post Mortem.

The abdominal organs were found to be healthy, with the exceptions noted.

The liver was undergoing fatty degeneration; the gall bladder was healthy and empty; the cystic duct was patent. The common bile duct was patent. Its lumen throughout its whole length was large and its walls somewhat thickened. It opened along with the atrophied remains of the duct of Wirsung into the ampulla of Vater. The diameter of the common bile duct at the ampulla was nearly $\frac{1}{4}$ in., whereas that of the duct of Wirsung was scarcely $\frac{1}{8}$ in. A probe could be passed along the duct of Wirsung from the duodenum for $1\frac{1}{2}$ in. only into the pancreas; the continuation of the duct then became too fine to admit of anything being passed along it. No trace of a duct of Santorini could be found.

The suprarenal capsules were normal in size and healthy; no microscopical changes could be found in them.

Kidneys.—The urine removed from the bladder reduced Fehling's solution to the yellow oxide of copper. The left kidney, with the exception of six or seven small vesicles projecting from the surface, as seen at the time of the operation in 1900, was healthy. Several small cysts such as are seen in cases of chronic interstitial nephritis projected from the surface of the right kidney. A tumour projected from its posterior surface in the form of a large circular plaque $2\frac{1}{2}$ in. in diameter. It was situated nearer to the hilum than to the outer border of the kidney.

The tumour was completely covered by the capsule of the kidney. Upon bisection of the kidney (Fig. 5) the tumour was seen to be localized, and to be surrounded by a well-defined capsule, which separated it from the kidney substance. It had, as it were, formed a bed for itself by thinning the middle portion of the kidney, leaving the poles unharmed. The tumour was yellowish, and unlike kidney tissue in consistence; minute spaces looking like small cysts could be seen throughout the section. Microscopically the tumour had all the features of a hypernephroma. There were no signs of malignancy.

The pancreas was removed *en masse* with the duodenum and gall bladder attached (Figs. 3 and 4). The specimen measured 8 in. in length by 6 in. in breadth at its widest part. The greatest circumference of the head was 11 in. The stump of the neck—all, in fact, to the left of the groove containing the superior mesenteric artery and vein (Fig. 4, D)—was converted into a large unilocular cyst. It had smooth walls and did not communicate with any of the other cysts. It contained 15 oz. of reddish-brown opaque fluid with slight amyloidal, but no proteolytic properties. It contained much albumin and old extravasated blood. The head of the organ, that is, all to the right of and in front of the groove containing the

mesenteric vessels, was converted into a multitude of small cysts separated from one another by septa of fibrous tissue and some pancreatic tissue. The largest of these cysts varied from the size of a walnut to that of a hazel nut. They were multilocular, each being composed of an aggregation of smaller cysts separated by perforated septa. They contained an opalescent greenish coloured fluid. Most of the cysts, however, were no larger than a pea or bean; they were unilocular and contained a clear watery alkaline albuminous fluid. No communication could be found either between the individual cysts or between them and the ducts of the pancreas. The head of the pancreas encircled the duodenum for about half its circumference, but did not compress it. There was every evidence of degeneration having advanced from the tail towards the head end; the cysts were larger towards the tail end, and the least altered pancreatic tissue was found between the head of the pancreas and the duodenum.

Microscopically there was an abundance of normal zymogenous pancreatic tissue situated between the cysts. There was no increase, as a rule, of fibrous tissue between its lobules or any sign of inflammation. In parts of the section some of the acini seemed to be opening up. A feature of the sections was the absence of the groups of cells known as the "islets of Langerhans." The fibrous tissue distribution followed and surrounded the ducts and vessels and formed a dense wall to the cysts of the neoplasm (Fig. 7). In the commencing cysts the epithelium was high and columnar of goblet form (Fig. 8). It much resembled the epithelium which lines the cysts of ovarian cyst adenomata.

In the larger cysts the lining cells were lower though still columnar. New groups of glandular tissue in the form of tubular canals could be seen in some parts of the sections adjacent to or in some cases projecting into already formed cysts (Fig. 6). Nothing to indicate malignancy could be seen in any of the sections.

REMARKS.

This case is, I believe, the only recorded case of massive multilocular cystic disease of the pancreas occurring in the British Isles. A few only are recorded in foreign journals. The special interest of the case lies in the speculation which naturally arises as to the pathology of the pancreatic tumour. It has undoubtedly a striking resemblance to the more common cystadenomata of the ovary, and was in all probability a benign multilocular proliferating cystadenoma of the pancreas.

Cases of this condition are recorded by Bozeman and Garrigues,¹ Riedel,² Paltuf and Selzer,³ Kühnast,⁴ Martin,⁵ Gussenbauer,⁶ Thiroloix and du Pasquier,⁷ Cibert and Poncet,⁸ Fitz,⁹ Dunning,¹⁰ Körte and Munzer,¹¹ Ransohoff,¹² and Vankreef.¹³ Cumston¹⁴ says that he has only been able to find records of fifteen instances of cystadenoma of the pancreas. Hartmann¹⁵ records a similar case, which was probably a cystic epithelioma; and Pye-Smith¹⁶ one which was described as a case of congenital cystic disease of the pancreas.

The formation of cysts could be traced microscopically in this case from a glandular neoformation, the cells of which were arranged in columns enclosing a lumen. By the enlargement of this lumen, probably by the pouring out of a secretion from the large columnar cells of goblet form, a cyst was formed. New cysts were formed by the proliferation of certain of the cells in the walls of this cyst to form fresh glandular spaces. By the bursting of these last formed cysts or others adjacent into the original one, a multilocular cyst would be formed. This is well shown in the photomicrograph (Fig. 6).

The subsequent growth of the cysts may have been mainly due to secretion and desquamation from their lining membrane, or in the case of the two large ones described to extravasation of blood into them.

The origin of the cells of the neoplasm must be purely speculative. It must suffice merely to suggest their origin from:

1. Certain primordial cells amongst (a) the cells lining the small ducts; (b) the specialized zymogenous cells of the islets of Langerhans, or the ordinary zymogenous cells, which are, according to Dale,¹⁷ Goodall and Earle,¹⁸ and Vincent,¹⁹ interchangeable under certain conditions.

2. Inclusion of fetal remains—for example, the Wolffian body (see Allbutt and Rolleston²⁰ and Dunning's case¹⁰).

3. Adrenal rests^{26 27} originally or by metastasis from the hypernephroma which was present. A hypernephroma is itself a distinctly rare tumour. Its presence may have been a pure coincidence. Doran,²⁰ Grafenberg,²¹ Guthrie and d'Este Emery,²² and Monsarrat²³ record cases of metastasis from hypernephromata. Lubarsch²⁴ found metastasis 20 times out of 29 cases in various organs, including the pancreas.

The microscopical findings do not accord with the suggestion that the cysts arose as retention cysts, caused by obstruction to the outflow from the small ducts, as (a) by a pathological secretion from the zymogenous cells, analogous to the ascribed cause of congenital cystic disease of the kidney, or (b) by chronic interstitial pancreatitis (see Robson and Moynihan²⁵). For it should be noted that in interstitial pancreatitis the islets of Langerhans usually escape atrophy, at all events until a very late stage (Robson²⁷), and there was no inflammatory process.

A feature of the case was the complete transformation of the pancreas into cysts. It would have been quite impossible to have enucleated the tumour or any part of it from the pancreas, as appears to have been done in some of the recorded cases (Dunning's case¹⁰).

Briefly, from a clinical point of view, the case was of interest because it showed the effect upon the economy of gradual loss of function of the pancreas in an otherwise healthy person, the outstanding features of the terminal part of the illness being the gradual wasting²⁶ of the body, especially of the muscles, unto death and the warding off of glycosuria until the end. The urine removed from the bladder after death contained sugar. It had always been free from it during life.

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Hospital, during the last three and a half years, in the practice of all the surgeons, 190 cases have been admitted. If strangulated external hernias of all kinds are excluded the number falls to 83. These figures exclude all cases in which the large intestine was obstructed, a fairly numerous class. The mortality in all cases of acute obstruction when they receive proper surgical treatment is given by Treves¹ as 50 per cent. The more recent statistics of Elsberg² give 30 to 40 per cent. as the correct mortality. In the herewith collected cases it was 19 per cent., but if the cases of external hernia are not considered, it rises to 24 per cent.

THE CAUSES OF OBSTRUCTION.

The following table shows the conditions leading to obstruction which were met with, the number of cases in which gut was found gangrenous, and the mortality in the several classes:

	No. of Cases.	Gangrenous Gut.	Deaths.
Inguinal hernia ...	50	6	5
Femoral hernia ...	46	11	7
Umbilical hernia ...	7	1	3
Ventral hernia ...	3	1	1
Obturator hernia ...	1	0	0
Intussusception ...	35	4	6
Adhesions not elongated into bands ...	22	4*	5
Bands ...	14	1	2
Meckel's diverticulum ...	3	0	0
Gall stones ...	1	0	1
Volvulus ...	1	1	1
Stricture ...	1	0	1
Hole in mesentery ...	1	0	0
Pressure by an abscess ...	1	0	1
Mesenteric thrombosis ...	2	2	2
Cause undetermined... ..	2	0	2
Total	190	31	37

* Actual gangrene was not present in these four cases, but the gut was so damaged that resection was deemed necessary.

External Hernia.

Under this heading few remarks need be made except to call attention to the fact that a femoral hernia, if not cured by operation, is more likely to become strangulated than an inguinal hernia. In spite of the much greater relative frequency of inguinal hernia, the number of strangulated cases dealt with is only slightly greater than the number of strangulated femoral hernias. This is because of the unyielding character of the margin of the crural ring. In inguinal hernias obstruction is most often caused by fibrosis round the internal ring at the upper extremity of the canal.

The number of cases of strangulated umbilical hernia is not large, but only those cases which had small intestine in the sac are included. The omentum is the first structure to enter into the sac of an umbilical hernia, then this drags in the transverse colon. Usually only after this has happened does small gut enter the sac.

Of the 3 ventral hernias 2 occurred through old laparotomy scars; the other one was in the middle line below the umbilicus. No operation had been performed, but there was some divarication of the recti muscles. The aperture leading into the abdomen was small and had hard margins. A loop of small intestine was strangulated to the point of gangrene.

Adhesions.

Next to external hernia and intussusception as a frequent cause of obstruction of the small gut, comes local peritonitis leading to the formation of adhesions. In the table the cases of obstruction due to adhesions which had not elongated to form bands are placed separately. Where definite bands were present, the cases have been grouped with cases of obstruction due to bands of other origin than

A Lecture

ON

ACUTE OBSTRUCTION OF THE SMALL INTESTINE.

DELIVERED AT THE MEDICAL GRADUATES' COLLEGE AND POLYCLINIC

By CHARLES A. PANNETT, F.R.C.S., M.D.,

SUPERNUMERARY OUT-PATIENT SURGEON TO ST. MARY'S HOSPITAL; ASSISTANT SURGEON, ROYAL FREE HOSPITAL.

Few serious abdominal conditions present more difficulties in diagnosis and treatment than obstruction of the small gut. Yet diagnosis must be early and treatment prompt if the conduct of the case is to lead to a successful issue. In the beginning signs and symptoms may be inconclusive; there is only a probability of obstruction being present. To wait until this probability becomes a certainty will, in many instances, cost the victim his life. If the possibility of intestinal obstruction were more obtrusive in the practitioner's mind when confronted with the complaint of abdominal pain, early diagnosis would be arrived at more often. But he can scarcely give the disease a greater prominence in his mentality because of the rarity of the condition in comparison with the multitude of other diseases with which he has to cope. In a hospital where the number of acute abdominal cases admitted is large, where such cases concentrate from an extensive surrounding district and from the practice of many men, the numbers do not reach a high figure. At St. Mary's