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HISTORY OF CANADIAN SURGERY

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ON THE AFTERNOON OF THURSDAY, March 26, 1885, at a place where the road running between Fort Carlton and Duck Lake crossed a coulee, a small party of Mounted Police and volunteers under Inspector Crozier faced a hostile band of Métis led by Gabriel Dumont, Louis Riel's chief lieutenant. Between the opposing lines the Inspector had opened a parley with some of the rebels advancing under a flag of truce when suddenly rifle shots cracked. Immediately the firing became general and half an hour later 18 lifeless bodies lay in the blood-stained snow, and many others had fallen wounded. Thus was signalized the beginning of the actual fighting in the North West Rebellion, but the shots that opened the Battle of Duck Lake also marked the passing of the old West. When the fighting ended a few weeks later, the native population had forever lost all chance of regaining possession of the prairies, the tide of immigration was ready to set in, the West had come of age.

Only an average lifetime separates us from that day, yet in the history of the West there is crammed into this span a development so remarkable that few parallels exist. There are some still with us whose lives have covered the full complement of those years, and there are many more whose passing is recent enough to leave their memory still fresh and green. One of the latter is Frank Hamilton Mewburn, whose life and work is woven into the very fabric of present-day Alberta.

On that historic March day, a young man of 27, he was in Winnipeg, then a city of about 20,000, where he was the first house surgeon ever appointed to the Winnipeg General Hospital. Ancestral influences had made his path into medicine almost inevitable and the record is one that can

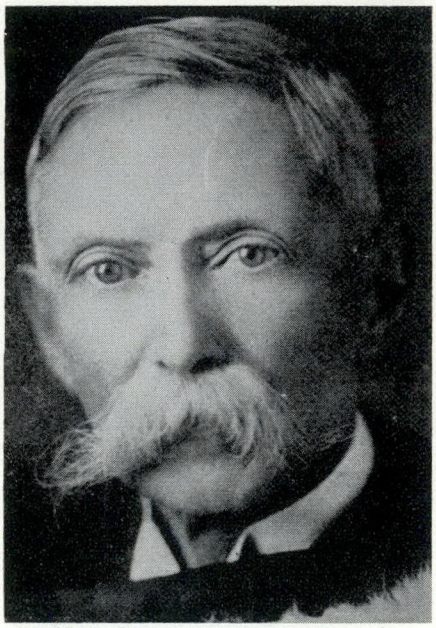

Fig. 1.—Frank Hamilton Mewburn.

have few equals. On January 8, 1765, James Mewburn, yeoman of Durham, England, apprenticed his 17 year old son, Francis, to Thomas Hornby for seven years. The latter undertook to ". . . find allow and provide to and for the said Francis Mewburn Good wholesome and sufficient Meat Drink and Lodging fit and convenient for him and also teach and instruct the said Francis Mewburn . . . in the Art Science and Mystery of an Apothecary . . .". On his part Francis agreed to serve his master faithfully and ". . . not to play at Cards Dice or any unlawful Game or Games or contract Matrimony."* The apprenticeship served, Francis practised in Whitby and, absolved from the injunction against matrimony, started a line of medical Mewburns that is now—two centuries later—in its sixth generation in the person of Dr. Robert H. Mewburn of Vancouver.

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*Professor of Anatomy, University of Alberta, Edmonton.

*From a photostat of the Indenture Agreement in the possession of the Mewburn family.

Fig. 2.—Interns at the Montreal General Hospital, 1882. *Seated:* John A. Macdonald and James Bell; *standing:* A. Henderson and F. H. Mewburn.

Francis's second son, John, acquired his medical training in London and when he obtained his M.R.C.S. he was "honourably noticed" by Sir Astley Cooper.[1] However, stirred by the call of a new country, he came to Upper Canada in 1832 and practised first at York (Toronto); then he moved to Stamford where he remained for the rest of his life. It is said of him that he was noted for his medical skill, and for being exceptionally warm-hearted, impulsive, fearless, and occasionally profane—a remarkable foreshadowing of his grandson.

When John Mewburn came to Canada he had a 15 year old boy, Francis Clarke Mewburn, who apprenticed himself to his father for five years, after which he took a year's course of lectures in medicine in Philadelphia. On the strength of this training he was admitted to licensure of the Medical Board of Upper Canada in 1838, and he practised in Weston till 1845 when he moved to Drummondville (Niagara Falls). He has left a short but vivid account of the status of medical practice in early Toronto.[1] His reputation must have been outstanding because he was awarded an honorary Doctorate in Medicine by the University of Buffalo. A very close friend was Frank Hastings Hamilton, the first Professor of Surgery at that institution, and it was no coincidence that when the youngest of the seven children was born in 1858 the boy was named Frank Hamilton Mewburn. With such a background he was sealed of medicine from birth.

McGill in the eighteen-seventies was outstanding on this continent for its School of Medicine, numbering among its distinguished staff the youthful Osler. This was where Frank Mewburn went for his medical training. He told us that early in his course he was very discouraged and ready to quit, when Osler had a talk with him restoring his courage and determination. No doubt this intimate encounter with a great teacher had a lasting influence; in any event, it laid the foundation for a lifelong friendship.

Graduation in 1881 was followed by a year of internship in the Montreal General Hospital. He and his fellow interns must have particularly desired to record this period for posterity and a photograph shows the four young men in studiedly careless poses, the young Mewburn already sporting the wide pointed moustaches that he kept to the end of his days (Fig. 2). One of his fellow interns, Andrew Henderson, became the first civilian practitioner in Calgary, and another, James Bell, was known to later generations as a famed Professor of Surgery at McGill.

Following internship he turned to the West. By 1882 Winnipeg had experienced a boom from the construction of the Canadian Pacific Railway and its little 20 bed hospital had become quite inadequate, so that the erection of a larger one was undertaken. Here Mewburn went as house surgeon. During his student days Lister's methods of surgical antisepsis, just introduced into Canada, were the subject of much controversy[2] but, as Mewburn would tell his classes 40 years later, his experiences with the injured from the railroad construction during that early Winnipeg period soon clinched the matter for him. The days must have been busy and profitable and three years had almost passed when the Riel Rebellion broke out in the North West Territories.

In Ottawa events moved with unusual swiftness. The Government immediately called for volunteers to constitute an expeditionary force and on Friday, April 3, Thomas Roddick, Mewburn's erstwhile Professor of Surgery at McGill, was appointed Chief of the Medical Staff in the Field. He left at once for Winnipeg where he arranged for the setting up of a base military hospital in some of the wards of the Winnipeg General, and he asked his old pupil and intern to take charge.[2]

Again Mewburn's decision was in the family tradition.[1] His great-grandfather, the apothecary, had held a commission in the volunteers when Napoleon threatened to invade England. His grandfather was an assistant surgeon in the Peninsular War and had treated the wounded after the Battle of Corunna in which Sir John Moore was mortally wounded. When he moved to Canada he again volunteered for service in the suppression of the Mackenzie Rebellion in 1837. Mewburn's father served two years as a medical officer and in 1866 was Surgeon Major to the 44th Regiment during the Fenian Raids. We may be assured that Roddick received an unhesitating and unqualified "Yes".

The Rebellion was shortlived and by the end of July the military hospital had finished its work and Mewburn had won his first military medal. But the spotlight had been turned on the West. In November of that year the last spike was driven for the C.P.R. route across Canada and Mewburn's gaze turned still further westward.

The North West Territories had been set up in 1870 and in 1882 Alberta had been created as one of its districts. But settlement had been slow and in 1885 the Alberta district had only about 15,000 inhabitants, including Indians and halfbreeds. However, the coal seams in the southern area had attracted attention and the North West Coal and Navigation Company had started mines at a place called Coal Banks, now named Lethbridge after the first president of the company.[3] They wished to get a doctor to establish permanent residence in the little community of miners and ranchers, and at the invitation of the manager, Mr. E. T. Galt, a son of Sir Alexander Galt, Mewburn travelled there in December 1885 to look over the prospects.

According to tradition he left Winnipeg in forty below zero weather and arrived at Lethbridge during a Chinook. This might have created a particularly favourable impression but in any event his mind was soon made up. He returned to Winnipeg to finish his term of service, to receive a handsome gold watch and chain from his professional colleagues, and to set off again for Lethbridge in the spring. His lifelong friend, the late Peter M. Campbell, wrote:

> "He was the only medical man in the town —calling it that. His medical neighbours were few and far between. To the west a Mounted Police surgeon at Macleod, 32 miles away; the same to the north at Calgary, 140 miles; also to the east at Medicine Hat, 110 miles; and to the south . . . the nearest was at Great Falls, Montana, 195 miles. That was quite an extensive area to serve, but fortunately for him there were very few people in it. It is probable that outside of the hamlets just mentioned, the population of the area was not as high as one person for every hundred square miles . . ."[4]

The young doctor plunged into what must have been a busy life. He became Assistant Surgeon to the Mounted Police, retaining a lively interest in the force until his death. He also served as doctor to the railway built by the Coal Company to Medicine Hat, and later he was similarly connected with the C.P.R., being their chief medical officer during the construction of the line through the Crowsnest Pass. All this was in addition to his work for the Coal Company and in the community. In a year his roots were struck deeply enough for him to get married and with this major step in life accomplished he was free to turn almost all his energies to his profession.

Although Alberta has been blessed with some outstanding pioneer doctors, none of those who arrived in those early years achieved a comparable reputation as a surgeon. While he carried on the full range of general practice, he was by temperament and training specially drawn to the surgical side of his work, which he pursued with ability and exceptional determination. He

subscribed to medical journals, read them carefully, and preserved them with care so that the Medical Library of the University of Alberta is fortunate, considering its youth, to have some long runs of journals as his gift. He also made great efforts to visit major clinics periodically. Twenty-seven years passed which brought him the reputation of the pioneer surgeon of the West.

It was the heroic age of surgery. Lister's great discovery had afforded the surgeon almost unlimited opportunity and—the intricate techniques of today not yet developed — the individual had a marvellous scope for initiative. Today's teamwork, while it has conferred great boons on surgery, has dimmed the glory of the individual. Given Mewburn's temperament and the circumstances of his time, his isolation was a blessing in disguise in that it threw him on his own resources, and developed his confidence in himself.

An example will illustrate this. In later years Mewburn told his students: "I had seen several patients die with 'perityphlitis', and I had also noticed articles appearing in the journals suggesting that the condition was essentially a purulent inflammation of the appendix, and early resort to surgery was advocated. I determined that the next such case that came along I would operate on without delay." The late W. S. Galbraith takes up the story:

"It was my privilege, then only looking on, to watch his development from surgery of amputations and abscesses to his first appendectomy in 1893. The patient had travelled 200 miles to have it done and it had evidently ruptured some time before, and everything was in a terrible mess . . . but the patient got well, and with increasing ease cases were offered for his skill; hernias in plenty, an ectopic gestation, which he reported, until December 10, 1903, came the climax, as he then thought, in a Cæsarean section. His progress from that point was continuous."[5]

The stories concerning him as a personality are legion and the anecdotal accounts are worth reading.[4-8] They reveal the hold he had on his fellows, and particularly on his patients, by the sheer force of character. But such qualities have marked the good doctor in all ages. What was it that brought him to the forefront? It was not manual dexterity for he was a slow, though exceptionally careful operator. He did have, however, a remarkably acute diagnostic sense and coupled with this was an equally remarkable ability to sense just how much a patient could stand. Behind this there lay still deeper qualities, and to these his close associate, W. S. Galbraith has again testified from first-hand knowledge:

"His success marks him as belonging to that class which ignores difficulties and lays tribute upon his daily work to produce the material for his own education and training . . . He was never satisfied with having 'got by' . . . Dr. Mewburn was certainly a living example of (the) dictum 'succeed with what you have'. As a colleague he was inspiring, and obliged one to give his best and be certain about it, but he made most of those who worked with him very warm friends, as his straightforwardness to friends and foes alike made his friendship highly prized. In the mining camp of forty years ago, the Lethbridge of today, his thoroughness is still a tradition."[5]

In 1913 at the age of 55 he moved to Calgary and limited his practice to surgery. But the move was barely accomplished when once more the bugles sounded and his response was again immediate. An anecdote that is absolutely characteristic is contained in a quotation from a letter written by a cousin, Brig. Gen. S. G. Mewburn:

"I remember . . . he sent a wire to Sam Hughes, then Minister of National Defence, offering his services. Sam replied, thanking him for the offer but regretting he was too old. The doctor sent a reply saying: 'Reference your wire—go to hell! I am going anyway.' He cabled Sir William Osler, a great personal friend, and the first I knew he telephoned me from Toronto early in 1915 that he was leaving for New York. He went over at his own expense and made a marvellous record overseas.[6]

His worth was quickly recognized and he was placed in charge of the Surgical Division of the Military Hospital at Taplow. Here he was able to renew his friendship with Osler, who was medical con-

sultant to the hospital. For his services he received in November 1918, from the hands of the King, the Order of the British Empire.

He returned to Calgary in 1919 ready to start practice once more but an abrupt change occurred in his pattern of life. The University of Alberta was preparing to extend its medical course so as to carry its students through to graduation and it was necessary to fill the clinical chairs. For surgery the happy choice fell on "The Colonel", as he was now known to all, and he accepted.

His days as a teacher crowned his life's work. His was a personality that a student encounters rarely. Over the years the facts he taught have faded, but the subtle force of his character and example has steadily maintained and increased its power. None of his students could fail to be influenced by the joyous way in which he went into battle for his patient. His continued effort to keep up with the progress of medicine was a potent stimulus. Above all was his whole-souled devotion to the art and craft of healing, for he was—in the modern phrase — completely "patient-centred". I have never known a physician so thoroughly devoted to his patient's interest, so regardless of social or economic status, or any other extraneous thing. He was first, last, and always the doctor.

He remained active to the last when, getting a severe chill after a strenuous morning in the operating-room, he developed a pneumonia which carried him to his death on January 29, 1929. He was buried at Edmonton on a sunny cold Alberta day, in the Western land he had done so much to develop, and as the casket was lowered a firing party sounded a soldier's farewell.

His traits are well epitomized by his memorials. The Mewburn Medal in Surgery marks his interest in students; the Mewburn Military Pavilion of the University Hospital commemorates both his clinical and military life; in front of the Galt Hospital in Lethbridge there is a cairn on which is carved the tribute of the community he served so well. But when that cairn was unveiled in June 1937, a very revealing incident occurred.[9] From a band of the Blood Indians, who had so often called on the services of "The Little Doctor," there stepped forward in full regalia their leader, Chief Shot-on-Both-Sides, who placed at the foot of the cairn a simple wreath of western wild flowers.

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ORIGINAL ARTICLES

ISLET CELL TUMOURS AND PEPTIC ULCERS
A REPORT OF TWO CASES OF ZOLLINGER-ELLISON SYNDROME

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THE ASSOCIATION of a tumour of the islets of Langerhans with peptic ulceration of the upper gastrointestinal tract was first characterized as a syndrome by Zollinger and Ellison in 1955.[1] At that time they reported two patients with primary peptic ulcers of the jejunum associated with islet cell adenomas of the pancreas and collected four similar cases published by others. Subsequently (1956) Ellison reported on 24 cases, including five new cases and 17 collected from the literature, of co-existing peptic ulcer and islet cell tumour.[2]

This association is generally designated "the Zollinger-Ellison syndrome", an eponym proposed by Eiseman and Maynard.[3] Further reports[3-11] have brought the total number of cases to approximately 35, the exact number depending somewhat upon the criteria used for inclusion in the syndrome. From these cases, the general features of the new clinical entity have become apparent:

FEATURES OF THE ZOLLINGER-ELLISON SYNDROME

1. *The Peptic Ulcer*

In almost all cases, the presenting picture is that of a peptic ulcer or one of its complications. The ulcer diathesis is intense, with marked increase in both volume and acidity of the gastric secretion. The site of the primary ulcer is often "atypical", and multiple ulcers are not uncommon (Fig. 1).

Apart from the above peculiarities, the gross and microscopic features of these lesions are those of any peptic ulcer. The surgeon's attention is often directed to the entity by stomal ulceration, which recurs repeatedly as long as any acid-secreting mucosa remains.

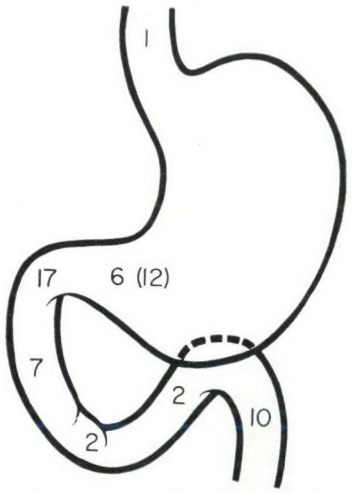

Fig. 1.—Diagram showing location of 57 primary ulcers in 34 cases of Zollinger-Ellison syndrome. The ulcers are frequently multiple and "atypical" in location. One patient had 12 chronic gastric ulcers.

II. *The Pancreatic Tumour*

The islet cell tumour is not, as a rule, an insulin-producing growth. Beta granules are usually absent, and some authors have reported that the alpha-type cell predominates. The neoplasm is malignant in more than half the cases, and metastases are often seen. Even when the growth is benign, multiple tumours may be present.

III. *The Patient*

Patients with the Zollinger-Ellison syndrome do not usually show clinical evidence of hypoglycæmia, but some exceptions have been reported. Most of the

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patients have been in the fourth and fifth decades of life, although the extremes have been 19 and 78 years. The sex distribution is approximately equal. Patients present, as a rule, with pain of an acute primary or stomal ulcer or with a complication of peptic ulcer. In a few cases ulcer symptoms were present for many years, but more often the peptic ulceration runs a fulminating and lethal course over a period of a few months. These cases can often be recognized in retrospect by a characteristic history of acute episodes, multiple unsuccessful operative procedures, recurrent ulceration, and fatal termination.

Another interesting feature of the entity is the finding of adenomas or hyperplasia of one or more other endocrine glands in approximately one-fifth of the cases. The parathyroids, the anterior pituitary, and the adrenal cortex have been chiefly involved, and in some cases the other endocrine tumours have been functioning.

Case Reports

Two cases of the Zollinger-Ellison syndrome are herewith reported:

Case 1.—Mr. T.C., a 29 year old married clerk, was admitted to the Royal Alexandra Hospital, Edmonton, on December 17, 1948, for upper abdominal pain of five months' duration. He was shown by barium meal examination to have a duodenal ulcer, and he was discharged on medical management.

He was readmitted on April 25, 1950, with burning epigastric pain of one year's duration. The pain had been relieved by food until one week before admission, when it became constant despite a milk diet and was accompanied by nausea, vomiting, heartburn, and waterbrash. His bowels had been "loose" for a month, but the character of the stool had been normal, except for one tarry stool passed two weeks previously.

The only physical findings of note were some epigastric guarding and tenderness. Barium meal examination revealed a prepyloric ulcer and marked pylorospasm. Gastrectomy was advised in view of his severe symptoms and the location of the ulcer.

Subtotal gastrectomy was carried out by Dr. W. S. Anderson on May 18, 1950, for a large, benign gastric ulcer with penetration of the pancreatic head. In the distal portion of the pancreas there were two nodules, respectively measuring 1.5 and 2.0 cm. in diameter. These were excised along with a rim of normal pancreatic tissue and were reported, on examination of frozen section, to be benign adenomas.

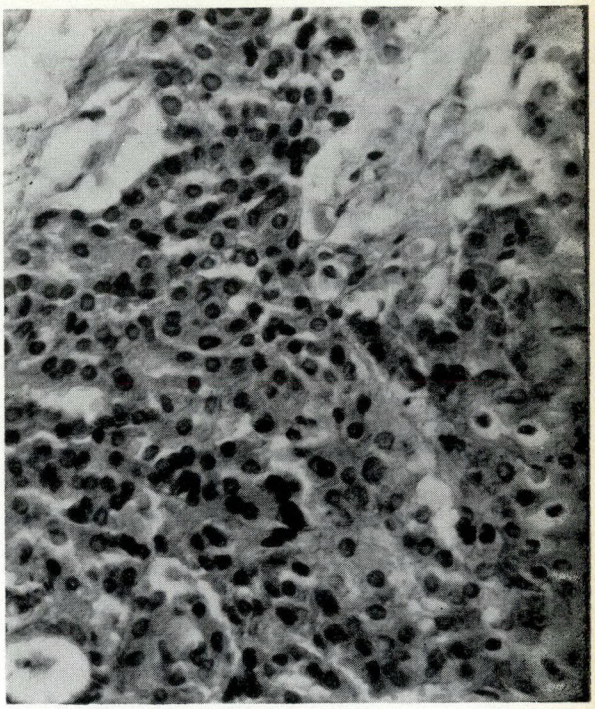

Fig. 2.—Case 1: Islet cell carcinoma of low grade malignancy—pancreas (H & E stain).

Subsequent microscopic examination of the two nodules from the pancreas by Dr. J. H. Sturdy showed them to be composed of low grade carcinoma of the islets of Langerhans. Invasion of adjacent exocrine parenchyma and stroma was evident in some areas.

Further study of this pathologic material disclosed an infiltrating tumour within pancreatic tissue, composed of nests, ribbons, and solid alveolar groups of polygonal and cuboidal cells, almost all of which displayed moderately well defined cell boundaries, acidophilic, finely granular cytoplasm, and a round or oval nucleus containing one or several small nucleoli (Fig. 2). Cell size corresponded approximately to that of normal islet cells. Mitotic figures were rare. Supporting fibrous stroma was abundant in most areas. With Masson's trichrome stain and Bensley's aniline, acid-fuchsin and methyl-green stain, a moderate number of tumour cells were found to contain small red cytoplasmic granules, a feature which suggested some kinship to alpha cells. No argentaffin granules were demonstrated by coupling with the stable diazotate

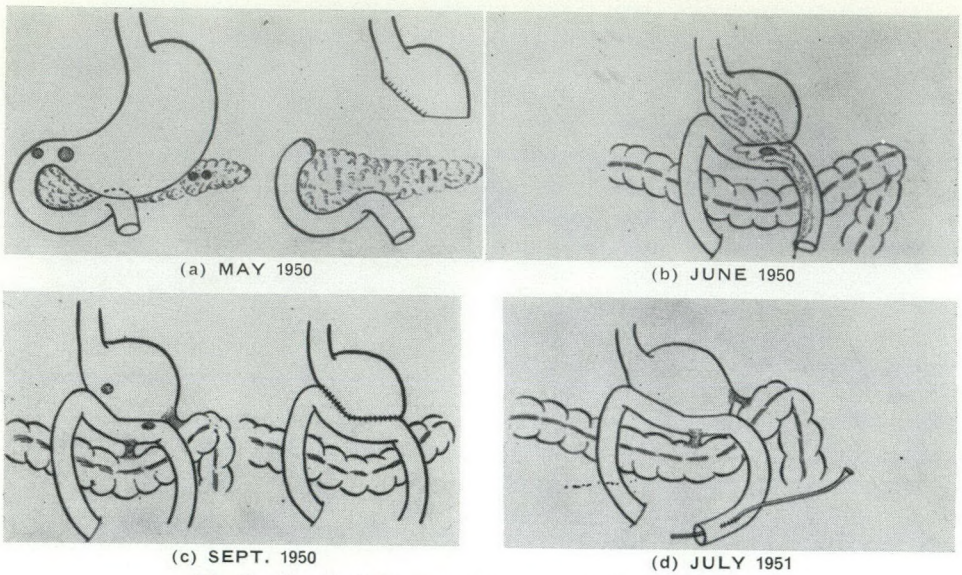

Fig. 3.—Case 1: Diagrammatic representation of clinical course.

of 5-nitroanisidine (Fast Red salt B) or by Schmorl's ferric ferricyanide method.

Chemical analysis of the tumour tissue by Dr. A. M. Fisher at the Connaught Laboratories, Toronto, showed that it contained about 0.8 unit of insulin per gram. This is a low insulin content for islet cell tissue.

Microscopic examination of the gastric ulcer showed the usual features of a chronic benign gastric ulcer.

The patient's hospital stay was uneventful. Blood glucose determinations and urinalyses for sugar were normal during his postoperative period and during all subsequent hospital admissions.

He was readmitted to the Veterans' section of the University of Alberta Hospital on June 5, 1950, having vomited about a quart of dark red blood. He was in shock on admission, and his hæmoglobin level was 4.3 g. %. He was transfused and treated with diet, sedation, antispasmodics, and x-ray therapy to the stomach.

Because the patient had continuous epigastric pain, he was re-explored by one of us (W.C.M.) on September 12, 1950. Operation revealed: (1) a gastric ulcer with penetration of the liver, (2) a gastrojejunal ulcer penetrating the anterior abdominal wall, and (3) gastrocolic and jejunocolic fistulæ. Involved tissue was resected and a new gastrojejunal anastomosis was established. His early postoperative course was not remarkable.

Subsequently, however, the intestinal fistulæ recurred. He suffered considerable pain and became addicted to narcotics and a psychiatric problem. He lost weight and eventually required a feeding jejunostomy. He died after a massive hæmatemesis on July 15, 1951—three years after his first symptom and 14 months after his initial operation. Landmarks in this patient's course are represented diagrammatically in Fig. 3.

At autopsy, a large gastrojejunal ulcer, and gastrojejunal and gastrocolic fistulæ, were found. There was an extensive inflammatory reaction throughout the upper abdominal cavity. No residual islet cell tumour was found, although the pancreas was not minutely examined by serial gross slices.

Comment

This is a case of a young man who had a peptic ulcer and a non-insulin-producing islet cell carcinoma of his pancreas, both treated surgically. The fulminating course from the onset of his initial ulcer symptoms until his death from the effects of peptic ulceration, uncontrolled by repeated surgical measures, is typical of many reported cases of the Zollinger-Ellison syndrome.

Case 1 is incompletely documented because a thorough search was not made for residual cell carcinoma at autopsy. Considering that the Zollinger-Ellison syndrome was not an established entity at that time, and that there was considerable inflammatory reaction in the upper abdomen, it is not unlikely that further small tumour

nodules were overlooked at operation or autopsy. On the other hand, it has not been unequivocally demonstrated that the islet cell tumour has any direct bearing on the pathogenesis of the fulminating peptic ulcer, and there is really no reason to assume that tumour must necessarily be present in the terminal stages of the disease. In Amendola's case,[12] the patient had an apparently complete removal of a cystic islet cell adenoma from the tail of the pancreas; no residual tumour was seen when the patient underwent surgery for a perforated gastric ulcer four years later.

CASE 2.—Mrs. B.R., a 54 year old housewife, was admitted to Binghamton City Hospital (Binghamton, New York) in June 1954 for investigation. She had a three year history of recurrent attacks of diarrhœa, associated with abdominal fullness and occasional vomiting, and accompanied by a 20 lb. weight loss. There was no history of pain or of blood and mucus in the stool. Investigation at that time was negative, except for some irregularity of the duodenal bulb on barium meal examination and a hyperchlorhydria on gastric analysis (120 mEq./l. of free acid in the fasting specimen and 136 mEq./l. 30 minutes after alcohol stimulation). Her condition was managed medically with some degree of success for 11 months.

She was readmitted on May 1, 1955, with an acute abdomen. She had experienced sudden, severe abdominal pain with vomiting and was found to have a rigid abdominal wall and moderate shock; radiography revealed intraperitoneal air. She was explored by one of us (B.L.M.), and a perforated jejunal ulcer was found 3 cm. from the duodeno-jejunal junction. The lesion was treated by wedge excision. The liver contained three hard, grey, umbilicated nodules, one of which was biopsied. She recovered after a stormy postoperative course.

The pathologist, Dr. Thomas A. Cope, Jr., reported the surgical specimens to be: (1) benign peptic ulcer of the jejunum, and (2) metastatic carcinoma to the liver, primary site not determined.*

She did well for an interval and then six months later on November 16, 1955, she again sustained a perforation of a jejunal ulcer. This was at virtually the same site as the previous perforation, the silk sutures used to close the bowel on the first occasion being seen at the edge of the second perforated ulcer. This was treated in identical fashion, and again the liver nodules were biopsied. As before, the pathologist reported the surgical specimens to be: (1) simple ulcer of the jejunum, and (2) metastatic carcinoma to the liver.

Postoperatively she continued to have abdominal distress and diarrhœa, and she was given a course of x-ray therapy to the stomach. In the meanwhile the entity described by Zollinger and Ellison had become known. A tentative diagnosis of islet cell tumour was made and the patient was explored on February 15, 1957.

A hard, multinodular tumour involving the tail and most of the body of the pancreas was discovered. The body and tail of the pancreas, along with the spleen and two para-aortic lymph nodes, were resected (Fig. 4). A liver nodule was again biopsied.

The pathologist, Dr. Frederick P. Becker, reported the surgical specimen to be: "islet cell carcinoma of the pancreas with metastases to liver and regional lymph nodes". Microscopically (Fig. 5) the tumour was composed of sheets and solid alveolar groups of somewhat pleomorphic, oval or polygonal cells, each with indistinct cell borders, faintly acidophilic, ground-glass cytoplasm, and a round or oval nucleus containing dust-like particles of chromatin and usually several prominent nucleoli. Few mitotic figures could be found. The tumour cells were devoid of specific cytoplasmic granulation (when stained by the methods employed in Case 1) and measured from one and a half to two times the usual size of islet cells. Supporting stroma consisted of narrow bands of dense collagenous tissue. Infiltration and destruction of pancreatic tissue was evident at the periphery of the neoplasm.

Postoperatively she had only transient improvement and then began to suffer from abdominal cramps, "bloating", and diarrhœa. She was again hospitalized for investigation in November 1957. On gastric analysis there were 98 mEq./l. of free HCl in the fasting specimen. Barium meal x-ray examination revealed a small hiatal hernia, prominent gastric mucosal folds, and severe jejunal and ileal dyskinesia. A glucose tolerance test gave values for blood sugar of: 130 mg. % fasting, 310 in 30 minutes, 354 in one hour, 320 in two hours, 223 in three hours, 155 in four hours, 97 in five hours, and 108 in six hours.

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*A morphological similarity to carcinoid tumour was noted. This resemblance between islet cell tumour and carcinoid has been noted by others;[5, 6] special stains are necessary for differentiation.

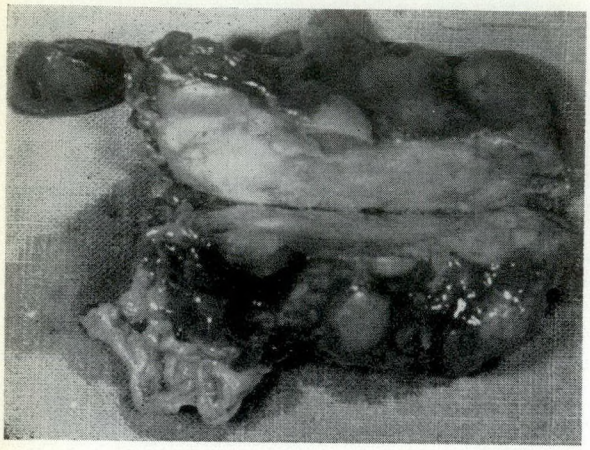

Fig. 4.—Case 2: Bisected surgical specimen (Feb. 15, 1957) consisting of a nodular tumour mass infiltrating the body and tail of the pancreas (x 1).

Serum calcium was 8.0 mg. %, serum phosphorus 4.0 mg. %, alkaline phosphatase 3.5 Bodansky units, and a urinary Sulkowitch test gave normal results with the patient on a low calcium diet. Radiography of the skull showed no enlargement of the sella turcica.

She was again operated upon on November 11, 1957. The three nodules in her liver, which had not become appreciably larger in two and a half years of observation, were resected. A jejunal ulcer was again found to be present. There was no evidence of recurrence of the primary malignancy. A 75% gastric resection with antecolic anastomosis was carried out, and a subdiaphragmatic vagotomy was done as well. Her hospital course was uneventful, and she was achlorhydric to an Ewald meal before discharge. At the present time the patient is well.

Dr. G. A. Wrenshall of the Banting and Best Department of Medical Research, University of Toronto, reported that the metastatic tissue removed from the liver contained less than 0.1 unit of insulin per gram. (Normal non-diabetic pancreas, extracted by the same method, yields 2.3 ± 0.2 units per gram.)

Special stains of the tissue removed from the liver showed cells with scant cytoplasm and a few mitoses, having the appearance of islet cell tumour. No specific granules could be identified. (Courtesy of Drs. F. P. Becker and J. Logothetopoulos.)

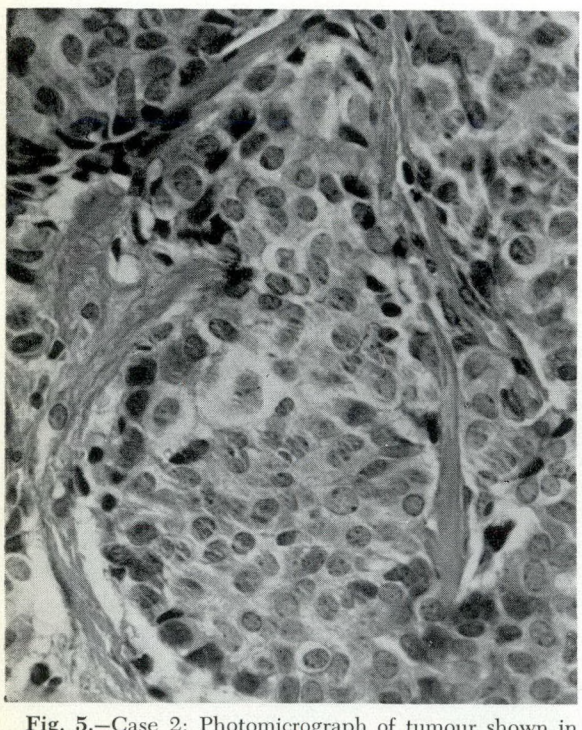

Fig. 5.—Case 2: Photomicrograph of tumour shown in Fig. 4. Islet cell carcinoma of pancreas with solid alveolar pattern (H & E stain).

Comment

This woman, too, has a typical history of repeated episodes of symptoms and complications of her peptic ulcer, associated with multiple operative procedures (Fig. 6). It is still too early to evaluate the results of the most recent surgical measures, but the fact that she is now achlorhydric makes us hopeful that she may now be relieved of recurrent ulceration.

This must be a slowly growing neoplasm, since the liver metastases did not increase in number or appreciably in size over a period of 30 months. There is considerable likelihood that her malignancy will recur, of course, since it was metastatic at the time of her first laparotomy. If it does recur, ACTH therapy, so effective in insulin-producing metastatic islet cell tumours of the pancreas,[13] will be contraindicated because of her ulcer diathesis.

Both of our patients presented with diarrhœa, as have five other patients in the literature on this syndrome. The mechanism is not settled, but it does not appear to be a steatorrhœa. Donaldson, vom Eigen and Dwight[7] attribute this symptom, also found in their patient, to the markedly elevated volume of gastric secretion, the effect of which they liken to the result of administering a saline cathartic.

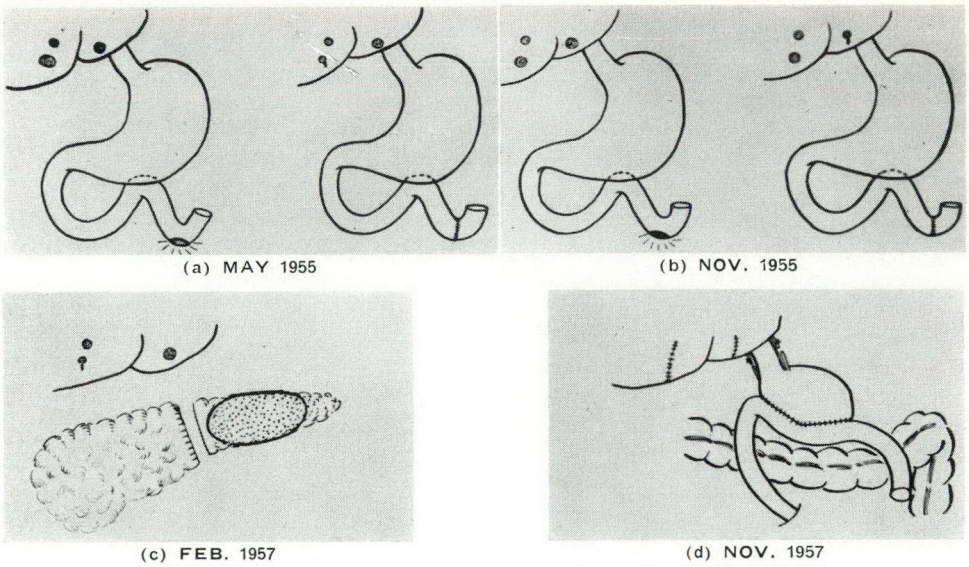

Fig. 6.—Case 2: Diagrammatic representation of clinical course.

Discussion

Etiology of the Peptic Ulcer

The pressing clinical problem in the Zollinger-Ellison syndrome, as far as the surgeon is concerned, is the fulminating peptic ulceration, frequently leading to the demise of the patient. Ideally, management should be contingent upon a knowledge of the etiology of the ulcer, but such information is lacking at present.

The most reasonable explanation for the etiology of the ulcer is that the islet cells secrete a substance that in some way promotes peptic ulceration. Insulin seems to be ruled out at once, since few of the reported patients were hypoglycæmic, since the tumours seldom contained beta granules, and since peptic ulcer is only rarely found in association with insulin-secreting adenomas of the pancreas,[14] despite the vagal stimulation which might be expected with the latter.

Poth *et al.*[15] (1950), on the basis of experimental work on dogs, suggested that secretion of glucagon by alpha cells may account for peptic ulceration under certain conditions. Although further work by Poth and Fromm[16] subsequently produced evidence against the ulcerogenic action of glucagon, the former concept was initially utilized by Zollinger and Ellison as a reasonable explanation for the co-existent islet cell tumour and peptic ulcer in their patients.[1] That the pancreas in some way promotes peptic ulceration is also suggested by Dragstedt's experiment, in which he demonstrated that total diversion of pancreatic juice by an external fistula produces peptic ulcer in 100% of dogs, but that total pancreatectomy was followed by ulceration in only 1.3% of 300 experimental animals.[17] In two of the reported cases of Zollinger-Ellison syndrome[1, 5] a hyperglycæmic factor with electrophoretic properties resembling glucagon was identified in the patient's serum. Subsequent work by Stunkard, Van Itallie and Reiss[18] and by Robinson *et al.*[19] indicated that glucagon inhibits gastric secretion and motility in both dogs and man. In the light of this recent evidence, it appears that peptic ulceration cannot be attributed directly to glucagon.

It may even be questioned whether the islet cell tumour plays any part in the production of the peptic ulcer in cases of Zollinger-Ellison syndrome. Survey of the literature reveals that there has never been a case in which total removal of the islet cell tumour, as the *sole* operative procedure, has resulted in complete relief of ulcer symptoms. In only one reported instance was an ulcer apparently "cured" by complete excision of an islet cell tumour as a supplementary operative procedure.

This was Strom's[20] patient, who presented with a marginal ulcer after a previous partial gastrectomy; he was well after removal of an islet cell tumour, but in addition 5 cm. of "duodenal stump" was resected. (Microscopic examination on the latter was not published.)

The co-existence of peptic ulcer and the islet cell tumour is possibly coincidental, since peptic ulcer is not only common but may occur in association with a variety of other disease processes. The "atypical" location of many of the ulcers and the peculiarly fulminating and persistent nature of the ulcer tendency, however, suggest that the relationship is not fortuitous.

Associated adenomas or hyperplasia of the parathyroids, the anterior pituitary, the adrenal cortex, and sometimes other endocrine glands, have been reported in about 20% of cases of the Zollinger-Ellison syndrome. As Fisher and Flandreau[5] point out, this figure probably errs by being too low, since the other endocrine tumours are not usually looked for.

When an islet cell tumour is found in combination with adenomas of other endocrine glands, such a case fits into the entity of multiple endocrine adenomatosis, as described by Wermer[21] and by Underdahl, Woolner and Black.[22] This syndrome is characterized by the occurrence of one or more adenomas in two or more endocrine organs, most often islet cells, anterior pituitary, parathyroids, and adrenal cortices. The various endocrine tumours may or may not be functional. Associated with multiple endocrine adenomatosis either peptic ulcer or gastric polyposis may be found, whether or not islet cell tumours exist.[21, 22] The Zollinger-Ellison syndrome, then, may be but one subdivision of a larger pathological grouping.

The possibility also exists that some of the other adenomas have a bearing on the pathogenesis of the ulcer.

Hyperparathyroidism is complicated by peptic ulcer in 24% of cases and by dyspepsia without demonstrable ulcer in another 15 or 20%, according to Haynes (quoted by Black[23]). In at least four cases of Zollinger-Ellison syndrome there has been a parathyroid adenoma or hyperplasia, and one patient presented with clinical hyperparathyroidism.[5]

In six of the reported cases patients have been shown to have a pituitary tumour or hyperplasia, and/or acromegaly.[2, 7] The neoplasia or hyperplasia may involve any of the three cell types in the adenohypophysis.

Five patients have had hyperplasia or adenomas of the adrenal cortex.[2,7] The role of adrenocortical hyperactivity in some cases of peptic ulcer is well established.[24] All in all, the role of several endocrine glands in the peptic ulceration of the Zollinger-Ellison syndrome remains to be elucidated.

We can only conclude that we do not know the mechanism by which the ulcer is produced, and in particular, we do not understand the role played by the islet cell tumour. Now that attention has been called to the syndrome, surgeons will undoubtedly recognize it with increasing frequency. A large number of detailed case reports on the Zollinger-Ellison syndrome may eventually help to clarify the pathogenesis of the ulcer.

Management of the Peptic Ulcer

If our approach to the management cannot be based on any real understanding of the etiology of the ulcer, it must be based on the limited clinical information available from reported cases. Certainly the first prerequisite is awareness of the lesion, in order that one can be prepared to cope with a peculiarly intractable type of peptic ulcer. The pancreas should probably be explored in any case in which the abdomen is opened for treatment of peptic ulcer, but particularly is pancreatic exploration indicated if the patient is a female, if the ulcer diathesis is severe, if the ulcer is in an atypical location, if there are multiple ulcers, or if there is a stomal ulcer.

Regarding stomal ulcer, we do not discount the importance of vagotomy, of excision of remaining antral mucosa, and of wider gastric resection in the management of recurrent peptic ulcer, but we would add exploration of the pancreas to these procedures.

When, in association with a primary or stomal ulcer, one or more islet cell tumours are found in the pancreas, they should be resected, if this can be done without risk to the patient. This should be undertaken primarily because a neoplasm is present and not in the expectation that this procedure alone will favourably affect the ulcer tendency.

The ulcer itself should be dealt with by means of a fairly radical gastrectomy, possibly combined with vagotomy, in an effort to render the patient achlorhydric. Zollinger and McPherson[10] now advocate total gastrectomy; this may be the only solution for a patient with recurrent stomal ulceration and a fulminating ulcer disease, but the procedure itself is too crippling to be employed in the primary operation.

Summary

The clinical and pathological features of the Zollinger-Ellison syndrome (associated peptic ulcer and islet cell tumour of the pancreas) are briefly reviewed.

Two case reports are added to the literature. Our first patient was a 29 year old man with duodenal and gastric ulcers and two small islet cell carcinomas of his pancreas. He died of fulminating peptic ulceration after a series of operative procedures over a 14 month period. Our second patient is a 54 year old woman who twice presented with a perforated jejunal ulcer and who had an islet cell carcinoma with metastases. She is living and fairly well after excision of all apparent tumour tissue and after a three-quarter gastrectomy and vagotomy.

Neither patient was hypoglycæmic, and histological and chemical studies suggested that the tumours were not insulin-producing. Diarrhœa was a prominent early symptom in both patients.

The etiology of the peptic ulcer is unknown and may not be related directly to the islet cell tumour. Adequate information as to the pathogenesis of the ulcer and the most effective method of management must await further studies and additional case reports.

For the present, it is our opinion that removal of the islet cell tumour should be carried out, if feasible, but that one must rely upon a fairly radical ulcer operation to deal effectively with the intense and often lethal peptic ulcer diathesis.

Addendum

Since completion of this manuscript, an unpublished case of Zollinger-Ellison syndrome has been presented at a surgical pathologists' conference in the University of Alberta. This patient is a 45 year old woman who had sustained a perforated duodenal ulcer four years previously. She presented with dyspepsia and with radiological evidence of a duodenal ulcer and cholelithiasis. Cholecystectomy was carried out by Dr. C. H. W. Weinlos, who also discovered and removed a tumour from the body of the pancreas. This proved to be an islet cell carcinoma.

We would like to thank Dr. W. W. Eadie and Dr. W. S. Anderson for permission to include a case report on their patient.

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RÉSUMÉ

L'association d'une tumeur des cellules des îlots de Langerhans et d'un ulcère peptique de la partie supérieure du tractus gastro-intestinal a été décrite pour la première fois comme une entité morbide particulière par Robert Zollinger et Edwin Ellison en 1955. De sorte que l'on parle volontiers dans ces cas de "syndrome de Zollinger-Ellison", caractérisé par: (1) un ou parfois plusieurs ulcères peptiques avec forte hyperacidité, de localisation souvent atypique, dominant la symptomatologie; (2) une tumeur des îlots de Langerhans, non productive d'insuline, constituée en majorité de cellules alpha, avec absence presque constante des cellules bêta. Ce néoplasme est malin dans plus de la moitié des cas: les métastases sont fréquentes.

Ce syndrome frappe de façon sensiblement égale les deux sexes aux alentours de la quarantaine ou de la cinquantaine. Ces malades souffrent d'un ulcère peptique ou d'un ulcère primaire à évolution rapide ne s'étendant que sur quelques mois pour aboutir à la mort. Des adénomes ou des hyperplasies de diverses glandes endocrines (parathyroïdes, cortex surrénal, hypophyse antérieure et autres) peuvent coexister.

Les auteurs présentent deux cas de cette maladie.

Le premier est celui d'un homme de 29 ans admis à l'hôpital pour une douleur du haut de l'abdomen apparue depuis 5 mois. L'examen radiologique permit de découvrir un ulcère duodénal et un traitement médical fut institué. Le patient fut réadmis 16 mois plus tard pour des douleurs épigastriques à type de brûlures, devenues permanentes malgré un régime lacté, accompagnées de nausées, de vomissements et de régurgitations acides. La radiographie mit en évidence un ulcère prépylorique: une gastrectomie partielle fut alors pratiquée, au cours de laquelle, on découvrit, outre un large ulcère pénétrant dans la tête du pancréas, deux petits nodules dans le corps de ce dernier. Ces nodules furent excisés et examinés: il s'agissait d'un carcinome des îlots de Langerhans de malignité faible, contenant peu d'insuline. Le patient guérit fort bien, mais dut être à nouveau réhospitalisé deux mois plus tard pour une hématémèse d'environ 1 litre. Une nouvelle exploration fit découvrir des ulcères multiples et des fistules gastro- et jéjuno-coliques; une anastomose gastro-jéjunale fut tentée. Bien que cette intervention fut supportée, les douleurs récidivèrent et devinrent atroces; le malade mourut un an plus tard d'une hématémèse massive.

A l'autopsie, on trouva de nombreux et larges ulcères et des fistules gastrojéjunales. Il est regrettable qu'un examen approfondi du pancréas n'ait pas été fait à ce moment, ce qui rend la présentation de ce premier cas incomplète.

La seconde histoire est celle d'une malade de 54 ans présentant un syndrome abdominal aigu, avec un passé de diarrhées, vomissements et perte de poids. Lors de l'admission à l'hôpital, on diagnostiqua la perforation d'un viscère creux, et la laparotomie d'urgence fit découvrir, outre un ulcère jéjunal perforé qui fut traité par excision, des nodules dans le foie. Ces derniers, enlevés et examinés histologiquement, étaient des métastases d'un carcinome indéterminé. Un nouvel épisode de perforation ulcéreuse survint six mois plus tard; peu de temps après, les auteurs ayant eu connaissance du travail de Zollinger et Ellison, décidèrent de tenter une exploration complète. Ils découvrirent une tumeur multinodulaire de la queue et de la majeure partie du corps du pancréas, qui fut réséqué. Cette tumeur possédait tous les caractères d'un carcinome des îlots de Langerhans. Ultérieurement, la malade subit alors une résection gastrique à 75% et une large excision de tous les nodules hépatiques que l'on put trouver, le tout associé à une vagotomie sous-diaphragmatique. Cette malade est actuellement en bonne santé.

Les théories actuelles sur l'étiologie de l'affection sont ensuite exposées. Il semble que le carcinome des îlots de Langerhans sécrète une substance capable de favoriser ou de provoquer les ulcères: si l'insuline semble être hors de cause, il n'en est pas de même du glucagon, sécrétion des cellules alpha. Les auteurs discutent longuement ce dernier point, ainsi que les interrelations endocrines possibles.

De tout ceci, il ressort que, désormais, le pancréas devra être soigneusement vérifié lors de toute laparotomie pour ulcère peptique ou primaire, tout particulièrement dans les cas à répétition et les récidives. Si des nodules tumoraux sont alors découverts, leur résection s'impose lorsqu'elle est possible. Quant à l'ulcère, il nécessite la résection gastrique quasi-totale associée à la vagotomie en vue de rendre le malade achlorhydrique.

CARCINOMA OF THE HEAD OF THE PANCREAS A STUDY OF TWENTY-ONE CASES

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CARCINOMA of the pancreas comprises from one to two per cent of all carcinomas, and approximately 80% of these originate in the region of the head of the pancreas.[1] Because the presenting symptom in the majority of these cases is obstructive jaundice, the general surgeon is not too infrequently challenged with this problem.

Since Whipple, Parsons and Mullins[2] in 1935 demonstrated the feasibility of pancreato-duodenectomy, a renewed interest has developed in the treatment of carcinoma of the head of the pancreas and ampulla of Vater. Many encouraging reports have appeared during the past 10 years, but notably so from Cattell and Warren of the Lahey Clinic,[3] Brunschwig of New York[4] and Rodney Smith of London.[5]

Although the operative mortality rate has been reasonable, survival in carcinoma of the head of the pancreas has been of short duration. On the other hand lesions limited to, or originating from, the ampulla of Vater or duodenal mucosa present a brighter picture, and quite a number of five-year cures have been reported.[6-8]

Cattell and Warren[3] in the largest personal series so far reported stressed, as did Whipple and others, the difference in operative mortality and postoperative prognosis, between carcinoma of the head of the pancreas and that of the ampulla of Vater. In a total of 76 cases resected the operative mortality was 13.6%. Out of 46 cases of carcinoma of the head of the pancreas, there were eight (17.6%) postoperative deaths.

Of the 38 survivors 22 died within one year and only two (5%) survived over five years. Of 30 cases of carcinoma of the ampulla of Vater there were two (6.6%) postoperative deaths. Of the survivors 11 (40%) lived three years or more and three (11%) were alive and well five years or more after operation. In Rodney Smith's[5] original series of 28 cases explored, seven radical pancreato-duodenectomies were performed with two operative deaths; the longest survivals were in the two cases of ampullary lesions—18 months each. More recently (November 1956) Smith[6] reported a total of 34 pancreato-duodenectomies for nine cases of carcinoma of the head of the pancreas with three (33.3%) postoperative deaths, and 25 cases of carcinoma of the ampulla of Vater and duodenum with no operative deaths. In this series he reported six five-year survivals, all with ampullary and duodenal lesions, except one cystadenocarcinoma of the body and tail of the pancreas.

Rhoads, Zintel and Helwig[8] reported 21 cases of pancreato-duodenal carcinomas with an operative mortality of 19%. There were six (29%) five-year survivals; of these lesions three were of the lower end of the common bile duct, two of the ampulla of Vater and one of the duodenal wall.

In my own series, the eight cases resected were classified as arising from the head of the pancreas. No true ampullary lesion was found by the pathologist.

It seems probable that there is an unwarranted delay in the diagnosis and management of many of these cases before surgery is contemplated; furthermore many surgeons are satisfied with simple palliative relief of the obstructive jaundice.

TABLE I.—Survival Rates After Pancreato-Duodenectomy

Patient	*Age*	*Duration of symptoms*	*Type of operation*	*Survived after operation*
Mr. G. M.	47	3 months	2 stage	15 months
Mr. W. S.	46	4–15 months?	1 stage	35 months
Mrs. E. C.	40	2 months	2 stage	14 months
Mr. G. H.	52	3 months	2 stage	17 months
Mr. J. C.	69	6 weeks	2 stage	18 months
Mrs. B. V. W.	68	4 weeks	2 stage	29 months (living and well)
Mr. R. D.	72	6 weeks	1 stage	Died 9th day after operation
Mr. L. LeG.	41	4 months	1 stage	14 months

TABLE II.—Survivals After Palliative Operations

Patient	*Age*	*Duration of symptoms*	*Type of operation*	*Survived after operation*
Mr. D. C.	74	5 weeks	Cholecyst-jejunostomy	7 months
Mrs. D. C.	74	4 weeks	1. Cholecyst-jejunostomy 2. Ant. gastroenterostomy	10 months
Mrs. C. M.	56	3 months	Cholecyst-jejunostomy	5 months
Mr. R. D.	70	4 weeks	Cholecyst-jejunostomy	2 months
Mrs. T. W.	65	2 months	Cholecyst-jejunostomy	2½ months
Mrs. M. W.	65	6 months	Cholecyst-gastrostomy	4 months
Mr. H. C.	48	6 weeks	Cholecyst-jejunostomy	7 months
Mrs. E. C.	78	2 months	Cholecyst-jejunostomy	5 months

For this reason, the experience obtained in a small series of cases of carcinoma of the head of the pancreas that occurred in private practice during the past six years is presented here.

There were 21 cases in all, seven in women and 14 in men. The average age was 60.5 years. Eight of the cases were found suitable for pancreato-duodenectomy, a resectability rate of 38%; eight patients had palliative operations and five were considered beyond operative relief.

Symptoms

Pain was usually the first complaint, although it was often of a bizarre nature, and it gradually increased in intensity. It varied in type from a mild colicky or spasmodic pain to a boring sensation; it was usually located in the mid-epigastrium or right hypochondriac region and was often referred in many directions. Occasionally, it was aggravated by the taking of food. Severe pain usually indicated an advanced stage of the lesion.

Jaundice was the presenting symptom or sign in all but one case, although it was not the initial symptom in a large percentage of cases. In a few cases it was intermittent, but always progressive.

Associated with these two main symptoms were anorexia, nausea and vomiting, fatigue, constipation and a constant loss of weight, often considerable.

Physical Findings

Apart from jaundice, the liver was enlarged in most cases and the gall-bladder was palpable in about one-third of the cases. No tumour was palpable except in a few advanced cases with metastases.

X-ray Findings

This diagnostic procedure was not considered to be of much assistance in this series. Barium meal examination was used in only seven cases, of which four showed some deformity or enlargement of the duodenal loop. Of the latter, all showing positive signs were advanced cases and only amenable to palliative procedures. Since most patients were intensely jaundiced and very ill, x-ray examination was not considered to be a justifiable procedure in all cases. However, I do feel that radiography could be a valuable diagnostic aid in ampullary or duodenal carcinomas.

Laboratory Findings

The majority of patients were only slightly anæmic, the hæmoglobin value ranging from 10.6 to 15.7 g. %; the average

serum bilirubin level was 16 mg. %; prothrombin time 20 seconds; alkaline phosphatase 28.5 units; cholesterol 220 mg. %; cephalin-cholesterol flocculation test 1+; thymol turbidity 1+.

Preoperative Therapy

Preoperative therapy consisted of administration of vitamin K, vitamins B and C, intravenous glucose solutions and blood transfusions when needed.

Diagnosis

There appeared to be an unexplained delay after the onset of symptoms before these patients sought medical advice or were referred to surgery. (Probably there was a little lethargy on the part of the patient, or the physician, or both). Three cases had been diagnosed and treated for infectious hepatitis and several more for cholecystitis with obstructive jaundice. These cases were treated for two weeks or more medically until a surgical opinion was requested. There were three diabetics in the series.

The diagnosis of obstructive jaundice was usually made on the clinical history and laboratory findings. If doubt existed after complete investigation and consultation, a laparotomy was performed. Other cases which presented difficulty were notably those with cholelithiasis and pancreatitis, one with homologous serum jaundice and cholangitis which followed a partial gastrectomy for duodenal ulcer, and two cases having painless obstructive jaundice with impacted calculi in the ampulla of Vater.

The finding of a discrete hard irregular mass palpable at operation in the head of the pancreas or ampullary area was almost pathognomonic of carcinoma. Usually the pancreas was œdematous and indurated because of obstruction of the main pancreatic duct. Lymph nodes constantly enlarged were the common bile duct node, and the subpyloric, cœliac and superior pancreatic groups. Histological examination of the lymph nodes in the operative (resected) cases was negative. Lesions located in the ampulla of Vater were easily diagnosed by opening the duodenum anteriorly; there was only one case of this type in the series.

Mobilization of the second part of the duodenum and thorough palpation of the head of the pancreas between thumb and finger was always carried out. If the growth was not fixed to the portal vein or superior mesenteric vessels and no evident metastases were present, a pancreato-duodenectomy was considered feasible.

Many of these patients were extremely ill, and in any case where jaundice had existed for more than two weeks, a biliary decompression operation was first carried out, the operation of choice being a cholecyst-jejunostomy. This of course, did not shorten the second operation or render it easier, but actually made it more difficult surgically. The advantage, however, was obvious, a "better operative risk". This was well illustrated in one of the resected cases (Case 6).

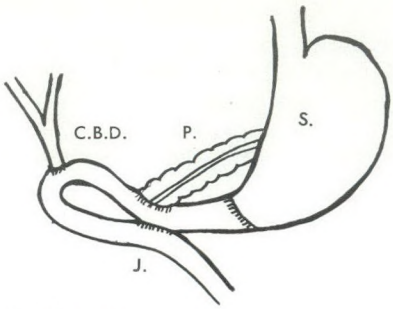
Pathology

The pathologist reported that all specimens of the resected cases showed ductal carcinoma; in only one did the growth ulcerate into the ampulla of Vater. The lesion in two cases appeared to originate in the distal portion of the common bile duct or in the pancreatic duct close to this region. No lymph node metastases were found in the cases resected.

Complications

Complications following pancreato-duodenectomy were minimal. The average hospital stay after operation was 17 days. One case developed a biliary fistula which closed on the 14th day and one had a pancreatic fistula for seven days. One other patient with an adenoma of the thyroid gland had sinus tachycardia which quickly responded to therapy.

There was one postoperative death in the resected cases. This patient had a one-stage pancreato-duodenectomy, and although he had been jaundiced for more than four weeks his general condition appeared good. The operation was comparatively easy and there was less than the usual blood loss, but in spite of this he went



S — Stomach
P — Pancreas
J — Jejunum
C.B.D. — Common bile duct

Fig. 1.

into postoperative shock and responded slowly. He developed anuria and died on the ninth postoperative day.

Summary of Cases Subjected to Radical Operation

Some interesting features are demonstrated in the case histories of those patients found suitable for pancreato-duodenectomy.

Case 1.—G.M., aged 47. This man became ill with "flu-like" symptoms followed by jaundice three weeks before he was admitted to hospital by his family physician. He was treated for infectious hepatitis and was discharged four weeks later somewhat improved, only to return again three weeks later with more intense jaundice. On examination he was found to have an enlarged liver and a grossly distended gall-bladder. At operation a mass was revealed in the head of the pancreas. This was considered to be operable. A cholecyst-gastrostomy was performed; he slowly improved and four weeks later a radical pancreato - duodenectomy together with a cholecystectomy was carried out. The superior mesenteric vein was inadvertently torn during the dissection, but this was repaired with little difficulty. He made a good recovery apart from having a biliary fistula for 14 days. He returned to work as a draftsman for 12 months, then developed signs of recurrence and died 15 months after operation.

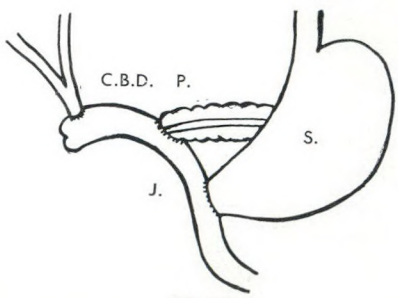


Fig. 2.

Case 2.—W.S., aged 46. This man came into hospital one year previously with a history of biliary colic and obstructive jaundice. A cholecystectomy and choledochostomy was performed, the common bile duct being literally impacted with many calculi; it was also noted at that time that the pancreas was diffusely swollen and indurated. He did well for four months, then again developed biliary colic and jaundice. When the abdomen was re-explored, the common bile duct was found to be grossly distended and the pancreas felt more swollen and lobulated but no definite mass was palpable in the head of the pancreas.

Biopsy of the pancreas showed chronic pancreatitis. (Biopsy was used in only two other resected cases, with negative results. No needle biopsies were done.) The common bile duct was reopened and a Cattell type of T-tube was inserted after exploring the ampulla of Vater. The T-tube was left *in situ* for four months and the patient appeared to be feeling well. After removal of the T-tube his symptoms recurred, with attacks of colicky pain associated with pyrexia and jaundice. The abdomen was again explored (i.e. one year after his first operation), and this time a definite hard mass was palpable in the peri-ampullary region. After one-stage pancreato-duodenectomy, he made an uneventful recovery and was discharged 14 days after operation. He was well and worked hard as a farmer for over two and a half years, then began to show signs of recurrence; he survived 35 months after his radical resection. This case demonstrated the difficulty in establishing a diagnosis; one wonders just when the carcinoma began to develop.

Case 3.—Mrs. E.C., aged 40. This woman was the mother of eight children. Two months before admission to hospital she became ill with a spasmodic pressure pain in the epigastric and right hypochondriac regions associated with nausea and vomiting. Soon after, she became jaundiced and was treated for infectious hepatitis by her family physician. On admission to hospital she was found to have an enlarged liver and an easily palpable gall-bladder. A cholecyst - jejunostomy was performed with marked improvement in her jaundice. Three weeks later a pancreato-duodenectomy was performed. A ductal car-

cinoma of the head of the pancreas pressing on the distal end of the common bile duct was demonstrated by the pathologist. She made an uneventful recovery and was discharged from hospital on the 14th postoperative day. Soon after discharge she became pregnant and nine months later was delivered of a normal baby, but shortly after her pregnancy she developed ascites and other signs of recurrence. She died 15 months after operation, and one wonders whether her pregnancy hastened the recurrence.

CASE 4.—G.H., aged 52. This man was referred with a 12 weeks' history of jaundice. He complained of vague upper abdominal pain, anorexia, fatigue and loss of weight. There was a history of duodenal ulcer for some years. The liver was enlarged but the gall-bladder was not palpable. At operation he was found to have a large posterior fixed duodenal ulcer and a mass in the head of the pancreas, and a cholecyst-jejunostomy was performed. After mobilization of the second portion of the duodenum the head of the pancreas was mobilized from the inferior vena cava and mesenteric vessels; although there were many firm adhesions and much inflammatory reaction, a radical operation was considered feasible. Two weeks later a pancreato-duodenectomy along with a sub-total gastrectomy and cholecystectomy was performed. He did well postoperatively and was discharged 18 days after operation. He survived 17 months.

CASE 5.—J.C., aged 69. This man was admitted to hospital with a six weeks' history of jaundice. This was preceded by mid-epigastric distress and anorexia. The liver was enlarged but the gall-bladder was not palpable. At operation a grossly distended gall-bladder and common bile duct were demonstrated. An irregular hard mass was palpable in the head of the pancreas.

A cholecyst-jejunostomy was performed and 14 days later a pancreato-duodenectomy. He made an uneventful recovery and survived for 18 months.

CASE 6.—R.D., aged 72. This man was admitted with a six weeks' history of jaundice and epigastric distress. Examination showed that his general condition was good, this including a complete investigation such as electrocardiogram, blood chemistry, and liver function tests. After the usual preoperative preparation a one-stage pancreato-duodenectomy was performed. The operation went well but in spite of this he developed postoperative shock and died of anuria on the ninth postoperative day. Biopsy of the specimen showed a well circumscribed ductal carcinoma of the head of the pancreas. There were no lymph node metastases. This patient probably should have had a biliary decompression before radical resection.

CASE 7.—Mrs. B.V.W., aged 68. This woman was admitted to hospital with a four weeks' history of jaundice preceded by vague epigastric pain and flatulence. The condition was initially diagnosed as infectious hepatitis by her family physician.

On examination, she was a large well nourished woman, intensely jaundiced, with an enlarged liver and a palpable gall-bladder. There was a palpable adenoma of the thyroid gland. On exploration the gall-bladder and common bile duct were grossly dilated and a 3 cm. mass was palpable in the head of the pancreas. Biopsy of a few regional lymph nodes and of the head of the pancreas failed to demonstrate neoplasia. A cholecyst-jejunostomy was performed, and three weeks later a radical pancreato-duodenectomy was carried out. The operation was difficult because of the obesity of the patient, but she made an uneventful recovery apart from sinus tachycardia. She is now living and well two and a half years after operation. The pathologist demonstrated that this was a well circumscribed lesion causing pressure on the terminal bile duct and duct of Wirsung.

CASE 8.—L.LeG., aged 41. This man's history was very interesting and instructive, since he was the only person in the series admitted without clinical evidence of jaundice. Four months previously he had been seen by his family physician complaining of spasmodic epigastric and right hypochondriac pain. At night the pain assumed a boring sensation referred to the 10th dorsal segment, and during the day the pain was referred in many directions. After a gastrointestinal investigation his appendix was removed. He returned two months later with an exacerbation of his symptoms, and was sent home on antispasmodics and an ulcer diet. Four weeks later he was readmitted to hospital. He had lost 20 lb. in weight, and was very depressed. This time he was seen by me in consultation.

A few findings pointed to pancreatic disease—namely a serum amylase value of 225 units, serum bilirubin 1 mg. %, and a positive occult blood reaction. At laparotomy a discrete mass was palpable in the head of the pancreas. A one-stage pancreato-duodenectomy was per-

formed. Some difficulty was encountered while dissecting the head of the pancreas off the mesenteric vessels, due to adhesions. Histological examination revealed a ductal carcinoma in the superior portion of the head of the pancreas, but the lymph nodes examined were negative. Except for a pancreatic fistula for seven days he made an uneventful recovery. This man returned to work as a printer for 11 months and then showed signs of disseminated recurrence and died 14 months after operation.

Among the eight patients found suitable for pancreato-duodenectomy, a one-stage operation was performed in three cases, and a two-stage operation in five cases. In all but one case the gall-bladder was removed. In the two-stage operation it was found easier to resect the cholecyst-jejunal anastomosis, this appearing to facilitate the radical resection en bloc. Thus a considerable segment of the common bile duct could be excised and a safer anastomosis accomplished between the common bile duct and jejunum with no common bile duct stump left to worry about.

Operative Procedures

Two methods were used: (a) In three cases an end-to-end (Billroth I type) gastro-jejunostomy was carried out, the pancreatic stump being implanted end-to-side into the jejunum just beyond this anastomosis. The common bile duct likewise was implanted into the jejunum some distance beyond the latter anastomosis and a side-to-side entero-enterostomy made opposite the site of implantation of the pancreas (Fig. 1).

(b) In the other five cases, the open end of the jejunum was closed, and the common bile duct, the pancreatic stump and the stomach were implanted (in that order from above downwards) end-to-side into the jejunum (Fig. 2).

The second method was found to be the preferable one, chiefly because it appeared to fit into the reconstruction more easily and reduced operation time by eliminating the entero-anastomosis. Postoperatively both procedures gave satisfactory function. There were few digestive complaints after either method.

Summary and Conclusions

A survey of 21 cases of carcinoma of the head of the pancreas, proven at operation, is presented. In eight of this series a radical pancreato-duodenectomy was performed with one operative death, while in eight other cases some palliative procedure was done. Of the seven patients who survived pancreato - duodenectomy, all remained alive and well for over one year, one patient being still alive 30 months after operation and enjoying good health. The average survival rate in the cases undergoing the palliative procedure was less than six months.

As a result of the experience gained in this series it is believed that pancreato-duodenectomy is a justifiable and indicated procedure in a considerable number of cases of carcinoma of the head of the pancreas.

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Résumé

L'auteur estime, après avoir passé en revue la littérature, que dans de nombreux cas de carcinome de la tête du pancréas, il existe des retards injustifiables entre le moment du diagnostic et le traitement. De plus, trop de chirurgiens se contentent d'une thérapeutique palliative de l'ictère par rétention. Son expérience se repose sur 21 cas de cancer de la tête du pancréas traités dans sa clientèle au cours des six dernières années.

L'âge moyen de ces malades—quatorze hommes et sept femmes—était de 60 ans et demi. Huit étaient justiciables d'une pancréato-duodénectomie; huit autres ne relevaient que d'interventions palliatives; les cinq derniers étaient inopérables. D'une façon générale, ces patients se plaignaient tout d'abord d'une douleur graduellement progressive; tous sauf un étaient ictériques, mais la jaunisse n'était habituellement pas le premier trouble. Le reste de la symptomatologie se résumait en anorexie, nausées, vomissement, fatigue générale, constipation et perte de poids. L'examen physique dénotait presque toujours un hypertrophie hépatique, et, dans un tiers des cas, la vésicule biliaire était palpable. La tumeur pancréatique n'était perceptible que dans quelques cas avancés. Les épreuves radiologiques ne furent pas d'un grand secours, bien qu'elles puissent apporter une contribution valable dans les cancers de l'ampoule ou du duodénum.

Il existait un retard inexpliqué entre l'apparition des premiers symptômes et le moment où le malade se décidait à consulter un médecin, ou celui où il était adressé au chirurgien. Le diagnostic et le traitement avaient été ceux d'hépatite infectieuse dans trois cas; et ceux de cholécystite dans plusieurs autres. Le diagnostic d'ictère par rétention fut en général posé d'après l'histoire clinique et les résultats de laboratoire, et, dans le doute, la laparotomie fut pratiquée. Les patients y furent préparés par l'administration de vitamines K, B, C, de glucose intraveineux et de transfusions sanguines si nécessaire.

A l'exploration, la découverte d'une masse dure et irrégulière dans la tête du pancréas ou dans la région de l'ampoule fut presque pathognomonique de cancer. Le pancréas était généralement œdémateux et induré, et les ganglions lymphatiques environnants toujours hypertrophiés. Chez les malades graves, et lorsque la jaunisse avait apparu depuis plus de deux semaines, l'opération était faite en deux temps. On provoquait d'abord une décompression biliaire par cholécysto-jéjunostomie; ceci ne facilitait pas la seconde intervention, mais en diminuait le risque. Les complications de la pancréato-duodénectomie furent peu importantes: un des patients souffrit d'une fistule biliaire temporaire et un autre d'une fistule pancréatique temporaire. L'anurie causa la mort d'un des opérés.

L'opération en un temps fut pratiquée dans trois cas, et celle en deux temps dans cinq cas. La technique de choix est de fermer le bout ouvert du jejunum et d'implanter de façon terminolatérale la voie biliaire commune, le moignon pancréatique et l'estomac dans le jejunum. Sept malades supportèrent la pancréato-duodénectomie; tous survécurent en bon état plus d'un an, et l'un d'eux est encore en vie 30 mois plus tard, jouissant d'une bonne santé. Le temps moyen de survie après les interventions palliatives fut de moins de six mois. L'auteur pense que la pancréato-duodénectomie est un traitement justifié et indiqué dans la plupart des cas de carcinome de la tête du pancréas.

SPINAL ANESTHESIA. John B. Dillon, Los Angeles, California. 61 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. $3.25.

In this sixty page monograph the author gives a clear description of his ideas on spinal anæsthesia derived from personal clinical experience. Each of the eleven chapters covers some aspect of the method in a few concise paragraphs followed by selected references. The illustrations are not many but instructive. The writer, an exponent of spinal anæsthesia, is apparently conservative in its use. Of timely interest is the statement that spinal anæsthesia is contraindicated for patients maintained on tranquillizers because of the unpredictable loss of vasomotor control. The use of tetracaine (Pontocaine) is advocated from the author's experience, it alone being described.

He states that "spinal anæsthesia should not be attempted by anyone who is not completely competent in the management of all types of general anæsthetic techniques", with which all anæsthetists should agree, but which may surprise some surgeons. This little book could provide a safe introduction for the anæsthetist interested in acquiring knowledge of spinal anæsthesia.

CHIRURGISCHE INDIKATIONEN: Rudolph zum 60. Geburtstage (Indications for Surgical Intervention. To Rudolph Nissen on his 60th birthday). 60 authors. 299 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1957. DM 42.

Dr. Nissen, who now exercises his surgical talents in Basel, Switzerland, is one of the great German wanderers. His early activities were in Munich and Berlin, where he was a favourite pupil of Sauerbruch. In 1933 he went to Constantinople and laid the foundations of thoracic surgery there. Later wanderings have taken him to New York, and finally to Basel. On the occasion of his sixtieth birthday his pupils and collaborators, including many eminent men from the United States, France, Germany, Switzerland, the United Kingdom, Scandinavia, Spain, Turkey, Egypt and Brazil, have contributed to a symposium on indications for surgery. Their writings cover many fields of surgical endeavour, including cardiac, thoracic, abdominal, urological, gynæcological, orthopædic and neurosurgery. They include contributions in French, German and English, so that it is necessary to be a good linguist to get full value from the symposium.

POSTOPERATIVE ACUTE PANCREATITIS*

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ACUTE PANCREATITIS is of interest to all medical men, but the disease as a complication after operation is of special interest to the surgeon. The writer has twice been embarrassed by the complication—once after performing a sphincterotomy and once after a partial gastrectomy.

CASE 1.—Mr. W.W., aged 69, was admitted to St. Paul's Hospital, Vancouver, on December 28, 1955. Several days later a laparotomy was performed and the preoperative suspicion of chronic relapsing pancreatitis was confirmed. The head of the pancreas was firm and in the region of the ampulla of Vater the firmness was so great that the presence of carcinoma was seriously considered. The gall-bladder was normal to inspection and palpation, as were the biliary ducts. Intraluminal exploration of the common bile duct, however, revealed a stricture at its termination. This stricture was dealt with by transduodenal sphincterotomy. The duct of Wirsung was not explored.

Postoperative progress was quite satisfactory for 24 hours. Immediately after this period, however, the patient became restless and began to suffer moderately severe abdominal pain. The pulse rate rose to 120. Within 12 hours the pain was excruciating, steady, and radiating. The pulse and temperature rose and the blood pressure fell to 80/60 mm. Hg. The return from the gastric suction was copious. The abdomen was tender, guarded and silent.

The differential diagnosis of the postoperative complications included coronary thrombosis, rupture of the duodenotomy closure, and acute pancreatitis. A serum amylase value of 64 (Winslow method) made the last diagnosis the one of choice.

Treatment included administration of oxygen, intravenous fluids, blood, meperidine (Demerol), and continuous Levin tube suction. Progress was unsatisfactory in spite of a temporary favourable response to therapy. The patient died on the eighth postoperative day.

Autopsy revealed hæmorrhagic pancreatic necrosis in the head and body of the pancreas with extensive necrosis of the retroperitoneal and mesenteric fat. There was no obstruction to the ducts of Wirsung or Santorini.

The case of Mr. W.W. illustrates the postoperative complication of acute pancreatitis in its severe hæmorrhagic and necrotic form. Of special interest were the early onset, the severity of symptoms, and the fatal termination.

CASE 2.—Mr. G.C., aged 50, was admitted to St. Paul's Hospital on April 7, 1956. The diagnosis on admission was of duodenal ulcer with penetration into the pancreas. At operation the preoperative diagnosis was confirmed. A partial gastrectomy was performed, dividing the duodenum proximal to the ulcer. The duodenal closure included insertion of a few reinforcing sutures into the adjacent pancreatic capsule. A Penrose drain was led down to the region of the duodenal stump.

The immediate postoperative progress was fairly satisfactory except that the patient experienced slightly more epigastric pain, tenderness, and muscle guarding than usual. The temperature and pulse rate remained mildly elevated. On the third postoperative day the Levin tube was removed but early vomiting necessitated its reinsertion. The patient was maintained in good biochemical and water balance but in spite of this the stomach refused to empty. A scout film of the abdomen showed an enlarged segment of small intestine in the left upper quadrant. A diagnosis of poorly functioning stoma or mechanical obstruction of the upper small bowel was made. Unfortunately the serum amylase value was not determined.

Reoperation was undertaken on the ninth postoperative day. The abdomen contained a small amount of clear peritoneal fluid. The head and body of the pancreas were firm and greatly enlarged. One small area of subcapsular hæmorrhage was seen. The retroperitoneal tissues were indurated and the base of the transverse mesocolon was three times its normal thickness. No areas of saponification were recognized. The proximal loop of jejunum was moderately dilated, as was the distal loop. The stoma appeared normal. An entero-enterostomy was performed between the proximal and distal loops in spite of the fact that the ileus appeared to be paralytic rather than mechanical.

At the close of the operation blood was withdrawn for a serum amylase test. The reading was a high normal at 16 (Winslow

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*Delivered before the British Columbia Surgical Society on May 3, 1957.

method). The postoperative course was uneventful.

The case of Mr. G.C. illustrates the postoperative complication of acute pancreatic œdema. The most significant feature is the comparatively mild nature of the symptoms. The case demonstrates how easy it is for this entity to go unrecognized unless the disease is constantly kept in mind.

Incidence

The incidence of postoperative acute pancreatitis is difficult to determine. It is certainly rare but probably not so rare as the reported cases would lead one to believe. Those who keep it in mind, and especially those who determine postoperative serum or urinary amylase values as a routine, find its incidence quite high. Millbourn[1] in 1949 reported an incidence of slightly under 10%. He performed a routine urinary amylase determination according to the Wohlgemuth procedure in 147 consecutive gastric resections. Thirteen cases had significantly elevated readings. Six of these cases were subclinical and had only transient diastasuria, two were clinically moderately severe, and five were clinically severe. Two of this last group ended fatally.

Warren[2] in 1954 reported seven examples with six deaths out of a total of 892 gastric resections, an incidence of slightly under 1%. He was forced to conclude that acute pancreatitis was the commonest cause of death after gastric resection at the Lahey Clinic for the period of study. Hallenbeck *et al.*[3] of the Mayo Clinic, reporting on biliary tract and pancreatic surgery for 1955, made reference to two cases of fatal postoperative acute pancreatitis, one after cholecyst-duodenostomy with biopsy of the pancreas and the other after sphincterotomy.

Pauls[4] reviewed the autopsy records in the Vancouver General Hospital for a 21 month period in 1955-1956. He found that acute hæmorrhagic pancreatitis had been the cause of death in nine cases, and of these four were in the nature of a postoperative complication. An analysis of the postoperative cases showed that one followed simple gastroenterostomy and three followed biliary tract surgery. The biliary tract surgery amounted to choledochotomy, with exploration of the common bile duct in each case and cholangiography in one case.

Schmieden and Sebening[5] in 1928 analyzed 145 cases of postoperative acute pancreatitis. The analysis showed that 91 cases were after gastric surgery, 38 after biliary surgery, seven after splenectomy, and four after biopsy of the pancreas.

MacKenzie[6] stated that in acute pancreatitis occurring without operation the incidence of the severe variety illustrated by Case 1 is 30%, and the incidence of the milder variety illustrated by Case 2 is 70%. It is probable that the same relative incidence occurs in the postoperative variety.

Etiology

The etiology of acute pancreatitis is not clear. Certainly there are many factors capable of bringing on the disease. Obstruction of the duct system by stricture or spasm of the sphincter of Oddi or by a stone impacted in the ampulla of Vater is an important factor. Reflux of bile up the pancreatic duct is undoubtedly an important factor too, but recent experimental work by Elliott, Williams, and Zollinger[7] suggests that the bile is only readily accepted within the pancreatic ducts if it has been previously mixed with pancreatic juice. In their animal experiments they found that the pancreas would readily accept, at low pressure, large quantities of an incubated mixture of bile and pancreatic juice. In their series, 100% of animals developed hæmorrhagic pancreatitis when subjected to this procedure. Other factors in etiology are a sudden increase in intraductal pressure, trauma, toxæmia, and ischæmia.

Certain special factors enter into the causation of the postoperative variety of acute pancreatitis. These factors will be dealt with under the section in this paper dealing with prevention.

Anatomical Factors in Etiology

Several aspects of the anatomy of the pancreas are worthy of special mention. The blood supply to the gland is so generous and its collateral circulation is so extensive that it is difficult to see how the occlusion

of any one artery supplying the pancreas could seriously interfere with its blood supply. Anatomists point out, however, that ligation of the gastroduodenal or the superior pancreatico-duodenal artery might result in ischæmia if certain anomalous arrangements of the blood supply should exist.

The duct of Santorini runs quite superficially in the head of the pancreas, sometimes within 0.5 centimetre of its anterior surface. The duct leaves the head to traverse the groove between the pancreas and the wall of the duodenum. It normally opens at the lesser papilla at least 4.5 cm. distal to the pylorus, but scar contracture of the duodenum may drag the papilla proximally.

The duct of Wirsung, as a rule, opens into the ampulla of Vater along with the common bile duct. Many investigators have made an attempt to determine how frequently the biliary and pancreatic ducts can be converted into a common channel by obstruction at the ampulla of Vater. Pauls[4] reviewed the operative and postoperative cholangiograms at the Vancouver General Hospital for 1956. Pancreatic reflux was demonstrated in 31 of 86 cholangiograms—an incidence of 36%. This is an average incidence for most of the reported series. Doubilet and Mulholland,[8] however, reported that they could visualize the whole pancreatic ductal system in 61% of operative cholangiograms.

Several other anatomical facts are worthy of note. The duct of Santorini, the so-called minor duct, is the larger of the two ducts in 10% of cases. This duct can act as the substitute for the duct of Wirsung whenever the two ducts communicate extensively within the gland. This substitution is possible in approximately one case out of three. On the other hand, the two ducts are entirely independent and fail to communicate within the gland in approximately two cases out of three.

Pathogenesis

The pathogenesis of acute pancreatitis is undoubtedly the same in the postoperative variety as in the disease occurring without operation. The initial lesion is in the duct either in the form of an increased permeability of its wall or a gross rupture of it. Following this, trypsin, lipase, and amylase are released into the surrounding pancreatic tissue. The activated trypsin acts on the blood vessels to produce hyalin degeneration and necrosis. Rupture of the blood vessels results, and pancreatic tissues become suffused with blood. Rupture of blood vessels also produces further ischæmia of pancreatic tissue and further release of enzymes. Once the process is initiated it becomes self perpetuating.

Pathology

The pathology of acute pancreatitis is well known and will not be elaborated upon in this paper. The first stage in the development of the disease is that of acute pancreatic œdema with its characteristic patches of fat necrosis. The second stage is that of acute pancreatic necrosis with its complications of thrombosis, hæmorrhage, suppuration and cyst formation.

Signs and Symptoms

The clinical picture of acute postoperative pancreatitis varies as to its severity and symptomatology. One of the most constant features, however, is the early onset of this complication. Acute pancreatitis occurs, as a rule, within 24 hours of operation. In the classic or extremely severe variety the pain is excruciating and shock comes early. Hyperpyrexia occurs, and death ensues in one to five days. In the moderately severe variety the pain is, as a rule, steady and upper abdominal. The pain often radiates to the flanks and back. Muscle guarding and tenderness are present. Vomiting occurs, and if the Levin tube is indwelling in the stomach there is a great increase in aspirated fluid. Paralytic ileus occurs and distension develops unless guarded against by continuous gastric suction. Rapid pulse and fever set in but shock is usually delayed. Death may or may not result. Case 1 is an example of the moderately severe variety.

In the mild type of acute postoperative pancreatitis the symptoms are slight, and often it is difficult to determine clinically the time of onset of the complication. The normal postoperative reaction might mask

the presence of mild acute pancreatitis. In this condition the upper abdominal or epigastric pain is slight and so are the tenderness and muscle guarding. Vomiting or an increase of gastric aspirations through a Levin tube occurs. Intestinal ileus is prone to set in, and a flat plate of the abdomen may show dilated loops confined to the upper jejunum. Clinical recovery usually takes place within two to ten days. Case 2 is an example of this type.

The serum and urinary amylase determinations assist in the diagnosis of acute postoperative pancreatitis and on the slightest suspicion of acute pancreatitis the tests should be performed. In the severe forms of the complication the test is invariably positive and in the mild form the test is positive at some time in the course of the disease.

Diagnosis

The diagnosis of postoperative acute pancreatitis should not be too difficult so long as the possibility of the complication is kept in mind. MacKenzie[6] stated that "cultivating an awareness of the lesion is of the greatest importance in the early diagnosis of acute pancreatitis." Actually, the signs and symptoms are the same as those of acute pancreatitis occurring at any other time, except in so far as they may be masked by the signs and symptoms normally present in a postoperative patient. A most important diagnostic point is the early onset. The serum and urinary amylase values are significantly raised.

Other postoperative complications such as cardiovascular accident, hæmorrhage, leak of an anastomosis, or rupture of a duodenal stump, enter into the differential diagnosis.

Prevention

The problem of preventing postoperative acute pancreatitis is a real challenge. Preoperatively and postoperatively the patient is maintained in a good state of nutrition and biochemical balance. In those cases particularly prone to the complication of acute pancreatitis, morphine, which causes spasm of the sphincter of Oddi, is withheld, and meperidine (Demerol) is used as a substitute. Duodenal stasis is reduced to a minimum by the use of continuous suction through a Levin tube.

The surgeon at the operating-table must take certain precautions lest his technical manœuvres should predispose to acute pancreatitis.

Gastric ulcer. — Mobilization of the stomach when there is a large gastric ulcer penetrating into the pancreas requires special care. Sharp dissection is permissible down to the point where the stomach and pancreas are apparently inseparably fused, but beyond this point blunt dissection is to be preferred. The thumb and index finger may be used to pinch the stomach from the ulcer bed. The ulcer bed is left alone and not excised, cauterized, or covered over.

Resection of the stomach for carcinoma occasionally requires a direct attack on the pancreas. Resection of the involved segment of pancreas is to be preferred to a superficial excision of invaded tissue.

Duodenal ulcer. — Operation performed for duodenal ulcer may occasionally be quite traumatic to the pancreas, its blood supply, or its duct system. Particularly hazardous in this regard is operation for deeply penetrating ulcer associated with much periduodenitis. In these cases the surgeon is well advised to act conservatively and to leave the ulcer intact. The procedure of choice more often than not is a gastric resection in which the duodenum is divided and closed proximal to the ulcer. McKittrick and associates,[9] however, recommend a two-stage operation. Dragstedt *et al.*[10] advocate gastroenterostomy and vagotomy.

In dissecting the duodenum from the pancreas and in closing the duodenal stump the following points in technique are worthy of mention.

1. The pancreas is treated with great respect, neither incised nor contused.

2. The base of a penetrating ulcer, like that of a gastric ulcer, is not excised, cauterized or covered over.

3. Sutures placed through the pancreatic capsule in an attempt to reinforce an otherwise insecurely closed duodenal stump are inserted with great care. Such sutures when placed in the scarred pancreas adjacent to the ulcer are probably not too traumatic.

but even the insertion of these is in principle wrong.

4. The gastroduodenal artery and its tributary, the superior pancreatico-duodenal artery, are identified and gently handled in case avulsion or needling should cause dangerous hæmatomata.

5. The ligation of either of these two arteries for one reason or another is performed only after consideration has been given to the possible presence of a significant anomaly of the blood supply to the pancreas.

6. The duct of Santorini is searched for in the ulcer base, so that the duodenal stump can be closed in such a way that the pancreatic ferments would not have a free exit to the peritoneal cavity. If the duct should be found within the ulcer base, the stump might be closed by the method popularized by Nissen.[11]

7. Attempting to identify both the major and the minor papillæ by palpation within the open duodenum is a worthwhile procedure, especially in those dissections which encroach upon the site of the minor papilla.

8. Great care is taken in mobilizing the duodenum from the head of the pancreas to identify the structures traversing the groove between the apposed organs. Any structure in this area is looked upon with suspicion lest it be the duct of Santorini. In this regard the findings of Schmieden and Sebening[5] are interesting. Eleven out of 91, that is over 12% of cases of acute pancreatitis following gastric surgery, were related to ligation of the duct of Santorini.

9. The site of the ampulla of Vater and hence the termination of the duct of Wirsung may require exact identification in difficult cases. In these, the common bile duct is opened and a catheter or the long arm of a T-tube is inserted as recommended by Marshall.[12]

In spite of all reasonable precautions, damage to the ducts does occur on occasion, but correction of the damage is usually not too difficult. Sometimes, leading a Penrose or sump drain down to the site of damage is sufficient. The damaged duct may be sutured over a T-tube or anastomosed to the jejunum. At other times an injured duct may be dealt with by ligation, but naturally one would not yield to the temptation of simply ligating the duct unless a functional connection between the two pancreatic ducts was demonstrated.

Biliary tract surgery.—Since surgery of the biliary tract carries with it the threat of postoperative acute pancreatitis, certain points in technique are worthy of mention. As regards cholecystectomy there is little to be said except that any concomitant disease of the common bile duct or the ampulla of Vater is not to be overlooked.

In common bile duct surgery the following points of technique are important:

1. Instrumentation of the duct by probe and mobilization of the head of the pancreas require gentleness.

2. Dilatation of the sphincter or transduodenal sphincterotomy is performed with consideration of the proximity of the pancreas.

3. Leaving a catheter or the long arm of a T-tube passing through the ampulla is probably safe if the right sized tube is used. It is only fair to point out, however, that the procedure has been condemned by some on the grounds that such a tube, on occasion, may block the pancreatic duct. Smith and associates[13] have reported cases of acute pancreatitis after the use of the long arm T-tube for transampullary biliary drainage. Cattell[14] of the Lahey Clinic stated: "I do not believe that the long arm T-tube blocks the duct of Wirsung. I use one somewhat smaller than the diameter of the duct."

4. Lavage of the common bile duct is undoubtedly safe if certain precautions are taken. It is obvious, for example, that too forceful a stream of water should not be used in lavage. A stream of moderate force may be directed proximally towards the liver but only the most gentle stream should be directed distally. Unless this precaution is taken, bile and debris may be forced up the pancreatic duct. The hazard of causing a retrograde flow up the pancreatic duct is increased whenever there is a distal obstruction, either within the ampulla of Vater or at the sphincter of Oddi. The writer became fully aware of this hazard in 1955 when a patient of his died of acute pancreatitis after lavage of the common bile duct and sphincterotomy. This case

was reported previously in this paper. Since then the rule has been formulated and followed that "lavage of the common bile duct in a distal direction is performed only after the patency of the duct has been determined or established." Ferris[15] of the Mayo Clinic emphasized the care which one must take in lavaging through a T-tube after the common bile duct has been closed around the long arm of the tube.

5. Operative and postoperative cholangiography should be performed by injecting a moderate volume of dye, slowly and under low pressure.

Pancreatic surgery.—Major surgery of the pancreas, strangely enough, is not too frequently followed by acute pancreatitis. Paradoxically, however, a minor procedure such as biopsy has been so frequently followed by this complication that in most clinics biopsy has been abandoned and reliance is now placed upon finger and thumb palpation to determine the disease process within the pancreas.

Treatment

The treatment of postoperative acute pancreatitis is as a rule medical, so long as the diagnosis can be made with confidence. The treatment of this postoperative complication must of necessity be compatible with the postoperative measures already adopted to take care of the particular needs of the patient. Prerequisites of good management are frequent assessment of the patient's condition and willingness to adjust or supplement established therapy.

The cardinal principles of therapy are relief of pain, supportive therapy, and suppression of pancreatic secretion. Meperidine (Demerol), which causes less sphincter of Oddi spasm than morphine, is the drug of choice for the relief of pain. If shock is present meperidine is administered intravenously. Amyl nitrite may be of help if no shock exists. Procaine blocks, either of the splanchnic paravertebral or continuous epidural varieties, may be employed.

Supportive therapy includes the administration of intravenous fluids, electrolytes, blood, calories, insulin, antibiotics, and oxygen.

Suppression of pancreatic secretion is worth while. All oral feedings are withheld and naso-gastric suction is established. An anticholinergic drug such as methantheline bromide (Banthine) is administered intravenously. Insulin is given in an attempt to combat hyperglycæmia, a condition which can cause overstimulation of the islet cells of the pancreas.

Prognosis

The outlook in the acute fulminating type is poor. Warren,[2] as pointed out earlier in this paper, reported six deaths in seven cases. Millbourn,[1] on the other hand, dealing mostly with the mild type, reported two deaths in 13 cases.

Summary

Two cases of postoperative acute pancreatitis are described; one patient died and the other recovered. The incidence, etiology, pathogenesis, and pathology of this disease are commented upon, as well as the signs and symptoms, diagnosis, prevention, treatment and prognosis. Considerable emphasis is placed on certain points of surgical technique considered important in the etiology and prevention of acute postoperative pancreatitis.

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Résumé

La pancréatite aiguë est une affection qui intéresse tous les médecins, mais lorsqu'elle apparaît comme complication post-opératoire, elle devient tout particulièrement importante pour le chirurgien.

L'auteur publie deux cas provenant de sa pratique personnelle. Le premier est celui d'un homme de 69 ans admis à l'hôpital pour pancréatite chronique, qui, le surlendemain d'une sphinctérectomie transduodénale pour stricture de l'ampoule, présenta une poussée de pancréatite aiguë (avec test de l'amylase à 64), et mourut huit jours plus tard malgré une thérapeutique active (oxygène, solutés physiologiques intraveineux, Démérol et aspiration continue par tube de Levin). Le diagnostic fut confirmé à l'autopsie.

Dans le second cas, il s'agissait d'un homme de 50 ans, admis pour ulcère duodénal pénétrant dans la tête du pancréas; ce diagnostic fut confirmé à l'exploration et une gastrectomie partielle fut pratiquée en soignant tout particulièrement les sutures du moignon duodénal et de la capsule pancréatique. Les suites post-opératoires furent médiocres, puis mauvaises: un syndrome d'iléus s'installa et, pensant à une obstruction mécanique au niveau de la bouche d'anastomose, on réintervint, ce qui permit de trouver un pancréas induré et œdémateux dont la capsule recouvrait quelques suffusions hémorragiques. La bouche était normale: il s'agissait donc de pancréatite aiguë accompagnée d'iléus paralytique. Dans ce cas les suites opératoires furent excellentes.

L'auteur passe en revue la littérature, d'où il ressort que la fréquence des pancréatites aiguës post-opératoires est sans doute plus grande qu'on ne le suppose généralement. Le tout est d'y penser. Il discute ensuite l'étiologie encore peu claire de cette affection, qui semble relever de l'obstruction ou de l'occlusion du sphincter d'Oddi et du reflux biliaire dans les voies pancréatiques. Il insiste sur certains détails de l'anatomie des canaux pancréatiques et de la vascularisation de la glande. La pathogénie de la pancréatite aiguë post-opératoire est sans doute analogue à celle de la pancréatite aiguë spontanée. Une perméabilité exagérée ou une lésion de la paroi du canal excréteur permet aux enzymes de passer dans le parenchyme du tissu glandulaire: une digestion des parois vasculaires se fait alors, qui entraîne la formation d'hémorragies, puis des ischémies locales suivies de nécroses qui augmentent de plus en plus; le processus, une fois déclenché, devient irréversible et se continue de lui-même. La pancréatite post-opératoire apparaît le plus souvent 24 heures après une intervention; la douleur est violente, siégeant à la partie supérieure de l'abdomen et irradiant vers les flancs; la défense musculaire s'installe; le choc est intense et rapide; l'hyperthermie est grave; les vomissements sont très fréquents. La mort survient dans les cas graves au bout de quelques jours. Dans les cas bénins, le diagnostic clinique peut être difficile du fait du peu d'intensité des symptômes. Une aide précieuse est apportée par le laboratoire: c'est le dosage de l'amylase, qui rend le dépistage de cette complication aisé à condition d'y penser.

La prévention de la pancréatite consiste à bien préparer le patient au point de vue métabolique, et à rejeter la morphine, capable de provoquer des spasmes du sphincter d'Oddi; enfin, l'aspiration continue évitera la stase duodénale. Pour ce qui est de la technique chirurgicale proprement dite, il conviendra d'être très prudent dans la dissection des ulcères gastriques pénétrant dans le pancréas et notamment de préférer à la dissection tranchante, la dissection "au doigt" ou "mousse". Dans les cas d'ulcères duodénaux avec périduodénite importante, il faudra savoir s'arrêter à temps et renoncer à des manœuvres trop compliquées ou dangereuses. Le pancréas lui-même ne devra jamais être incisé ou manipulé brutalement; le fond d'un ulcère adhérent ne sera jamais excisé ni enfoui, mais simplement cautérisé avec précaution; les sutures de la capsule pancréatique seront toujours effectuées avec la plus grande légèreté; les artères gastro-duodénales et pancréatico-duodénales doivent être reconnues, et il faut savoir que parfois, du fait d'anomalies anatomiques, leur ligature peut entrainer des troubles circulatoires au niveau du pancréas; le canal de Santorini doit être visualisé, et son ouverture ne sera jamais laissée béante.

Dans la chirurgie biliaire, les lavages des canaux seront faits avec délicatesse; d'autre part, il ne faut pas oublier que les tubes en T sont susceptibles de provoquer l'occlusion du canal pancréatique.

Le traitement de la pancréatite aiguë post-opératoire est médical. Il consiste en sédation de la douleur par le Démérol, injections de solutés intraveineux, transfusions en cas de besoin, insuline éventuellement, oxygénothérapie et aspiration continue par sonde. Le prognostic dépend de la gravité du cas.

THE EFFECT OF NARCOTICS ON THE SERUM AMYLASE*

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ACUTE PANCREATITIS must be considered in the differential diagnosis of any acute upper abdominal pain. An increased concentration of amylase in the serum may be diagnostic of this condition, but it has been stated that the administration of a narcotic for the relief of pain may, in itself, produce an elevated amylase.[1-3] Some experiments in animals[4, 5] and in man[6, 7] suggest, however, that narcotics do not cause an increase in the concentration of amylase. The obvious clinical significance of this question and the availability of a rapid method for the estimation of serum amylase led us to re-examine the problem.

METHOD

Thirty male patients between the ages of 19 and 60 years with no clinical evidence of pancreatic disease were the experimental subjects. In each of three groups of 10 patients the effect of one of the following pairs of tests on the concentration of amylase in the serum was investigated:

1. Morphine grain 1/6 without breakfast vs. meperidine (Demerol) 100 mg. without breakfast.

2. Morphine grain 1/6 with breakfast vs. meperidine 100 mg. with breakfast.

3. Morphine grain 1/4 with breakfast vs. morphine grain 1/4 without breakfast.

After the patient had fasted overnight a control amylase value was obtained, and this was followed immediately by the administration of the narcotic with or without breakfast. The concentration of amylase was then measured at one-half, one, two, and 24 hours after the narcotic had been given, and in a few patients after four hours as well. The two tests in each group were carried out on successive days, a table of random numbers being used to determine which of the pair would be done on the first day. In the first group of 10 patients one test was carried out in the morning before an operation and the other the following morning. The control values of these two tests, therefore, provided an estimation of the effect of the operative procedure on the serum amylase. The operations included hernia repair, drainage of abscess, removal of fibroma, triple arthrodesis, meniscectomy, closed reduction of fracture, lumbar sympathectomy, cholecystectomy, and cholecystectomy with exploration of the common bile duct.

The method of King[8] was used to measure the serum amylase because of the speed of its performance—10 minutes as compared to two hours for the method of Somogyi.[9] The King and Somogyi methods had been found in this laboratory to give almost identical results.

Standard statistical methods were used for the analysis.[10] Paired data were used to correct for individual variation in the control serum amylase value and in the response to the narcotic.

RESULTS

Two tests of the effect of a narcotic on the concentration of amylase in the serum were carried out on each of 30 patients (Tables I, II, and III). The mean of 59 control values of serum amylase was 121 ± 40 (S.D.) units with a range of 75 to 260 units. One unusually high postoperative control value, which is discussed below, was not included in the calculation of the mean because of the probable presence of acute pancreatitis.

Neither morphine nor meperidine (Demerol) had any significant effect on the amylase (paired data), and in fact its concentration after the administration of a narcotic only rarely differed from the control value. The combination of a narcotic with a meal, which provided a stimulus for pancreatic secretion, still did not produce an increase in serum amylase.

Major and minor operative procedures had no effect on the amylase with the exception of one case in which a small soft

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TABLE I.—Effect of Narcotics on Serum Amylase Concentration

		Morphine grain 1/6				*Meperidine 100 mg.*				*Pre-op.‡ vs.*
Operation	*Age*	*C**	*½ hr.†*	*1 hr.†*	*2 hr.†*	*C*	*½ hr.*	*1 hr.*	*2 hr.*	*post-op.*
Drainage of hand	30	100	0	−11	−11	123	0	+10	+10	+23
Medial meniscectomy	30	145	0	0	0	123	0	0	0	−22
Inguinal hernia repair	50	100	+14	+14	+14	114	0	0	0	−14
Removal palmar fibroma	60	134	0	0	0	133	−10	−10	−10	− 1
Triple arthrodesis	19	177	0	0	0	200	−22	−22	−40	−23
Inguinal hernia repair	19	178	0	0	0	145	0	0	0	+33
Cholecystectomy	51	107	0	0	0	107	0	0	0	0
Reduction of metacarpal fracture	19	107	0	0	0	114	0	0	0	− 7
Lumbar sympathectomy	34	200	0	0	0	179	0	0	0	−21
Cholecystectomy and exploration bile duct	19	100	0	0	0	2130	0	0	0	+2030

*C = Control serum amylase.
†½ hr., 1 hr., 2 hr. = change in serum amylase ½ hr., 1 hr., and 2 hr. after the administration of the narcotic.
‡Pre-op. vs. Post-op. = change in control serum amylase.

rubber catheter was passed through the ampulla of Vater into the duodenum in the course of an exploration of the common bile duct. On the first postoperative day a greatly increased amylase value (2130 units) was found, which slowly declined to normal in a week. The patient had no symptoms or signs of acute pancreatitis except for abdominal pain, which was no greater than that usually associated with the operative procedure. It is interesting that the administration of a narcotic did not change the amylase concentration in this situation. In the patient who underwent cholecystectomy without exploration of the common bile duct no increase in the concentration of amylase occurred.

Discussion

These results indicate that, in male patients with no known pancreatic disease, narcotics have no effect on the concentration of amylase in the serum even when the pancreas is secreting after a meal. Several investigators have found that narcotics do produce an increased concentration of amylase in some patients.[1-3] This variance between our results and those previously reported may have been produced by samples from different populations: we have used patients with no known pancreatic disease, whereas previous investigations have been carried out on patients with disease of the pancreas, biliary tract, duodenum, or stomach. In about one-third

TABLE II.—Effect of Napcotics + Meal on Serum Amylase Concentration

		Morphine grain 1/6 + meal				*Meperidine 100 mg. + meal*			
Diagnosis	*Age*	*C**	*½ hr.†*	*1 hr.†*	*2 hr.†*	*C*	*½ hr.*	*1 hr.*	*2 hr.*
Low back pain	34	160	0	0	0	133	0	0	0
Low back pain	27	188	0	0	0	100	0	0	0
Fracture tibia	18	89	—	+45	+56	100	0	0	0
Hammer toe	18	100	0	0	0	107	0	0	0
Low back pain	51	123	0	0	0	114	0	0	0
Multiple fractures	27	80	0	0	+43	94	0	0	0
Varicose veins	44	124	0	0	0	124	0	0	0
Osteochondritis dissecans	21	80	0	0	0	75	0	0	0
Low back pain	53	133	0	0	0	145	0	0	0
Medial meniscus tear	32	89	0	0	0	100	0	0	0

*Control serum amylase.
†½ hr., 1 hr., 2 hr. = Change in serum amylase ½ hr., 1 hr., and 2 hr. after the administration of the narcotic and a meal.

TABLE III.—Effect of Morphine Grain ¼ on Serum Amylase Concentration

Diagnosis	Age	Morphine grain ¼				Morphine grain ¼ + meal			
		C*	½ hr.†	1 hr.†	2 hr.†	C	½ hr.	1 hr.	2 hr.
Perianal abscess	43	80	0	0	0	80	0	0	0
Ischiorectal abscess	39	114	0	0	0	114	0	0	0
Fracture zygoma	22	80	0	0	0	75	0	0	0
Stasis ulceration	36	76	0	0	0	89	0	0	0
Pilonidal sinus	23	106	0	0	0	94	0	0	0
Chronic tonsillitis	19	100	0	0	0	80	0	0	0
Herniated disc	39	267	0	0	0	267	0	0	0
Acromioclavicular dislocation	21	100	0	0	0	100	0	0	0
Thrombosed hæmorrhoid	34	100	0	0	0	100	0	0	0
Neurofibroma	29	145	0	0	0	120	0	0	0

*C = Control serum amylase.
†½ hr., 1 hr., 2 hr. = Change in serum amylase ½ hr., 1 hr., and 2 hr. after the administration of the narcotic with and without a meal.

of such patients an increase in the concentration of serum amylase follows the administration of a narcotic. This result is of importance in the interpretation of the result of a serum amylase estimation in the patient who has the clinical picture of acute pancreatitis but who has previously received a narcotic for the relief of pain. In the absence of pancreatic disease the amylase concentration will not be increased by the narcotic; but, if pancreatic disease is present, the narcotic, if it has any effect, can only make this more evident by further increasing the amylase concentration.

The pathogenesis of pancreatitis may be discussed in the light of this difference between the response of normal patients and of patients with disease in the region of the pancreas. One hypothesis is that there is a common channel proximal to the sphincter of Oddi into which both the main pancreatic duct and the common bile duct empty, and that disease of this channel may produce increased pressure in the pancreatic duct and reflux of bile into the pancreas with resulting pancreatitis. The increased serum amylase observed in some patients after the administration of a narcotic is said to be caused by occlusion of the common channel by the resulting spasm of the sphincter of Oddi.[11-13] In none of our 30 patients without pancreatic disease was an increased amylase concentration found, and it would appear, therefore, that in none was there a common channel. On the other hand, Doubilet and Mulholland[13] demonstrated the presence of a common channel in all but three of 319 patients with pancreatitis. It can be concluded, therefore, that a functioning common channel is an infrequent occurrence in the general population, but that when it is present the chance of the individual's developing pancreatitis is greatly enhanced.

The finding of an increased concentration of amylase in the serum postoperatively in the one patient who underwent exploration of the common bile duct directed our attention to this phenomenon, which we have since observed on several occasions. This rise is probably caused by œdema of the ampulla of Vater or by our handling of the head of the pancreas. It has not, however, been associated with any appreciable increase in morbidity.

Summary

In 30 males with no evidence of pancreatic disease the administration of a narcotic with or without a meal did not produce an increase in the concentration of amylase in the serum. It is, therefore, unnecessary to consider these factors in the evaluation of the clinical finding of an increased amylase concentration. It was also deduced that a common channel for the biliary and pancreatic ducts proximal to the sphincter of Oddi was not present in any of these patients, but that when it did occur the chance for the development of pancreatitis would be enhanced.

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RÉSUMÉ

Dans tout syndrome douloureux de l'étage supérieur de l'abdomen, le chirurgien doit penser à la pancréatite aiguë; une élévation dans le taux de l'amylase du sérum peut confirmer le diagnostic. Toutefois on a prétendu que les narcotiques donnés pour calmer la douleur peuvent par eux-mêmes augmenter l'amylase et fausser la valeur de cette épreuve. L'auteur a voulu se rendre compte par lui-même de la valeur de ces assertions.

Trente hommes âgés de 19 à 60 ans, et ne souffrant d'aucune lésion pancréatique connue ont reçu des doses de 1/4 à 1/6 de grain de morphine, ou 100 milligrammes de Démérol, à jeun ou après un repas. La concentration d'amylase fut déterminée après 1/2 heure, 1 heure, 2 heures et 24 heures. La méthode de King, qui prend 10 minutes alors que la méthode de Somogyi en prend 120, fut employée. Les deux épreuves donnent des résultats presque identiques.

L'analyse statistique des résultats montra que l'amylase sérique demeura dans la moyenne normale après l'administration de morphine ou de Démérol. La combinaison d'un narcotique avec un repas, qui stimule la sécrétion pancréatique, ne change pas les résultats.

L'auteur conclut de cette étude qu'en l'absence de trouble pancréatique, l'amylase sérique n'est pas augmentée par un narcotique; mais s'il y a lésion du pancréas, le sédatif peut la faire ressortir en en augmentant le taux dans le sérum.

PRINCIPLES OF GENERAL SURGICAL MANAGEMENT. H. A. F. Dudley, University of Edinburgh. 203 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1958. $4.70.

The techniques employed and the clinical wisdom to judge when to use them in the care of surgical patients on the ward form a very important part of a surgeon's training. "Principles of General Surgical Management" is an outline of the present practices at the Royal Infirmary of Edinburgh as developed by house surgeons under Sir James Learmonth and Professor John Bruce. Preoperative preparation, shock, antibiotics, chest complications, the care of wounds, postoperative care, thrombo-embolism, intravenous therapy, urinary complications are discussed and the practical procedures used are given in detail, often with sketches and photos.

Interns will appreciate the clear descriptions of procedures and laboratory tests carried out in investigation and treatment outside the operating-room, the list of proprietary and approved names of newer drugs and the table of normal values and samples required for various blood tests. The clinician may find himself surprised by the way the interns' work has changed since his time, and though he may differ with some opinions expressed, must be stimulated by this description of the practices carried out at one of the great surgical schools of the world.

A SIMPLE PLAN OF POSTOPERATIVE PARENTERAL FLUID THERAPY*

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Discussions of the metabolism of water and electrolytes are often complex and difficult to follow. Attempts to base practical therapy on such discussions commonly result in the collection of large quantities of biochemical data and the placing of a severe strain on medical, nursing and laboratory facilities without proportional benefit to the patient. Some degree of simplification is essential if current knowledge of water and electrolytes is to be effectively applied to routine medical care.

Postoperative patients who have abnormal gastrointestinal losses and cannot take food or fluids by mouth form the largest group requiring attention to the metabolism of water and electrolytes. The purpose of this communication is to present a simple plan of postoperative parenteral fluid therapy applicable to the majority of these patients. No simple plan can be used when there are marked deficits of water and electrolytes prior to operation. Under these circumstances, the treatment in each case must be adjusted to meet specific requirements. However, most patients at the time of operation have no serious deficits. In spite of this, severe deficits demanding intensive specific treatment develop all too frequently in such patients when temporary dysfunction of the gastrointestinal tract prolongs the period of parenteral fluid therapy. There is thus a clear need for a simple plan of postoperative fluid therapy which can be ordered for most patients and which will prevent the development of water and electrolyte imbalance even if prolonged intravenous therapy should prove necessary.

It is well known that disturbances of water and electrolyte metabolism are rare once the patient is able to eat and drink. This suggests that the regulatory mechanisms of the body can conserve and eliminate water and electrolytes in accordance with needs, provided these substances are supplied in adequate and safe amounts. Talbot and his colleagues[1] determined the physiological minimum requirements and maximum tolerances for sodium, potassium, chloride, lactate, phosphate and water. They suggested[2] the use of a solution of 5% glucose containing amounts of these electrolytes within the safe working ranges, namely each litre of the solution to contain 40 mEq. of sodium, 35 mEq. of potassium, 40 mEq. of chloride, 20 mEq. of lactate and 15 mEq. of phosphate. It is of interest to compare the intake of electrolytes when the patient is on a soft diet with that obtained from 2 litres of Talbot's solution (Fig. 1). The only major dissimilarity is in the amounts of calcium and phosphate. This is unimportant since calcium and phosphate are poorly absorbed from the intestine and there are adequate stores available in the skeleton. The soundness of this approach prompted trial of the solution developed by Talbot *et al.*[2] in a simplified plan of postoperative fluid therapy for adult patients in our hospital.

Outline of Plan of Postoperative Fluid Therapy

Phase 1

On the day of operation, the patient receives 2 litres of 5% glucose in water.

Phase 2

Thereafter, if the 24 hour urinary output is greater than 500 ml., the patient receives daily 2 litres of Talbot's solution* (to cover

*Ionosol-T, Abbott Laboratories

*From the Departments of Metabolism and Surgery, The Montreal General Hospital.
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†Since submission of this article, Dr. Bauld has met with a fatal accident on July 20, 1958.
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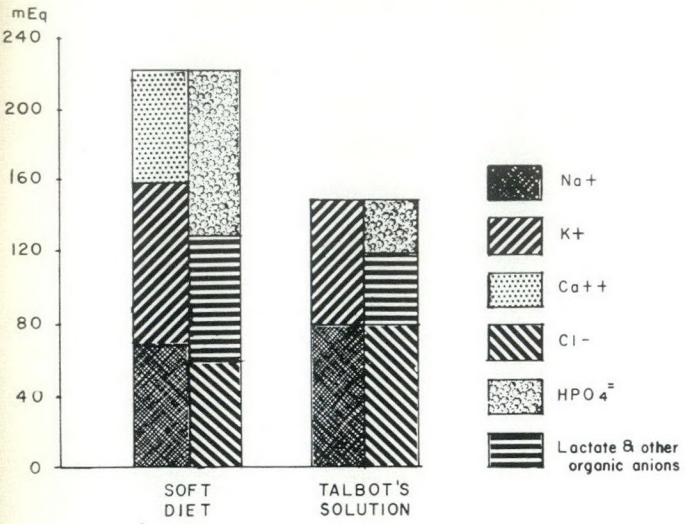

Fig. 1.—Comparison of electrolyte intake from typical soft diet and from Talbot's solution (2 litres).

urinary and insensible loss) plus volume for volume replacement by Talbot's solution of gastrointestinal losses up to 1.5 litres. Gastrointestinal losses greater than 1.5 litres are replaced quantitatively with 0.9% saline in 5% glucose containing 1 g. of calcium gluconate per litre.

Blood is given as required.

No oral intake is permitted while the plan is in force. This applies whether the patient is intubated for gastrointestinal suction or not.

This plan is based upon the following considerations:

1. *Use of 5% glucose in water on the day of operation.*—Water is supplied in sufficient amount to cover urinary and insensible loss. Sodium is not included because of the marked retention of this ion in the immediate postoperative period and the common practice of giving saline with blood in the operating-room. Potassium is avoided because of the possibility of acute renal failure due to shock or other complications.

2. *Use of Talbot's solution.*—Once the possibility of acute renal failure has been eliminated by a urinary output greater than 500 ml. per 24 hours, sodium and potassium within the safe working range are provided in the form of Talbot's solution.

3. *Use of supplementary saline.*—Gastrointestinal fluids contain much more sodium than potassium.[3] Since Talbot's solution contains almost equivalent amounts of sodium and potassium, its use alone to replace very large gastrointestinal losses results in the administration of too much potassium and too little sodium. To avoid this, gastrointestinal losses in excess of 1.5 litres are replaced quantitatively with 0.9% saline (in 5% glucose).

4. *Use of calcium gluconate.*—Calcium cannot be incorporated in Talbot's solution because of the presence of phosphate. Large and long continued gastrointestinal losses may lead to calcium deficiency.

5. *Avoidance of oral intake.*—While the patient is on this plan, the need for water is being met parenterally. If water or other fluid is given by mouth, the intake will exceed the requirement and water intoxication may develop. With patients on continuous gastric suction, there is the additional well-known danger of electrolyte depletion from gastric lavage.

Method of Assessment of Plan

Selection of Cases

The plan has been used routinely in the care of adult patients in the surgical wards of our hospital for two years.

Ten cases were selected for special biochemical studies. These were patients who had undergone major abdominal operations and required intravenous fluid therapy for at least four days postoperatively. None had major deficits before operation, but for at least four days after operation all had abnormal gastrointestinal losses. Their ages ranged from 30 to 72 years. Seven were older than 50 years, and one (Ch.) had pre-existing renal disease.

Special Biochemical Studies

The following estimations were made in the 10 cases selected for special studies:

Before operation—

Blood urea nitrogen; serum sodium, potassium, bicarbonate, calcium and inorganic phosphorus.

After operation—

1. Serum sodium, potassium and bicarbonate on the day after operation and on alternate days thereafter;

2. Serum calcium and inorganic phosphorus, and blood urea nitrogen on the second day after operation and on alternate days thereafter;

3. Urine volume, osmolarity, sodium, potassium, titratable acidity and ammonia daily.

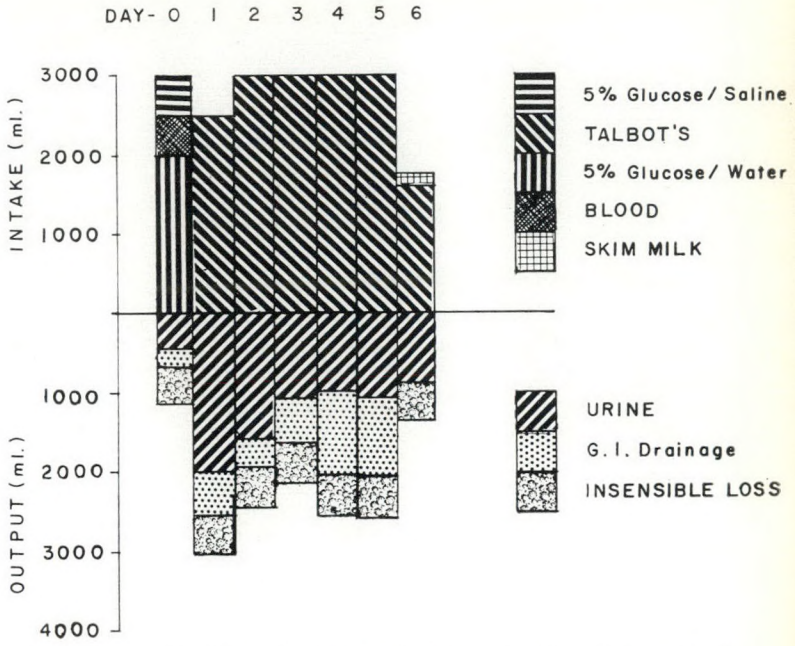

Fig. 2.—Case Br. Chart of intake and output: resection of sigmoid colon.

Results

The plan has been used routinely in the care of many hundreds of surgical cases in our hospital. From the clinical standpoint, the results have been excellent. No patient has developed a deficit. Pulmonary œdema attributable to intravenous therapy has not been encountered. The gastrointestinal tract has been put at rest for adequate periods of time with a consequent reduction in the incidence of postoperative ileus. The number of biochemical tests has been greatly reduced.

The special biochemical studies in the 10 selected cases support this clinical assessment. The results in Table I show that abnormalities of serum electrolyte concentrations were minor and transitory. The results in Table II show the rates of urinary output of water, electrolytes and total solids to have been almost invariably within the physiological ranges. Thus the normal serum electrolyte values were achieved without taxing the renal reserves.

Illustrative Case (Br.)

The daily fluid balance of a patient maintained on the plan is shown in Fig. 2. The patient was a woman, aged 70, with a carcinoma of the sigmoid colon. There was no evidence of preoperative deficits. The insensible fluid loss was estimated as 1000 ml. Routine gastric suction was employed for six days after the sigmoid resection. Oral intake was not permitted until the sixth postoperative day.

As shown on the graph, 2000 ml. of 5% glucose in water were given on the day of operation (Phase 1 of the plan). On subsequent days, only Talbot's solution was used (Phase 2), in 2500 to 3000 ml. quantities depending on the volume of the gastric drainage. Since gastrointestinal losses never exceeded 1500 ml. per day, no supplementary saline was required.

This patient was one of the 10 cases selected for special biochemical studies. Results of these are shown in Tables I and II (Case Br.). All values were normal throughout the course of therapy. It should be emphasized that treatment was ordered from day to day according to our plan and not on the basis of these laboratory determinations.

Discussion

Parenteral fluid therapy in the postoperative period is commonly based on the use

TABLE I.—Blood Studies

	*Serum Na mEq./l. (135-150)**				*Serum K mEq./l. (3.5-5.0)**				*Serum HCO_3 mEq./l. (21-31)**				*Serum Ca mg./100 ml. (9.0-11.0)**				*Serum P mg./100 ml. (2.5-4.5)**				*Blood urea nitrogen mg./100 ml. (10-20)**			
Day		*Postop.*				*Postop.*				*Postop.*				*Postop.*				*Postop.*				*Postop.*		
Patient	*Pre-op.*	*+1*	*+3*	*+5*	*Pre-op.*	*+1*	*+3*	*+5*	*Pre-op.*	*+1*	*+3*	*+5*	*Pre-op.*	*+2*	*+4*	*+6*	*Pre-op.*	*+2*	*+4*	*+6*	*Pre-op.*	*+2*	*+4*	*+6*
Ba	144	139	135	132	4.7	4.7	4.6	5.1	21	18	21	21	9.0	8.0	9.2	9.9	3.6	2.8	2.1	2.9	34	22	15	14
Br	144	140	141	136	4.2	4.6	4.5	4.5	22	26	26	29	9.7	10.2	9.2	10.6	2.7	3.6	4.0	4.4	12	14	17	25
Ol	145	135	138	138	4.4	4.5	4.1	5.0	14	20	24	25	9.4	10.8	9.8		2.8	2.9	3.6		20	16	15	
Wa	143	135	136	141	4.9	4.4	4.5	4.0	18	22	22	23	11.0	10.2	10.8		2.6	2.8	3.1		11		14	
Ge	142	136	140		4.5	4.0	4.2		19	24	12		9.7	9.8	9.5		2.7	2.6	3.0		14	20	14	
Ch	139	137	136		4.3	4.6	4.9		17	20	17		8.9	8.7	10.8		3.5	5.2	5.2		24	50	48	
Al	139	149	136		4.1	4.1	3.9		26	25	24		10.5		9.7		3.7		2.6		15	14	8	
Be	138	134	139	133	4.5	3.7	3.9	4.5	23	27	29	29	10.9	11.7	10.4		2.8	2.9	3.8	2.7	11	9	12	15
Ma	147	139	144	129	4.2	4.3	3.1	4.6	26	25			9.8	9.3	9.6		3.1	2.4	3.0		21	29	17	
Mck	140	136	128	136	3.5	3.5	3.6	4.6	29	33	30	23	9.9	10.0	9.9	9.3	2.7	2.1	3.1	3.8	12	18	24	36

*Range of normal values.

of solutions similar in composition to extracellular fluid to maintain serum electrolyte concentrations at normal levels. Such procedures present two serious defects. Firstly, extracellular and intracellular fluids differ markedly in composition (Fig. 3) and the volume of intracellular fluid is more than twice the volume of extracellular fluid. Use of solutions resembling extracellular fluid therefore cannot adequately meet total needs. Secondly, attempts to maintain normal serum electrolyte concentrations in-

TABLE II.—URINE STUDIES

	*Urine volumes ml./m²/24 hr. (500-7500)**					*Urine Na mEq./m²/24 hr. (10-500)**					*Urine K mEq./m²/24 hr. (10-500)**					*Urine ammonium mEq./m²/24 hr. (10-130)**					*Urine osmolarity mOsm./l. (100-1425)***				
Postop. day / *Patient*	*+1*	*+2*	*+3*	*+4*	*+5*	*+1*	*+2*	*+3*	*+4*	*+5*	*+1*	*+2*	*+3*	*+4*	*+5*	*+1*	*+2*	*+3*	*+4*	*+5*	*+1*	*+2*	*+3*	*+4*	*+5*
Ba.....	1280	2760	1490	1460		72	203	167	132		62	48	38	72		15.5	26.4	23.0	28.0		472	298	435	396	
Br.....	1430	900	610	550	580	16	20	15	17	38	33	48	42	43	56	16.3	12.5	19.6	16.6	8.1	251	365	539	615	627
Ol.....	1850	1250	920	1300		122	70	43	86		73	63	42	57		45.4	79.1	56.8			407	451	459	426	
Wa.....	530	720	580	465	535	29	70	43	31	54	53	51	35	30	40		36.8	23.1	17.4	21.1	785	752	727	820	
Ge.....	1030	1200	1000	855		46	25	41	57		48	37	39	40		40.0	25.0	19.1	23.2		420	239	326	403	
Ch.....	1140	1840	1620	2035		55	125	131	155		56	78	67	86		14.0	17.0	13.0	17.0		432	413	460	444	
Al.....	600	480	925	1100		29	70	41	39		39	66	39	31		17.6	39.2	52.8	45.0		818	577	419	502	
Be.....	890	600	500	490	430	78	55	32	60	28	63	50	41	60	56	44.0	39.8	37.7	34.4	25.7	606	401	550	1069	908
Ma.....	480	1100	1005	1605		29	36	74	88		39	48	28	42		33.6	19.5	9.0	8.6		704	280	266	208	
Mck.....	800	1140	420	1000	935	62	62	65	16	26	62	80	37	43	37	7.4	10.0	4.4	7.3	9.6	417	372	420	260	359

*Physiological minimum-maximum rates of urinary output expressed per square metre of body surface (m^2) per 24 hours.[4]
**Physiological minimum-maximum expressed as millimoles of solute per litre of water.

volve laborious collection of specimens, large numbers of biochemical tests and calculations which are often theoretically unsound. For example, serum sodium values do not reflect the needs of the body for sodium in the presence of dehydration[6] or œdema.[7] These discrepancies between serum sodium concentration and total circulating sodium can be overcome by measurement of plasma volume.[8] This is, however, a technically difficult procedure. Another illustration of the unreliability of

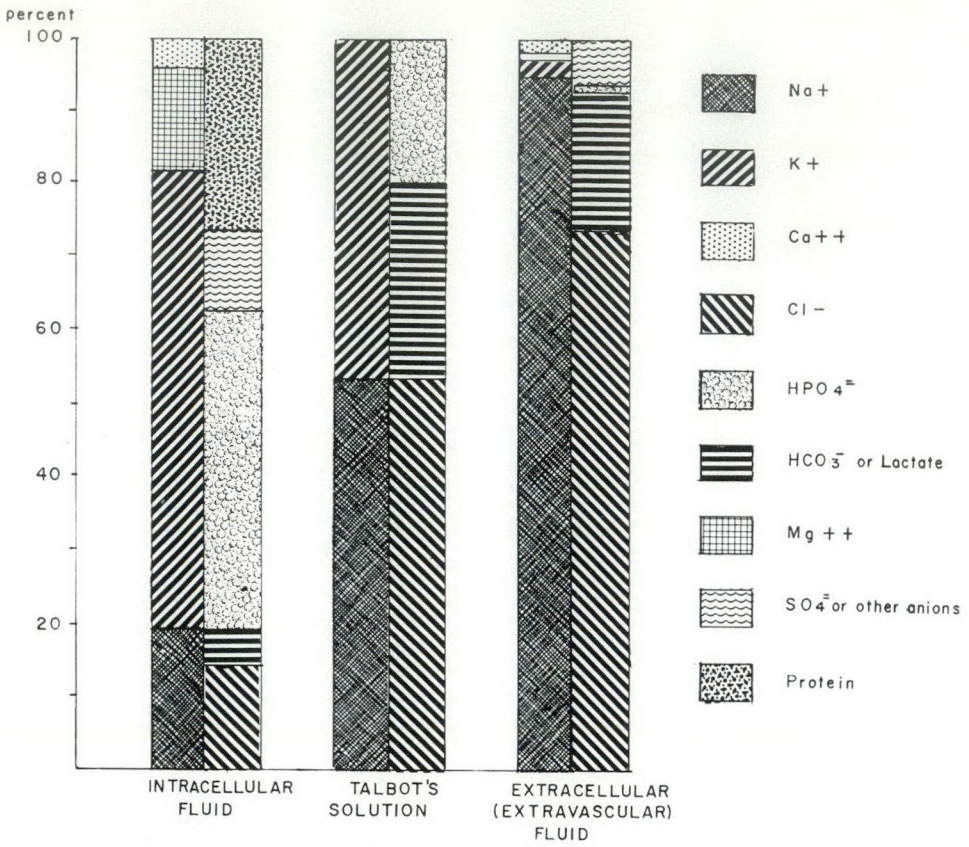

Fig. 3.—Percentage electrolyte content of Talbot's solution and body fluids.[5]

serum electrolyte concentrations is provided by potassium. In acidosis the serum potassium is raised by transfer of this ion from the cells, even when the body potassium is markedly depleted; the reverse occurs with alkalosis.[9]

These disadvantages have led others[3] to base parenteral fluid therapy in the postoperative period on the use of solutions similar in composition to the fluids lost. This procedure also presents certain defects. Individual variations in the composition of gastrointestinal fluids are so great[3] that accurate estimations of losses cannot be made without performing daily analyses. When such analyses are not done, the potassium loss is often grossly underestimmated.

The plan described in this paper does not involve the use of a solution similar in composition to extracellular fluid. Indeed, Talbot's solution has a composition intermediate between that of extracellular and that of intracellular fluid (Fig. 3). The plan is not based on measurements of electrolyte concentrations in serum or gastrointestinal fluids. It is therefore not dependent upon complex procedures requiring specially trained teams of biochemists, surgeons and nurses. It can be used in the majority of postoperative patients and adequately maintains water and electrolyte balance even when gastrointestinal losses are great. If parenteral therapy is prolonged, the plan must of course be supplemented by the provision of protein and other essential nutrients.

It must be emphasized that our plan is not designed to correct pre-existing deficits of water and electrolytes. Although it will eventually accomplish this, rapid correction of deficits requires specific replacement.

Summary

A simple plan of parenteral fluid therapy has been devised for postoperative

patients who have abnormal gastrointestinal losses and cannot take food or fluids by mouth. This plan is suitable for patients without serious deficits of water and electrolytes before operation. Its adequacy has been proven by satisfactory clinical results in many hundreds of cases and by detailed biochemical studies in ten patients.

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Résumé

L'étude théorique du métabolisme de l'eau et des électrolytes est compliquée, et il est presque impossible d'étayer sur elle des règles ayant une valeur clinique réelle sans surcharger considérablement les équipes médico-chirurgicales par une foule de tests et de dosages de laboratoire. Dans ce domaine, une certaine simplification est indispensable dans la pratique des traitements.

La majorité des patients justiciables de cette thérapeutique est celle des opérés, privés de toute ingestion par la bouche et ayant de fortes déperditions au niveau du tractus gastro-intestinal. Dès qu'une alimentation normale peut être rétablie, il n'y a plus de troubles à craindre: il est certain que l'organisme est tout à fait capable de choisir et d'utiliser ce dont il a besoin, à condition que les matières premières nécessaires lui soient fournies. A cet effet, Talbot, après avoir déterminé les besoins physiologiques minima en sodium, potassium, chlorures, lactates et phosphates, a mis au point une solution destinée à l'usage parentéral, dont la formule est rappelée.

Le plan de traitement post-opératoire par injections liquidiennes qui est proposé par les auteurs se résume ainsi: (1) Le jour de l'opération, le patient reçoit 2 litres d'une solution aqueuse de glucose à 5%. Ceci vise a compenser les pertes cachées et les excrétions urinaires. A ce stade, on supprime le sodium par crainte de sa rétention post-opératoire et le potassium à cause des possibilités d'insuffisance rénale. (2) Par la suite, si l'excrétion urinaire est supérieure à 500 c.c./24 heures, on donne journellement 2 litres de solution de Talbot plus une quantité de cette même solution égale à celle des pertes gastro-intestinales, jusqu'à concurrence de 1.5 litres. D'autre part, si la déperdition gastro-intestinale dépasse 1.5 litres, on administrera une solution aqueuse de chlorure de sodium à 0.9% et de glucose à 5%, additionnée de 1 g. de gluconate de calcium par litre. Le sang sera transfusé en cas de besoin; les ingestions orales seront interdites. La solution de Talbot, employée exclusivement, entraînerait un excès de potassium et une insuffisance de sodium; de plus, le calcium ne peut y être ajouté à cause des phosphates qu'elle contient.

Ce plan a été appliqué chez tous les patients chirurgicaux du Montreal General Hospital depuis deux ans. Parmi eux, une dizaine a été étudiée à fond au point de vue biochimique. Il s'agissait de grands opérés abdominaux, dont l'âge variait entre 30 et 72 ans, traités par injections parentérales pendant quatre jours. Un ensemble d'examens biochimiques fut pratiqué chez eux avant et après l'intervention; les résultats en sont fournis dans des tableaux. Un de ces cas est exposé plus en détail à titre d'exemple.

Les fluides intra- et extra-cellulaires de l'organisme diffèrent de façon marquée dans leur composition et leur volume. C'est pourquoi la solution de Talbot, dont la formule est intermédiaire entre celles de ces deux fluides, permet de rétablir les équilibres physiologiques sans nécessiter de recourir à des analyses de contrôle innombrables et compliquées. Ce plan est donc simple et sûr; bien entendu, il est applicable seulement chez des sujets sains du point de vue humoral et lorsque des déficits existent avant l'opération il faut en entreprendre le traitement spécifique.

PERFORATION OF THE SMALL INTESTINE FROM NON-PENETRATING TRAUMA

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PERFORATION of the small intestine from non-penetrating abdominal trauma, which may be caused by a blunt force, blow, or fall, is occasionally referred to as subcutaneous rupture of the bowel. This is not a common occurrence, and in view of the fact that frequently there may be absence of early signs of intestinal injury, diagnosis and treatment in these cases are often delayed. Because the morbidity and mortality are high in this condition, early recognition of the perforation, and its immediate surgical treatment are necessary.

Penetrating wounds of the abdomen – percutaneous injuries – are more common during wartime, and the possibility of injury to the intestinal viscera is apparent. The injury to the bowel may be caused by bullets, knives, and other objects. In civilian practice non-penetrating wounds of the abdomen are more common, and present a more complex problem in diagnosis and management.

Non-penetrating abdominal trauma appears to be increasing, because of the more frequent use of mechanized equipment in industry and farming, and the increasing number of automobile accidents. In many of these accidents there may be quite severe concomitant injuries, and the possibility of intestinal rupture is not considered until the signs of peritonitis are quite marked; whereas in abdominal injuries due to penetrating trauma, the patient is always carefully observed. Thus it is essential that all patients with non-penetrating abdominal trauma be admitted to hospital for careful and repeated examinations of the abdomen by the same surgeon. In patients with abdominal injuries due to traffic accidents, Root and Christensen[10] have recommended immediate surgical exploration in patients with abdominal symptoms persisting or increasing in severity, irrespective of the development of signs and symptoms which involve other systems.

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HISTORY

Aristotle was aware of the extreme fragility of the intestine in animals, and stated that "A slight blow will cause rupture, without injury to the skin." In the seventeenth century, post mortem reports appeared in the literature, of intestinal perforation due to kicks by horses, blows, and falls, which often appeared to be trivial. The first successful operation for subcutaneous rupture of the intestine is said to have been done by Sacherus, in 1720. In 1923, Massie[8] reported 34 cases occurring over a 24 year period at Guy's Hospital, London, with a mortality of 78% in the 31 who consented to operation. This series included four perforations of the stomach and one of the cæcum. Subcutaneous rupture of the jejunum was reviewed by Counseller and McCormack[5] in 1935, and in 1942, Poer and Woliver[9] collected from the literature a group of 1476 cases of perforation of the small bowel due to non-penetrating trauma. The mortality rate in this series was 72%.

MECHANISM OF PRODUCTION

The mechanism of production of rupture of the small bowel from non-penetrating trauma may be difficult to determine. Three chief methods have been proposed: (1) It may be due to a crushing force, in which the intestine is caught between the traumatic agent and some fixed structure such as the spine or pelvis, and the direct force is applied perpendicular to the abdomen. Aird also stresses the importance of a hernia as a predisposing cause, which fixes a portion of the bowel in the hernial sac. (2) A tearing force applied tangentially to the abdominal wall may cause the bowel to be torn from its attachments, and often tears the mesentery as well. A tear of the mesentery does not appear to influence the prognosis, except when it lies along the line of attachment to the bowel, and the blood supply of the bowel is interrupted. (3) A bursting force may arise from increased

intra-intestinal pressure, exerted by fluid or gas caught in the bowel between angulations of the wall. Previous disease or deformity, such as peptic ulceration or diverticulum, does not appear to increase the likelihood of rupture or injury at these sites. Injury to the duodenum is a serious lesion, as the intestinal contents may escape extraperitoneally and cause widespread infection of the retroperitoneal tissues. The injury to the small bowel may be a complete transection, perforation, rupture of the outer coat, or contusion. Contusion, though the least severe, may be the most dangerous, as symptoms and signs may be delayed for several days when a quiet perforation occurs.

Diagnosis

In some cases, the diagnosis of this condition may be obvious, the signs of peritonitis developing immediately after injury. Frequently the abdominal signs may be delayed for hours or days, and the ultimate in surgical judgment is required. The diagnosis may be obscured when there are other severe injuries requiring immediate treatment, and the management of these cases may be extremely difficult. When an intra-abdominal injury is suspected, careful and repeated examinations are necessary to establish a diagnosis. This must include examination of the hernial sites, as well as rectal examination and, in the female, bimanual examination, to determine the presence of peritoneal irritation or bulging in the cul-de-sac. Auscultation of the abdomen is an important diagnostic aid. The absence or marked reduction of bowel sounds in one quadrant of the abdomen may indicate a localized injury to the bowel. A roentgenogram of the abdomen will demonstrate free gas in the peritoneal cavity in 50% of cases, and, if indicated, an emergency cystogram serves to establish the diagnosis of a ruptured vesical bladder. In view of the high mortality associated with delay in the diagnosis, a diagnostic laparotomy is indicated, if there is any doubt concerning the possibility of rupture of a hollow viscus.

Delay in the onset of symptoms and signs may be due to the size of the opening, and the portion of the bowel involved. The wounds may vary from small contusions to large perforations and ragged tears, and the signs and symptoms are typically those of chemical or bacterial peritonitis. In the delayed cases, it has been suggested that a mesenteric hæmatoma may develop, which cuts off the blood supply of the bowel. Subsequently, necrosis and gangrene of the intestinal wall occur, with perforations several hours or even days after the original trauma. Spillage of the intestinal contents is facilitated by the onset of peristalsis after the intake of food or fluids. Cope has suggested that intestinal paresis follows the injury to the bowel, and during this period the exudate of plastic lymph seals off the perforation if it is small. After the patient recovers from shock, or takes food, the peristaltic action is resumed, with consequent leakage. This may account for the early presence of peristaltic sounds, as well as the absence of abdominal findings. Spillage of the intestinal contents may be prevented by a plugging of the opening by the mucosal layers of the bowel; in cases of complete transverse division of the bowel, the contraction of the circular muscles of the divided end may temporarily prevent leakage. In 1950, Johnson and Cherniack reported the complete transection of the bowel at the duodeno-jejunal junction, which was successfully repaired. The higher the location of the injury in the gastrointestinal tract, the more chemical will be the nature of the peritoneal irritation, whereas bacterial contamination will occur in the lower small bowel.

Results

At the Toronto Western Hospital, from 1942 to 1956, there were 23 cases of subcutaneous rupture of the small bowel, which is approximately two cases yearly. The age incidence ranged from 10 to 86 years, with 19 males and four females. The size of the bowel perforation was usually small, approximately 1.5 cm. or less in diameter, one case having two perforations. As noted in Table I, there were seven patients with herniæ, six inguinal and one a postoperative ventral hernia. In six of these cases, the bowel ruptured into the peritoneal cavity, and in one case the operative note did not

report the site of perforation. As pointed out by Aird, a blow to the abdomen increases the intra-abdominal pressure, but when the abdominal cavity is completely shut off, the pressure is equalized in the bowel and the peritoneal cavity. If there is an outlet in the hernial sac, rupture of the bowel is more likely, as the pressure is not equalized in the peritoneal cavity and in the hernia. As a result, rupture of the bowel is apt to occur in the abdominal cavity, as demonstrated in our group of cases.

TABLE I.—Subcutaneous Rupture of Small Bowel (Toronto Western Hospital, 1942-56)

Rupture of the small bowel	23 cases
Operations	22 "
Hernia	7 "
Mortality	3 (13%)

The mortality in the 23 cases was 13%. This included two postoperative deaths, and one patient who was admitted to the hospital in shock, with a large ventral hernia, and died 16 hours after the onset of pain. The admission diagnosis was "dissecting aneurysm", and the abdomen was not explored. At post mortem, the small bowel in the ventral hernia was intact, but rupture had occurred in the abdominal cavity. In one of the two postoperative deaths, operation was delayed 10 hours after perforation of the terminal ileum, and in the remaining case, a man 86 years of age had two perforations in the terminal ileum with operation 18 hours after trauma. The most interesting case in this series occurred in a 57 year old hospital employee, who gave a history of gastric resection for duodenal ulcer 13 years before admission to the Toronto Western Hospital. His symptoms began about 15 minutes after consuming a large meal, along with generous amounts of alcohol. He presented himself to the Emergency Department six hours after the onset of symptoms, with generalized abdominal pain and rigidity. There was no immediate history of trauma, and in view of his previous history of peptic ulcer a preoperative diagnosis of "perforated stomal ulcer" was made. In this case, the rupture of the intestine was located about 18 inches (45 cm.) from the ileocæcal region, and the perforation was oversewn with a double layer of gastrointestinal suture. The patient promptly recovered, with no complications. Subsequently a history was obtained of a blow to the right lower quadrant three days before admission, at which time he had moderately severe pain, which gradually passed off during the day. A biopsy was taken at the time of operation, and this showed normal mucous membrane at the site of perforation.

TABLE II.—Type of Trauma

Fall	6 cases
Blow	6 "
Traffic accident	7 "
Kick	2 "
Football accident	1 case
Not stated	1 "

The type of trauma varies considerably (Table II). In recent years, car accidents associated with multiple injuries have increased, and in this group many of the perforations have occurred in the mid portion of the small bowel. Nevertheless, the most common sites are within the first and last two feet (60 cm.) of the small bowel, near the fixed points of the small intestine (Table III). The surgical complications in this group of cases are few. The most serious was a subphrenic abscess one month after operation, and in two other cases there were superficial wound infections.

TABLE III.—Site of Intestinal Rupture

Duodenum	1 case
Upper jejunum	6 cases
Lower ileum	8 "
Mid small bowel	4 "
Not stated	4 "

Treatment

The treatment of perforation of the small bowel is usually simple. Small perforations can usually be closed with a two-layer suture of the wall, in a transverse direction. Resection may be required with larger perforations and transection of the bowel. Careful search of the bowel is often necessary to locate the rupture and to avoid missing multiple lesions.

SUMMARY

The diagnosis of subcutaneous rupture of the small bowel may be exceedingly difficult. All cases of non-penetrating abdominal trauma, no matter how trivial, should be kept under close observation, and if there is any doubt, laparotomy should be carried out within six to eight hours. Although there may be concomitant injuries, the hazards associated with delay greatly exceed the risks of surgery. The perforation is usually single, and tends to occur in the upper jejunum and the terminal ileum, which are near the fixed points of the small intestine. The prognosis appears to be better in lesions of the upper jejunum which are operated on early. The mortality rate in this series is 13%.

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RÉSUMÉ

La perforation du petit intestin par contusion, aussi appelée rupture sous-cutanée de l'intestin, se constate surtout dans la vie civile, par opposition à la rupture par plaie pénétrante de l'abdomen qu'on rencontre surtout dans la pratique militaire. La lésion se retrouve surtout dans les accidents de la route et de la ferme; dans plusieurs de ces accidents, les lésions concomitantes sont plus évidentes et ce n'est que lorsque les signes de péritonite apparaissent qu'on est porté à penser à la perforation, alors que dans les plaies perforantes de l'abdomen, la rupture intestinale est systématiquement recherchée.

Poer et Woliver, en 1942, ont colligé 1476 cas dans la littérature, avec une mortalité de 72%. Le mécanisme de perforation peut être difficile à établir. On l'a attribué à l'écrasement, l'arrachement et l'éclatement. On a constaté que la rupture siège surtout dans le premier pied (30 cm.) et dans les deux derniers pieds (60 cm.) du grêle, près des points fixes d'attache du petit intestin. Il semble que l'existence d'une hernie prédispose aussi à la perforation, à cause d'une différence de pression dans les segments sus- et sous-jacents au sac herniaire.

Une lésion, en soi pas toujours grave, peut être dangereuse à cause de l'apparition tardive des phénomènes péritonéaux. Dans certains cas, le diagnostic est évident, les symptômes de péritonite apparaissent tôt après le traumatisme. Fréquemment les symptômes tardent à apparaître; si une lésion intra-abdominale est soupçonnée, des examens répétés et attentifs sont nécessaires. Il faut examiner les points herniaires, faire des touchers rectaux et chez la femme des touchers vaginaux qui peuvent montrer une collection dans le Douglas. L'auscultation et la radiographie apportent de précieux éléments de diagnostic. S'il y a le moindre doute, la laparotomie est indiquée.

Dans bien des cas la réparation en deux plans suffit; on fera une résection si la lésion est étendue. L'examen méthodique de tout le petit intestin est des plus importants car il évitera de laisser passer inaperçue une petite perforation surprise.

L'auteur rapporte une série de 23 cas qui se sont présentés au Toronto Western Hospital de 1942 à 1956. Dans la plupart des cas la perforation mesurait 1.5 cm. Sept patients avaient en plus une hernie, soit 30%. Il y eut quatre décès, soit 13%, dont deux décès après opération.

REHABILITATION OF THE ELDERLY AMPUTEE

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REHABILITATION of the elderly patient after lower limb amputation presents a difficult and time-consuming problem. Success can be judged best by the use made of a prosthesis. This paper reviews a series of appropriate cases, indicates the results obtained and suggests how rehabilitation may be facilitated.

The literature contains little material dealing with this particular subject. McKenzie,[1] however, has written an informative paper, which confirms many features recorded herein. Few other articles discuss the matter beyond the stage of healing of the amputation. Two alternative impressions are left — that no problem arises after wound healing or that the problem is insurmountable. The truth appears to lie somewhere between.

The sequelæ of arteriosclerotic peripheral vascular disease — infection, ulceration, gangrene or persistent pain due to ischæmia — usually necessitate high amputation. It is such amputees who present the greatest rehabilitation problem, since the lesion necessitating operation is merely a local and obvious manifestation of cardiovascular degeneration.

REVIEW OF CASES

At Sunnybrook Hospital, Department of Veterans Affairs, Toronto, during 1948-1956 over 170 major lower limb amputations were performed. Selection of cases for review was based on the following criteria:

1. The amputation was necessitated by arteriosclerotic peripheral vascular disease.
2. The patient was over the age of 55 years at the time of operation.
3. Amputation was performed above the level of the knee joint.
4. Amputation was not bilateral.

Patients with diabetes were included, as were those in whom embolism may have initiated gangrene.

Eighty-five patients, all males, were thus selected. In six instances, follow-up information was inadequate. Seventy-nine therefore remained for study (Table I). In most instances, those still living and possessing a prosthesis were interviewed.

Requirements of successful function with a prosthesis were minimal. Its use out-of-doors twice a week, with canes if necessary but not crutches, was accounted satisfactory. Mere wearing of the prosthesis around the house was not considered to indicate successful use. The minimum satisfactory time requirement was six months from the time of discharge from treatment. This period was chosen since few patients progressed from amputation to discharge from treatment in a lesser time. Indeed, if illness supervened — and this was not rare — the interval was longer. We considered that the duration of successful use of a prosthesis should equal at least an average time spent in recovery and convalescence.

Regardless of level of amputation, cases were divided into five groups (Table II).

GROUP I: *Patients who died within four months of amputation — 13.*

The average age at amputation was 66 years.

In the main, the cause of death was degenerative cardiovascular disease. There were no operative deaths, although amputation was never refused, no matter how poor the patient's condition. In only three instances — one pulmonary embolism, one pneumonia and one myocardial infarction— could the operation be implicated as precipitating an early demise.

GROUP II: *Patients not considered fit enough to use a prosthesis — 29.*

The average age at amputation was 72 years.

The number deceased within two years of amputation was 12 (41%). The reasons for unfitness were as follows:

Marked mental and/or physical debility 5; degenerative diseases (mainly cardiovas-

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TABLE I.—Types of Amputation in 79 Cases Studied

Gritti-Stokes amputations	68
Low or mid-thigh amputations	11
Total	79

cular, but sometimes multiple) 17; inadequate circulation in the opposite leg 5; deformity of the opposite leg 1; malignant disease elsewhere 1; total 29.

Group III: *Patients whose training was commenced but later discontinued — 8.*

The average age at amputation was 71 years.

The number deceased within two years of amputation was 4 (50%).

Reasons for discontinuing training: Degenerative diseases 4; inadequate circulation in the opposite leg 2; death 2; total 8.

Almost half the total number of cases is contained in Groups II and III. It is speculative how many might have become ambulant under an easier training regimen. It is of interest that one man in Group II who was visited had used crutches for six years after amputation. He seemed to have been more mobile during that period than many of those accounted successful in Group V.

Group IV: *Patients trained and discharged, but who did not use their prosthesis adequately — 17.*

The average age at amputation was 68 years.

The number deceased within two years of amputation was 8 (47%). Five patients died before the minimum requirement period of six months was up. It was difficult in some of the remainder to elicit the exact cause of failure to use the prosthesis. Indeed, several gave more than one reason. The main causes *stated* were as follows: "Shortness of breath" 5; symptoms referable to the other leg 4; fear of falling 2; amputation of the other leg 1; death (as noted) 5; total 17.

TABLE II.—Results of Amputation in 79 Cases

Group I:	Patients who died within four months of amputation	13
Group II:	Patients not considered fit enough to use a prosthesis	29
Group III:	Patients whose training was commenced but later discontinued	8
Group IV:	Patients trained and discharged but who did not use their prosthesis adequately	17
Group V:	Patients who used a prosthesis successfully for at least six months	12
Total		79

It is significant that fear of falling was noted by four others. It was felt from questioning that this fear was a bigger factor than indicated. Stump pain was not a major concern of any. Although there is no common cause for failure in this group, degenerative disease and/or fear may be cited as the reasons in most instances. Again, an easier and simpler program might prove more fruitful.

Group V: *Patients who used a prosthesis successfully for at least six months — 12.*

The average age at amputation was 68 years.

The average duration of use of the prosthesis was 2 years (1-4 years). There were no deaths within two years of amputation. This last fact is particularly noteworthy. It probably indicates that degenerative changes, notably cardiovascular, were less advanced in this group. Edwards[2] has noted from examination of arteriograms that if a localized block is present in the limb artery, the progress of the arteriosclerotic process is slower and the prognosis for life and limb better than when the arterial disease is diffuse. In this latter situation, deterioration of the patient's condition is much more rapid. The use of an arterial by-pass graft will save some limbs which show a segmental arterial block. If not, selection of cases for prosthetic training after amputation may be aided.

When interviewing patients in the last two groups an impression was gained that, although a physical difference may have been present, there was also a psychological difference. Those in Group IV seemed more easily upset and frightened

than those in Group V, who showed stouter moral fibre.

Discussion

It is important for purposes of comparison with other series that the figures used in determining success or failure be defined accurately. Possible variations in calculation are shown in Table III. A true picture can be obtained only if the number in whom limb fitting was attempted is compared with the number accounted successful by *follow-up*. In this series, the incidence was 32.5%. McKenzie,[1] in patients of similar age and using the same definition of figures for computation, obtained an incidence of 49.7%. However, he included all levels of amputation from all causes, and noted 8.4% improvement in the rehabilitation rate of below-knee as opposed to above-knee amputees. Thus, there is less difference between the two series.

TABLE III.—Assessment of Success or Failure in Use of Prostheses in 79 Cases

Total number of patients	79
Number in whom training was attempted	37
Number discharged using prosthesis satisfactorily	29
Number who continued to do so	12

Possible Interpretations

Total No. of patients	*Accounted successful*	*Total No. of patients*	*Proved successful*
79	29 (36.5%)	79	12 (15.0%)
No. of trainees		*No. of trainees*	
37	29 (78.5%)	37	12 (32.5%)

Watters[3] has reviewed a series of fifty Callander amputations. Most of his patients were similar to those now under review. Several, however, had had amputation performed at a much younger age because of Buerger's disease. When allowance was made for these, a success rate of 38% remained. In many ways Watters' review corroborates the fundamental theme and findings of this paper.

McGoey[4] has emphasized the difficulty of rehabilitation following amputation. He states that few patients over 70 years of age are able to use an artificial limb and that failure to recognize this point results in "needless effort and bitter disappointment to older amputees".

Thus rehabilitation of elderly lower-limb amputees is an accepted problem. The factors mainly responsible for the problem — degenerative disease and fear — suggest that the training program should be as short, as simple and as easy as possible. Measures directed to this end may be considered under three headings:

1. Amputation below the knee.
2. Simplification of the prosthesis.
3. Geriatric management.

Amputation Below The Knee

The more distal the amputation, the more successful the prosthetic training. Members of the Orthopædic Service at Sunnybrook Hospital have shown the merits of Syme's amputation. Even in elderly patients a highly satisfactory result may be obtained in properly selected cases. Although the number of cases is small, the procedure warrants serious and more frequent consideration.

There is no doubt that below-knee amputation provides a more functional stump than section through or above the knee. The "improved incidence" of rehabilitation as a result is well recognized. It is said, however, that such amputations in the elderly are unwise for two main reasons:

1. Satisfactory healing is difficult to obtain.

2. Skin breakdown occurs easily with use of a side-bearing prosthesis.

Such objections are disputed by many authors. Bickel[5] noted uncomplicated healing in 68% of below-knee amputations performed for arteriosclerotic vascular disease. He urged that such amputations be considered more often because of the easier rehabilitation. Silbert and Haimovici[6] reviewed a series of elderly leg amputees, most of whom were diabetics. They reported primary healing in 70% and delayed healing in 27%, while re-amputation was necessary in only 3%. They noted further that they "knew of no pressure sores from use of a prosthesis" and that "no well-healed stump had broken down". Shumacker and Moore[7] stated that they were in favour of more attempts to preserve the knee joint. They pointed out in agreement with other writers[5, 8] that pop-

liteal pulsation is not a *sine qua non* of successful leg amputation. Perlow and Roth[9] had already noted little difficulty with healing in below-knee amputations, even in the presence of a weak popliteal pulse. More recently, Kelly and Janes[10] concluded that if rehabilitation was likely, one might be justified in performing below-knee amputation under less than ideal circumstances. They noted that 41.3% of leg amputees used a prosthesis while only 16% of above-knee amputees did so.

These favourable (and perhaps optimistic) reports are in contrast with the views of Mandelberg and Sheinfeld[11] who felt that efforts to obtain a below-knee stump courted unnecessary risks and were usually of no avail. Although it cannot be denied that this is true in some cases, it appears to be an unnecessarily despondent outlook in others.

It seems worth while, therefore, to strive for amputation below the knee. The following factors may help to further that aim:

1. Efficient and adequate treatment of impending or early gangrene.

2. Satisfactory medical care with proper control of diabetes, improvement in cardiac function, etc.

3. Lumbar sympathectomy, which may allow amputation at a lower level or improve the healing of the skin flaps. Key[12] considers that arteriography provides valuable prognostic information regarding the merit of such a procedure. If there is evidence of good collateral circulation, sympathectomy will be of value and vice versa. Further, the more distal the block, the more favourable the result of operation.

4. Surgery directed to the vascular lesion, with particular reference to the use of arterial by-pass grafts, designed primarily to save the limb. Although this goal may not be attained in some instances, a more distal amputation may be permitted.

5. Emergency guillotine amputation, which may be advantageous in certain cases. This simple and rapid procedure removes the detrimental influence of a gangrenous and often infected extremity. The patient's general condition improves, diabetes can be controlled and infection combated. A more distal definitive amputation may then be possible.

At times, a decision regarding level of amputation can be difficult. There are no infallible criteria. Most surgeons agree that clinical examination and experience are the most reliable guides.

This problem has led to a suggestion which may have certain merit — the "cut and see" technique.[5, 7] The limb is prepared and draped for performance of amputation below and above the knee. No tourniquet is used. Below-knee skin flaps are outlined and operation is commenced. If skin and muscle bleeding is poor, the attempt is abandoned and higher amputation carried out. The few additional minutes taken thus should not jeopardize the outcome of operation in patients sufficiently well for rehabilitation to be considered.

Simplification of Prosthesis — the Peg-Leg

For the sake of clarity, the term artificial leg will be used as distinct from peg-leg. The term prosthesis will be used to refer collectively to both.

If success does not attend efforts to save the knee-joint, the more frequent use of a peg-leg seems likely to improve the rehabilitation rate in elderly amputees. It was noted in the present series that many of those accounted successful did not do any more with their artificial leg than they could have done more easily and quickly with a peg-leg.

The philosophy of many is well embodied in a statement by one of them — "I didn't want to do much — just get around a bit."

The advantages of a peg-leg are as follows:

1. It is two to three pounds lighter.

2. It is the method of ambulation requiring *least* physical effort when used with crutches or canes.

3. It is more stable. Fear of falling due to buckling of the knee-joint as in an artificial leg is avoided.

4. It may be fitted early.

5. Its use can be taught more rapidly. A patient can become independent in three

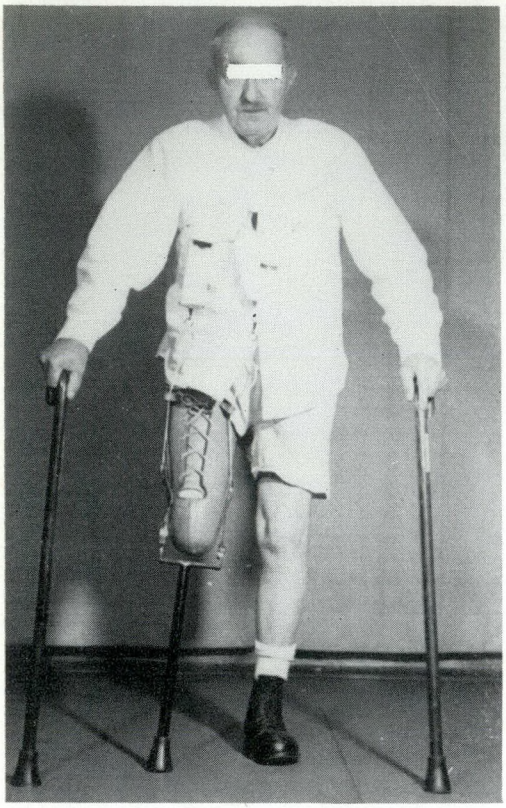

Fig. 1.

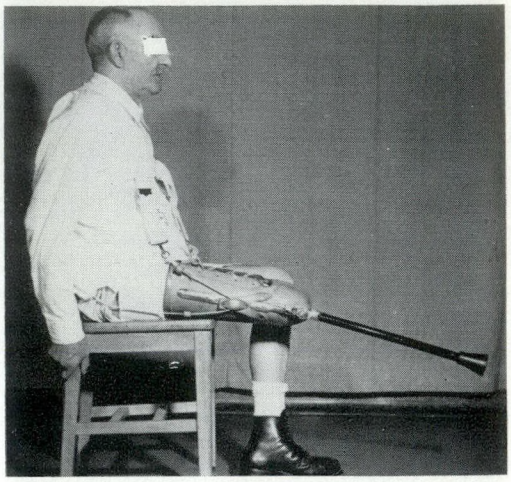

Fig. 2.

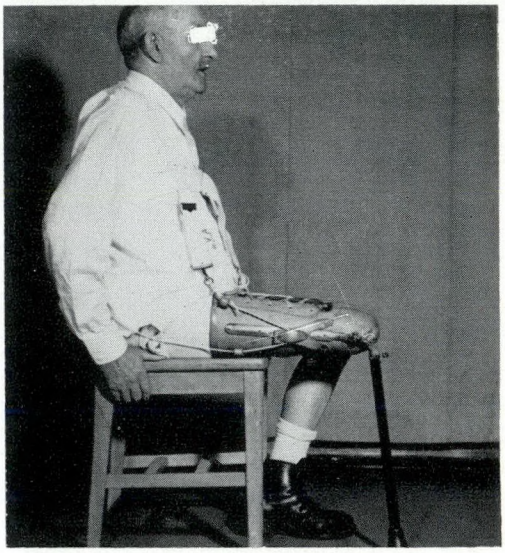

Fig. 3.

Figs. 1-3.—This patient had forsworn the use of a conventional peg-leg. He had neither the aptitude nor the fitness necessary to use an artificial leg. However, he now wears the type of peg-leg illustrated quite happily.

to four months in contrast to the six months noted earlier.

6. It can be made more quickly and, therefore, more cheaply — 17 man-hours as opposed to 42 man-hours for an artificial leg.

7. It is the best method for shrinking a stump and also for overcoming a hip flexion deformity.

8. It is a good yardstick by which to judge individual fitness for a permanent prosthesis. If a patient cannot use a peg-leg well, he will not be able to use an artificial leg to advantage.

A "home-made" peg-leg or pylon can afford valuable evidence of a patient's potential. Such an appliance can be made easily with a plaster bucket, incorporating the lower half of a crutch, and a canvas strap.

The disadvantages of a peg-leg are few:

1. Cosmetically it is less pleasing.

2. It is said to cultivate a bad walking habit which makes any subsequent training with an artificial leg more difficult. This problem has been exaggerated and may be overcome without great difficulty. In any case, a bad walking habit at the age of 65 or 70 years is of no moment.

3. Stump shrinkage as a result of early fitting necessitates alteration of the bucket — this is a simple procedure.

4. The main objection of most wearers is that a peg-leg sticks out when they sit down, making travel by automobile, for instance, well-nigh impossible.

This objection is a real one and has been overcome with satisfaction in two trial cases by incorporating a knee-lock (Figs. 1-3). Fitting a knee-lock into an artificial leg was considered. It was felt, however, that such a prosthesis would still be heavy, complicated, expensive and awkward.

It is interesting to note the sequence of events in two patients. In one, with a Gritti-Stokes amputation, an artificial leg was prescribed. The patient was trained and then was discharged. A few months later he was admitted to hospital with a crutch palsy, having been unable to use his leg satisfactorily. It was exchanged for a peg-leg, from which he obtained better use. The second patient, also a Gritti-Stokes amputee, had a peg-leg prescribed and in due course, apparently as a result of satisfactory progress, he graduated to an artificial leg. The patient felt that he could not master his new leg and after a few unhappy months, culminating in a fall, he went back to using his peg-leg quite happily.

Geriatric Management

It is not proposed to discuss detailed geriatric care. However, certain features, with particular reference to amputation, may be emphasized. In the elderly, recovery and convalescence are slow after amputation. Proper healing, shrinking and the development of strong stump muscles take time. Enforced inactivity is tolerated poorly by elderly patients, both physically and mentally. Long periods in hospital and the slow, arduous training necessary for prosthetic usage are not well accepted. It was noted previously that an average time from amputation to discharge from treatment was six months. Watters[3] found a similar interval. Six months is a long time at this stage of life.

It is therefore necessary to start training at an early date to maintain mental acuity and physical capability. Failure to "keep the patient going" results in loss of incentive and independence. Muscles become weaker, joints stiffer and bones more osteoporotic. He becomes frightened, and is fearful of falling. Loss of confidence follows and rehabilitation may become impossible.

As Bell[13] noted, it is the aim of all amputees to obtain an artificial leg and to become ambulant as soon as possible. Few, however, are capable of the sustained effort required. It is very helpful to discuss this problem with each patient soon after, or even before, amputation. It is surprising how well patients accept quite adverse thoughts concerning their physical powers. However, explanation must be given. They should be assured that all efforts will be made to make them ambulant, consistent with assessment of their capabilities. Thus understanding is reached, disappointment avoided, and the way paved for earlier and easier training with a simple prosthesis.

Conclusions

1. The number of elderly above-knee amputees who can be rehabilitated is limited. The primary pathological condition—degenerative cardiovascular disease—might lead one to expect this.

2. Rehabilitation therefore must be easy, simple and early.

3. Above-knee amputees suitable for training should start with a peg-leg. If warranted, they may progress to an artificial leg.

4. Age cannot be used as a guide for selection of cases.

5. Patients who might forego the peg-leg stage are rare and should be selected carefully.

6. The trial use of a pylon and crutches should be encouraged, within reason. Such a simple exercise should not produce adverse effects. Many patients, although unsuccessful, would be happier in that they had tried.

7. Time and effort should not be spent in foolhardy attempts to rehabilitate those too debilitated, unwilling, or unable to use a pylon. A wheel chair should be advised without hesitation.

Summary

A series of 79 above-knee amputations has been reviewed.

Only 37 of these patients were considered fit enough to warrant prosthetic training.

As judged by follow-up, only 12 obtained satisfactory use from a prosthesis.

Measures to improve this situation are suggested – amputation below the knee; use of a peg-leg; rational geriatric care.

ACKNOWLEDGMENTS

We wish to acknowledge the help of Major C. A. Bell, Department of Veterans Affairs, whose inquiry regarding prosthetic usage stimulated our investigation.

We are grateful to the Department of Veterans Affairs, Sunnybrook Hospital, for assistance with the necessary follow-up of patients.

ADDENDUM

After submission of this paper for publication, we were very interested to read an article by Grynbaum, Gordon and Bluestone.[14] They discussed the same subject with more emphasis on the role of physical medicine. There is close similarity of thought and conclusion in the two presentations.

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RÉSUMÉ

La réhabilitation des patients âgés ayant subi une amputation du membre inférieur est toujours longue et difficile. On trouve dans la littérature deux opinions diverses sur cette question: ou bien on estime qu'il n'y a aucun problème une fois que la cicatrisation cutanée est obtenue; ou bien on estime que le problème est insoluble.

L'auteur passe en revue les cas qui furent opérés entre 1948 et 1956 à l'Hôpital Sunnybrook de Toronto. A cet effet, il en fait une sélection basée sur les critères suivants: (1) l'amputation est nécessitée par un trouble vasculaire artério-sclérotique périphérique; (2) l'âge du patient est au moins de 58 ans; (3) l'amputation est faite au niveau du genou; (4) l'amputation est unilatérale. Il fut ainsi possible de retracer l'histoire de 85 malades, dont un grand nombre fut réexaminé. On put les classer en cinq groupes: (a) 13 patients qui moururent dans les quatre mois suivant l'intervention, dont l'âge moyen était de 66 ans. Il convient de signaler que le décès fut toujours causé par des complications cardio-vasculaires évolutives, sans rapport avec l'acte opératoire. (b) 29 patients, âgés en moyenne de 72 ans, chez lesquels on jugea inutile d'essayer une prothèse pour des raisons diverses telles que insuffisance physique ou mentale, troubles circulatoires de l'autre membre, etc. (c) 8 patients, d'un âge moyen de 70 ans, auxquels une prothèse fut donnée, mais dont la ré-éducation fut abandonnée secondairement pour divers motifs. (d) 17 patients reçurent leur prothèse et furent ré-éduqués avec succès; cependant, ils abandonnèrent ultérieurement l'usage de leur membre artificiel, se plaignant d'essoufflement, de troubles dans l'autre jambe, de peur de tomber, etc. (e) Enfin, 12 patients, âgés en moyenne de 68 ans, furent totalement réhabilités et utilisèrent leur prothèse avec plein succès. Il est à remarquer que tous les malades de ce groupe possédaient un moral et une énergie supérieurs à ceux du groupe précédent.

De l'examen de tous ces cas, il est permis de tirer les conclusions suivantes:

Niveau de l'amputation.—Il est certain que plus l'amputation est basse, plus les chances de succès sont grandes. On a objecté à cette proposition que la cicatrisation parfaite est difficile à obtenir sur les moignons en dessous du genou, et que les déhiscences cutanées y sont fréquentes. Pour pallier à ces éventualités, il faudra penser à adjoindre au traitement général nécessité par l'état du malade (diabète, maladies cardio-vasculaires, etc.), la sympathectomie lombaire et même les anastomoses artérielles. En outre, l'amputation d'urgence dite "à la guillotine" permet de remonter le patient et de procéder dans un deuxième temps à une bonne "recoupe" dans de meilleures conditions. Comme il est parfois difficile d'apprécier avec exactitude le niveau où devra porter la section, on peut aussi s'aider du procédé suivant, dit "coupe et regarde"; le malade est préparé comme il se doit, mais sans garrot; on commence l'amputation en dessous du genou: si les muscles saignent peu, on n'insiste pas et l'on pratique alors l'amputation au-dessus du genou.

La prothèse.—L'auteur propose de revenir à des prothèses plus simples que les membres artificiels actuels. Il a en effet constaté que, d'une façon générale, les patients porteurs d'une jambe

artificielle ne faisaient guère plus que ceux qui étaient seulement dotés d'un pilon. Ce dernier est plus léger, demande moins d'effort physique pour son emploi; il est plus stable, et supprime la crainte de la chute; il peut être appliqué de façon plus précoce; il est bon marché; et enfin, il permet de juger dans quelle mesure le malade serait éventuellement capable de s'adapter à une jambe artificielle plus perfectionnée. La philosophie de ces amputés vient d'ailleurs corroborer l'opinion de l'auteur, car ces patients ne demandent en somme que "peu de chose, juste de pouvoir circuler un peu çà et là".

Traitement gériatrique.—Il est de la plus haute importance de commencer la ré-éducation de l'amputé de façon aussi précoce que possible pour maintenir leur moral et le bon état physique local. Le plus grand désir de la majorité de ces malades âgés est de redevenir rapidement indépendants.

THE SURGICAL TREATMENT OF RECURRENT VARICOSE VEINS

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Because an hereditary trait is involved, with passage from generation to generation, the problem of varicose veins will always be with us. Improved methods of treatment have greatly reduced the incidence of the disabling complications of ulceration, eczema and varicose indurations but the progressive nature of the underlying disease in some cases has tended to nullify the results of treatment. No surgeon can guarantee permanent cure but the surgical methods employed will, in great measure, determine the eventual results. There are good surgical methods and there are bad ones; there are careful surgeons with a good understanding of the problem and there are those who apparently know little of the fundamental problems. The latter will invariably have poor results.

At the present time, the most important point in the treatment of original varicose veins is the preoperative assessment. An exact knowledge of the degree of venous involvement of the leg will dictate the proper management. Is the great saphenous vein the only one involved or is the small saphenous similarly affected? Are there any incompetent communicating veins and where are they located? Is there any history or evidence of previous deep venous damage due to phlebitis? Most surgeons agree that the correct present day management of incompetent varicose veins is a flush ligation of the great and/or small saphenous veins followed by a stripping procedure to the foot. Incompetent perforating veins are ligated and excised at their predetermined locations.

Assessment of Case

Every surgeon with an interest in this problem is constantly seeing cases where previous operation has been carried out but partial or complete recurrence has taken place. It is with this group of patients that this presentation is concerned. In these, an even more careful preoperative assessment is indicated before further therapy is determined. Table I indicates the many possible factors which should be known in each case. Those patients who show a marked

TABLE I.—Factors in the Recurrence of Varicose Veins

1. Was the original surgeon a good or indifferent one?
2. At what age did the varicose veins first appear?
3. Were all the involved veins dealt with?
4. Are the incisions so placed as to indicate that correct flush ligation was performed?
5. Has the small saphenous vein been overlooked?
6. Is there any evidence of incompetent communicating veins?
7. Was the operation mistakenly done on secondary varicose veins, congenital arteriovenous fistula, etc.?
8. Do the recurrent veins show a positive Trendelenburg test, or are they small and unusually located?
9. Has there been an original reduplication of the saphenous vein, only one of which has been dealt with?

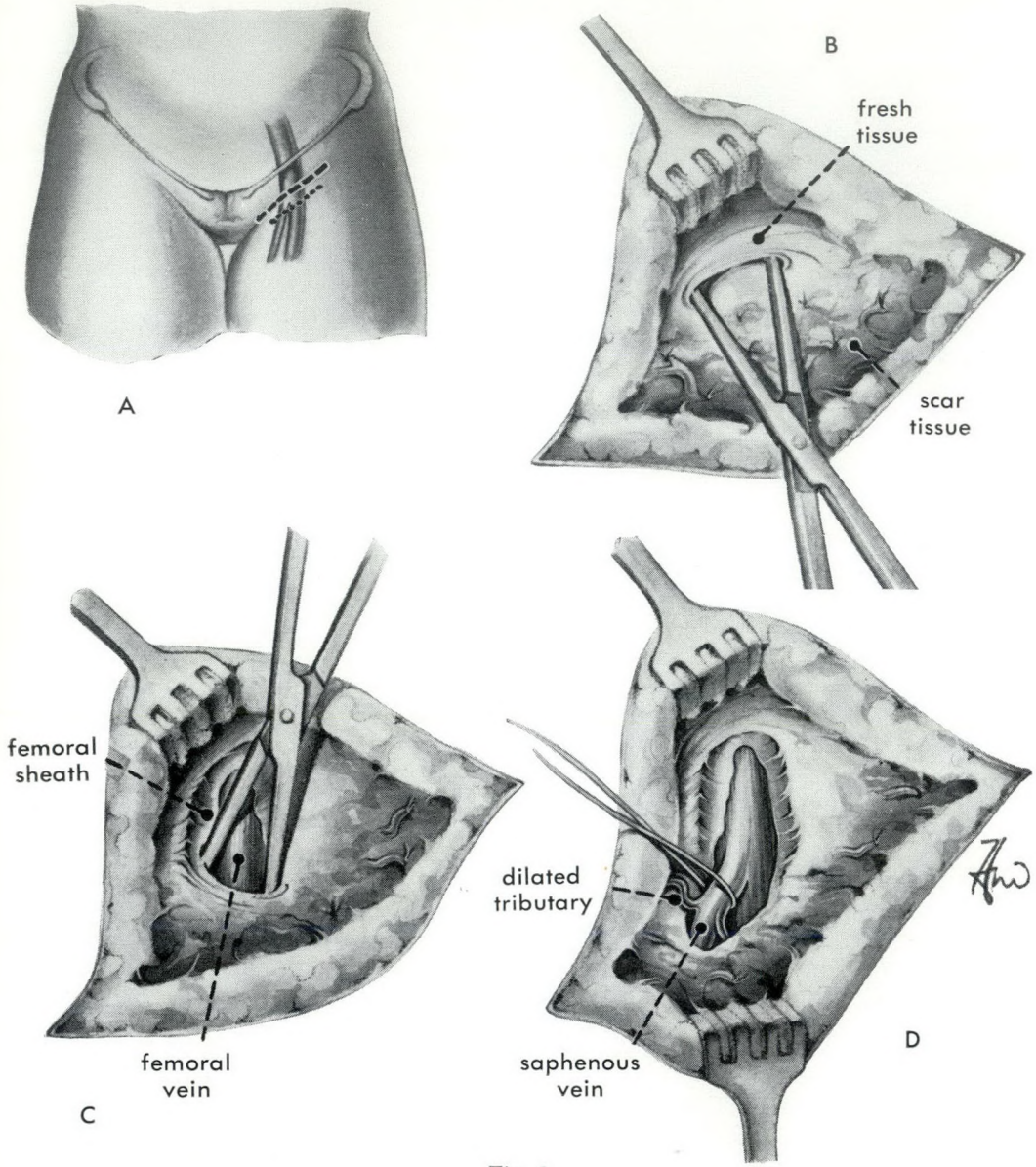

Fig. 1

degree of varicosities in their late teens or early twenties are difficult ones to manage over a long period. A major degree of the hereditary fault has been transmitted and will continue to produce varicosities despite the best of initial treatment. People whose dilated veins appear initially in the forties have received a lesser hereditary legacy and, with good treatment the long term results are usually excellent. A low groin incision will usually mean an inadequate ligation of the great saphenous, leaving behind the various tributaries in that region, and these are usually obvious on inspection. Palpation in the popliteal area and upper calf will often indicate an enlarged small saphenous vein which has been overlooked. The Trendelenburg test will indicate incompetence of the valvular mechanism in the remaining veins, and the multiple tourniquet test together with palpation will determine the origin of most of the incompetent communicating veins. We are strong advocates of the plan that at the initial operation the

stripper should be passed both from groin to foot and vice versa, as we believe that in 15 to 25% of cases the great saphenous vein is duplicated in part of its course. Stripping in one direction will leave behind one of those duplications. Always in mind should be the thought that the original veins are secondary in nature, either follow-a previous deep phlebitis, associated with arteriovenous fistulæ or secondary to cirrhosis of the liver or early heart failure.

Treatment

Treatment of these recurrent varicosities will depend on the individual findings. If the Trendelenburg test is still positive and there is evidence of continuing great and/or small saphenous incompetence, or if incompetent communicating veins can be demonstrated, then further surgery should be recommended. If, on the other hand, the result of the Trendelenburg test is doubtful or negative or the recurrent veins are superficial, tortuous and bizarre in location, then local sclerosing therapy is indicated. Associated compression therapy may be needed if complications are present.

Re-exploration of the saphenofemoral junction can be a most difficult procedure depending on how close the original surgeon had been to the junction. Scar tissue obliterates the landmarks and especially the areolar tissue which ensheathes the veins, making the dissection next to impossible. The recurrent veins in the scar are thin-walled, friable and tortuous. Resulting troublesome bleeding harasses the surgeon and, with the distorted anatomy, the femoral vein can be easily damaged. The following technique (Fig. 1) has been devised by us to facilitate the procedure and to ensure a correct high ligation of the saphenous vein.

The previous incision is re-opened if it is placed in the fold of the groin. If the original scar is lower in the thigh a new incision in the fold is made. After division of the scarred subcutaneous fat, the dissection is then angled upward beneath the upper flap, leaving undisturbed the previous operative area. The upward and inward dissection is carried out through undisturbed tissue and the common femoral vein is sought just distal to the inguinal ligament. The femoral vein is not difficult to identify as it lies inside the femoral sheath medial to the palpable femoral artery. During this phase of the operation and during the subsequent stripping, the Trendelenburg position will be of assistance in reducing venous pressure and lessening possible damage to the femoral vein. After the femoral sheath is opened the anterior half of the common femoral vein is seen. The usual surrounding areolar tissue about this vein has been undisturbed by the original operation and permits easy dissection downward to the saphenofemoral junction. If a correct high ligation has been previously performed, scarring is again encountered at the fossa ovalis but, by keeping close to the sides of the femoral vein inside its areolar envelope, the exposure can be carried below the junction. The femoral vein is now exposed above and below the saphenous junction and it is a simple matter to pass a silk ligature around the saphenous to achieve a flush ligation in continuity. The saphenous tributaries can be disregarded once correct proximal ligation has been carried out.

The remainder of the surgical procedure consists in isolating the great saphenous vein at the medial side of the knee or any other level where it can be seen or palpated. The stripper is passed upward toward the groin and can be extricated from the scar in that area. Stripping is also carried out distally from the knee incision as far as possible. The lower end of the great saphenous is then isolated just distal to the medial malleolus, and the stripper passed upward. It frequently follows an entirely different venous channel than that discovered at the medial side of the knee and emphasizes the finding that saphenous reduplication is not uncommon. Stripping in these recurrent cases is not easy and frequently only produces short segments of veins, especially in those cases where sclerosing injections have previously been given. The surgeon should not hesitate to excise local vein masses, as this is almost invariably necessary. It is in these "blow-out" masses that incompetent communicating veins are frequently found, and this

portion of the procedure should be carefully and painstakingly performed. The small saphenous is stripped to behind the lateral malleolus if indicated. Hæmatomas are evacuated, the wounds irrigated and closed, and an elastic bandage applied from toes to groin.

Results

From 1937 to 1950, all cases of varicose veins were treated by us with the technique of high ligation and retrograde injection. Various low ligations at the site of incompetent communicators and small saphenous ligation and injection were associated in about half the cases. The recurrence rate in subsequent follow-up appeared to be greater than should be expected; consequently, in 1950, the stripping technique was adopted and has been continued to the present time. Recurrences following stripping have taken place in our cases because of two main causes, namely failure to remove a duplicated section of saphenous and the missing or new development of an incompetent communicator. All patients after vein surgery show the development of new veins in subsequent years, and this is to be expected because of the continuation of the hereditary fault. All our patients are requested to report yearly because of this fact, and usually one or two sclerosing injections are necessary to obliterate the veins which have newly developed.

Since 1950, 728 vein strippings have been performed. Seventeen of these patients have returned in subsequent years with a major recurrence showing a positive Trendelenburg test. This is not to say that only this number have had a major recurrence, as a detailed follow-up of all cases has not been carried out. Of these 17, the recurrence was due to a missed reduplication of the great saphenous in seven, missed or new incompetence of the small saphenous vein in five, and missed or new development of incompetent communicating veins in five cases. They were treated by further appropriate operations. Of the total group of 728 cases, 612 were new (surgically untouched) and the remaining 116 patients had had previous operation. The majority of these recurrent cases had had various ligation procedures with and without the use of sclerosing fluid injections. The reasons for recurrence included all the factors outlined in Table I. Twenty-seven of this recurrent group had been operated upon by us during the years 1937 to 1950. Of the 116 recurrent cases re-operated upon, we have been able to follow up 92 over the subsequent years. Seven (7.6%) have again shown major recurrence, as indicated by a return of a positive Trendelenburg test. All seven (probably rightfully so) have shown a disinclination for further surgery and are being treated palliatively with periodic courses of injection therapy.

Summary

The importance of a good preoperative assessment of the case with varicose veins is emphasized as the greatest single factor in producing lasting good results.

The reasons for major recurrence after varicose vein surgery are discussed; the fault lies chiefly in improper assessment and consequent inadequate surgery. The degree of hereditary fault acquired by the individual is also important.

The methods of therapy for a case of recurrent varicose veins are given, including a new surgical re-exposure of the saphenofemoral junction. The difficulties and hazards of re-operation on this junction are markedly reduced by this technique.

Our series of 728 vein strippings is discussed. Seventeen major recurrences were observed to follow stripping procedures on 612 fresh cases. In 116 cases, previous operations had been performed by a variety of surgeons, mainly employing the older technique of multiple ligations. These patients presented themselves with a major recurrence and were re-operated upon as described. Seven of these have again shown a major recurrence.

Résumé

Le traitement des varices récurrentes variera selon les cas. Si l'épreuve de Trendelenburg est positive, il faudra recourir à la chirurgie, tandis que s'il est négatif ou douteux, les injections sclérosantes suffiront. La ré-exploration de la jonction saphéno-fémorale peut constituer une procédure des plus laborieuses. Le tissu cicatriciel modifie les points de repère et les veines sont friables et tortueuses. L'opération peut être sanglante et la veine fémorale, lésée. La technique ci-après décrite est celle de l'auteur.

Si l'incision originale est assez haute, elle sera rouverte, sinon une nouvelle incision adéquatement placée au pli de l'aine sera exécutée. Après division de la graisse cicatricielle sous-cutanée, la dissection est amorcée vers le haut afin d'identifier la veine fémorale lorsqu'elle passe sous le ligament inguinal en dedans de l'artère. La position de Trendelenburg est adoptée durant ces manœuvres. De là, en tissus sains, la dissection se poursuit vers la jonction saphéno-fémorale. S'il y a eu antérieurement ligature adéquate, on trouve du tissu cicatriciel au niveau de la *fossa ovalis* mais en adhérant strictement à la veine fémorale, il est possible de dépasser la jonction. Celle-ci exposée, il est alors facile de pratiquer une ligature au niveau de la crosse de la saphène.

Le reste de l'intervention consiste à isoler la saphène interne au genou ou ailleurs si on peut la palper ou la visualiser. Le "stripper" est dirigé vers l'aine et retiré du tissu cicatriciel à ce niveau. La manœuvre est répétée ensuite vers le bas à partir du genou aussi loin que possible. La saphène est ensuite identifiée à la malléole interne et le "stripper" dirigé vers le haut. Cette manœuvre permet l'exérèse d'une saphène double qui se rencontre assez souvent. Le "stripping" dans ces cas n'est pas facile et ne ramène assez souvent que de courts segments veineux, surtout s'il y a eu auparavant quelques injections sclérosantes. Il faut alors faire des excisions veineuses en masse car c'est à ces endroits que se trouvent les perforantes. La saphène externe, si elle est variqueuse, doit être réséquée. Les hématomes sont évacués, les plaies irriguées et suturées, et finalement un bandage élastique appliqué des orteils jusqu'à l'aine.

PATENT DUCTUS ARTERIOSUS
A REVIEW OF THIRTY-SIX CASES TREATED BY SURGERY*

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OF ALL CONGENITAL abnormalities in the cardiovascular system, patent ductus arteriosus is one of the most amenable to successful surgical treatment.

Closure of a patent ductus arteriosus was first suggested by Munro[1] in 1907, but it was not until 1938 that Gross[2] successfully performed the operation. While Gross first ligated the ductus in continuity, because of the possibility of recurrence, he later performed division and suture of the divided ends, which he now does in all cases.[3] He reports a surgical mortality in uncomplicated cases of less than 0.5% in a series of 525 surgically treated cases.[4]

Thus patients with patent ductus arteriosus are now being operated upon in many centres throughout the world with excellent results and with little risk.

NATURE OF THE LESION

During fetal life, blood is shunted away from the unexpanded lungs from the pulmonary artery into the aorta via the ductus arteriosus. After birth, with expansion of the lungs, the pulmonary arterial pressure diminishes, so that blood flow through the ductus ceases and normally the ductus undergoes a process of obliteration.

If obliteration does not occur, the aortic pressure rises over that in the pulmonary artery, and blood is shunted from the aorta into the pulmonary artery. The amount of blood diverted varies according to the size of the ductus and to the gradient of pressure from aorta to pulmonary artery. In some patients, this flow may amount to as much as 70 to 90% of the left ventricular output.

The cause of the failure of the ductus to close is not known. It is interesting to note, however, that German measles affecting the mother early in pregnancy may result in her bearing a child with a patent ductus arteriosus.

SYMPTOMS AND COMPLICATIONS

The majority of children with a patent ductus arteriosus have no symptoms. However, as they grow older, they may begin to tire and have slight shortness of breath on exertion. Many of them are small for their age.

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†Former Resident in Surgery, the Children's Hospital, Winnipeg.

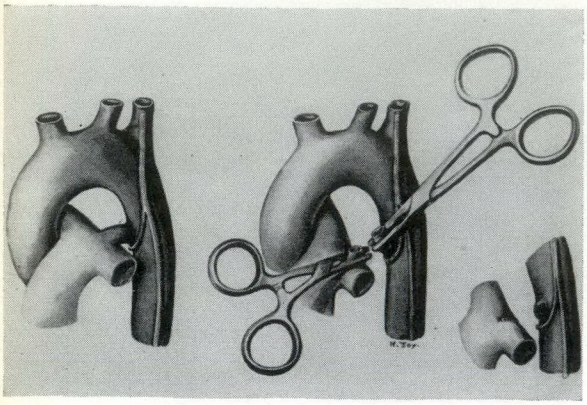

Fig. 1.—Diagrams illustrating method of division and closure of patent ductus arteriosus using Potts multi-toothed clamps.

While it is true that a child with a small uncomplicated patent ductus can live a life of normal activity and duration, Keys and Shapiro[5] report that two-thirds of such individuals develop serious difficulties before the age of 40 years.

The complications which may be produced by a patent ductus arteriosus are briefly summarized below.

1. Occasionally in infants, as reported by Ziegler[6] and by Lyon and Kaplan,[7] a patent ductus arteriosus may be the sole cardiac lesion responsible for severe intractable heart failure.

2. Children may have retardation of growth,[8] diminished exercise tolerance, and recurrent pulmonary infections.

3. With increased cardiac output and strain, left heart failure may result.

4. Subacute bacterial endarteritis may occur, usually in the pulmonary artery at the site of the ductus.

5. With continued increased pulmonary blood flow, pulmonary vascular changes may occur and produce pulmonary hypertension, reversal of ductal flow, cyanosis, and right heart failure.

6. Rarely, a ductus may undergo aneurysmal dilatation or rupture.

Diagnosis

In well over 90% of patients, patent ductus arteriosus can be diagnosed in a few minutes on physical examination. In these, a very characteristic murmur is heard, which is aptly described as being machinery-like in character. The murmur is continuous throughout diastole and systole, but has a systolic accentuation. It is best heard at the second left interspace along the left sternal border. In approximately half of all patients there is an accompanying palpable thrill.

While systolic blood pressure is usually at a normal level, the diastolic pressure is low because of the continuous shunting of blood from the systemic into the pulmonary circulation. With this wide pulse pressure, a bounding pulse may easily be detected.

Examination of the heart by x-ray shows slight enlargement, and typically there is a prominence in the region of the pulmonary artery. The pulmonary vascular markings are increased.

The electrocardiographic tracing is usually normal or shows evidence of slight left ventricular hypertrophy.

In a small number of patients with patent ductus arteriosus, however, the above mentioned diagnostic points may be either absent or atypical. This is particularly apt to be the situation in small infants or in patients who have developed complications.

A systolic murmur, in an otherwise normal infant, may eventually be shown to be of no significance or may be due to one of several cardiac abnormalities including patent ductus arteriosus. If the baby has no symptoms and progresses normally, there is no need to carry out a full investigation early in life. If the murmur is due to an open ductus, the characteristic murmur may subsequently appear and the diagnosis thus become clear.

In other infants, however, there may be marked retardation of development and cardiac failure may be present. In these, it is extremely important that early diagnosis be made, so that life-saving surgical intervention may be carried out. When a patent ductus arteriosus is suspected, the diagnosis can be confirmed either by retrograde aortography or by cardiac catheterization.

In our experience, if a small infant in heart failure has a loud continuous murmur, the lesion is more likely to be a truncus or an aortic-pulmonary septal defect than it is to be a patent ductus arteriosus.

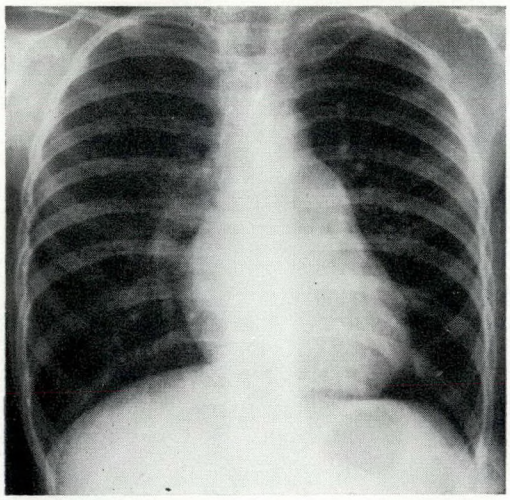

Fig. 2.—Usual x-ray appearance of the heart in patent ductus. The heart is a little enlarged, the pulmonary artery is prominent, and the pulmonary vascular markings are slightly increased.

In older patients with continued large ductal flow, the pulmonary artery pressure may increase to the point where it approximates the aortic diastolic pressure. Thus flow through the ductus takes place only in systole and only a systolic murmur is heard. In these individuals a diagnosis is usually not possible without cardiac catheterization.

Indications for Surgery

Because of the high incidence of complications and since the risks of surgical closure are slight, all patients with an asymptomatic patent ductus arteriosus should be operated upon. Ideally, this can best be accomplished when the patient is from two to eight years of age, although of course many cases are not diagnosed and thus not operated upon until later in life. Infants in cardiac failure due to the presence of a patent ductus should be operated upon early.

Older patients with complications must be assessed individually. In almost all, surgical closure of the ductus is indicated, except when pulmonary vascular changes have reached the stage where there is either no significant shunt, or where reversal of the shunt has occurred. In these, closure of the ductus is contraindicated.

Surgical Technique

The patients are positioned on the operating-table with the left anterior chest uppermost. A left-sided antero-lateral submammary thoracotomy incision is made through the third intercostal space. The costal cartilages adjacent to the sternal border of the second and third ribs are divided to increase the exposure. Exploratory palpation over the pericardium and great vessels for the detection of thrills is then routinely performed. With the left lung retracted downwards, an incision is made through the parietal pleura posterior to the left phrenic nerve in the region just above the left pulmonary artery. The vagus nerve and its recurrent laryngeal branch are identified. This latter structure courses around and below the ductus. The ductus is then carefully dissected clean of adventitious tissue on all sides, so that it may be completely exposed. In small infants in cardiac failure, when operating time should be as short as possible, we believe that multiple well spaced ligatures are satisfactory for closure of the ductus. In all others, closure

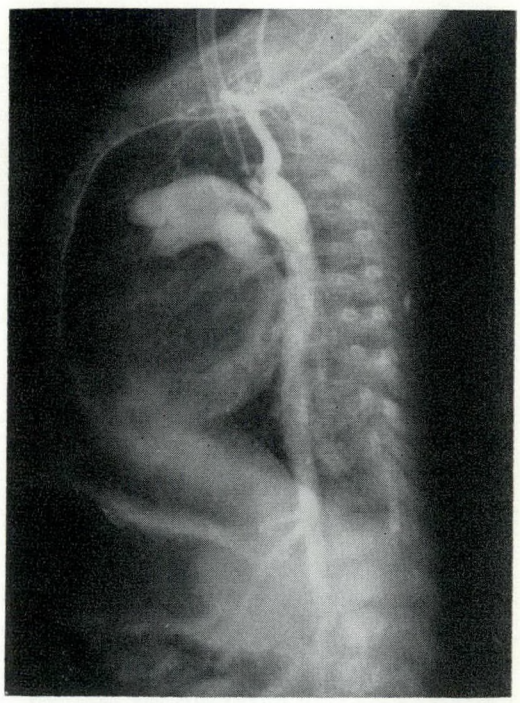

Fig. 3.—Retrograde aortogram performed through the left brachial artery shows radiopaque material passing from the aorta, through the open ductus into a large pulmonary artery.

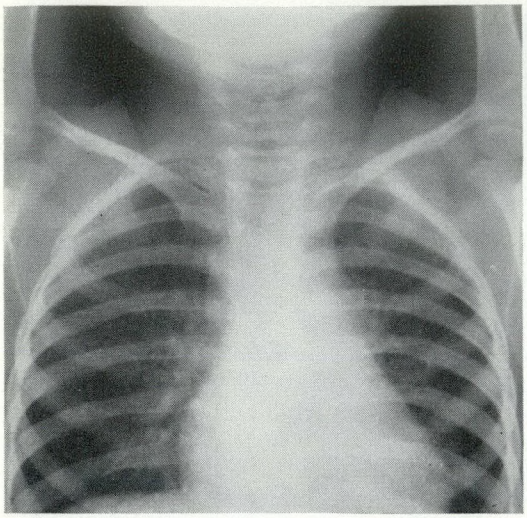

Fig. 4a.

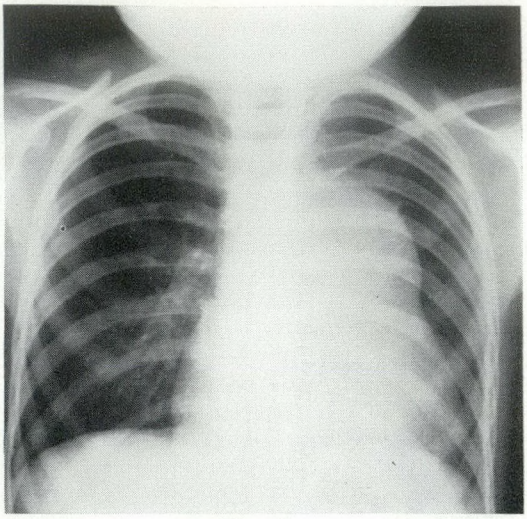

Fig. 4b.

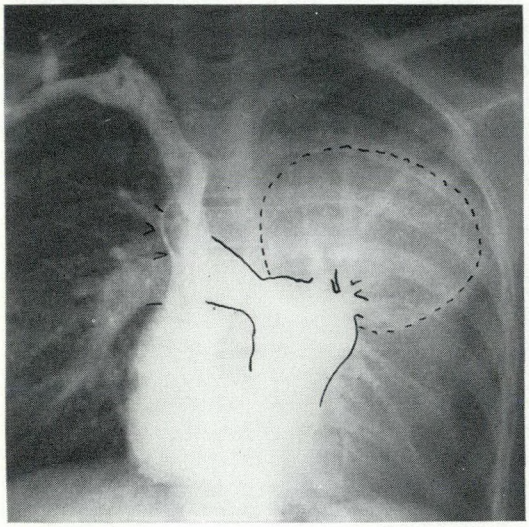

Fig. 4c.

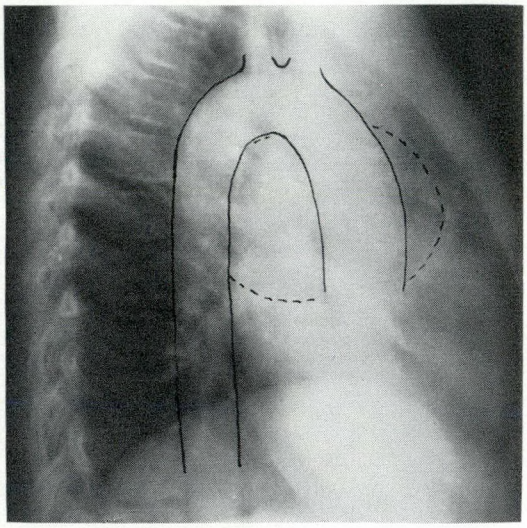

Fig. 4d.

Fig. 4a.—Chest radiograph of four year old child admitted to hospital with heart murmur and fever. Child responded well to antibiotics. **Fig. 4b.**—Chest radiograph of the same patient four weeks later reveals the development of a large mass in the region of the pulmonary artery. **Fig. 4c.** and **Fig. 4d.**—Subsequent antero-posterior and lateral films taken during angiocardiography show visualization of the pulmonary arteries and of the aorta without filling the mass. At thoracotomy, this mass was found to be a thrombosed aneurysm of the ductus arteriosus.

of the ductus by division and suture is preferred.

Potts[9] multitoothed ductus clamps are applied as widely apart as possible across the pulmonary and aortic ends of the ductus. The ductus is then divided between these clamps, and the ends are oversewn with a continuous interlocking suture of 5-0 arterial silk. After the clamps are removed, a small piece of muscle obtained from the thoracic wound is inserted between the divided ends. This insures against the possibility of recurrence. The parietal pleura is approximated, and after palpation of the structures to ascertain the disappearance of the thrill, the chest wound is closed with intercostal catheter drainage.

Clinical Material

Thirty-six patients with patent ductus arteriosus have been operated upon by one of us (C.C.F.) in Winnipeg during

the past four years. Twenty-nine of the patients were female; this female preponderance of the lesion is in accord with other reported series.

In 17 patients, growth was definitely retarded. In most instances, the diagnosis was relatively straightforward, the characteristic murmur being present in 31 individuals.

In three infants with systolic murmurs only, the diagnosis of patent ductus was made by retrograde aortography. In two older patients with atypical findings, the diagnosis was established by cardiac catheterization.

The average age at the time of operation was nine years (seven weeks to 40 years).

Of the 36 patients operated upon, 27 had division and closure performed, eight had multiple ligation, and in one the lesion was considered inoperable.

Four patients had subacute endocarditis. In two of these the condition responded well to antibiotics, and elective division and closure of the ductus was subsequently done. In the other two patients, however, the infection failed to respond to treatment until surgical closure of the ductus had been accomplished.

There were no complications during operation except in three instances. In one patient, after closure of the ductus, temporary cardiac irregularity occurred. In another, there was serious bleeding from the aorta but this was eventually controlled. The third patient at operation developed right-sided atelectasis, which responded to immediate bronchoscopy.

There was one fatality in the total series. This occurred in a seven week old premature infant weighing only 4 lb., who had been in cardiac failure since birth. The ductus was closed successfully but at the conclusion of the operation there still remained a prominent thrill over the anterior surface of the heart. At autopsy, a large atrial septal defect was found.

One patient at thoracotomy was considered inoperable because of the presence of a large thrombosed aneurysm of the ductus.

Postoperative complications were minor in all cases, the worst being a stitch abscess requiring subsequent removal of a deep costal cartilage suture. The average postoperative stay in hospital was 11 days (eight to 18 days). Except for the one death in the series, all other patients made uneventful recoveries.

Follow-up examinations have been carried out on all patients, though obviously the period of observation has not been very long. One patient has continued to have repeated pulmonary infections and has not done as well as had been hoped. All other patients are well, free of symptoms, and have resumed normal activity. The characteristic murmur has disappeared in all, although four patients have residual systolic murmurs. In one of these, it is known that there is a small ventricular septal defect present.

Blood pressures have returned to normal, and the heart size and pulmonary vascular markings as seen by x-ray have diminished in all patients.

Summary

The symptoms, signs, methods of diagnosis, and surgical treatment of patients with patent ductus arteriosus have been reviewed. The results of surgery in 36 cases have been presented.

One patient with an aneurysm of the ductus was considered inoperable.

The only death in the series occurred in a 4 lb. infant who had an additional cardiac abnormality.

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Résumé

De toutes les anomalies congénitales du système cardio-vasculaire, celle du canal artériel demeure la plus encourageante à traiter chirurgicalement. L'oblitération d'abord conçue par Munro en 1907 ne fut réalisée qu'en 1938 par Gross. De la simple ligature, celui-ci est passé à la division avec suture, qu'il emploie maintenant dans tous les cas, avec une mortalité de moins que 0.5% dans les cas compliqués.

Après un rappel de la pathogénie, de la symptomatologie et des méthodes de diagnostic, les auteurs exposent les indications opératoires comme péremptoires chez l'enfant, à cause du risque minime en regard de la fréquence élevée des complications. Chez l'adulte, l'opération est indiquée, sauf si les pressions paraissent égales ou encore si la pression pulmonaire est plus forte.

La technique chirurgicale est décrite et les auteurs insistent sur la mise en place d'un fragment musculaire entre les segments divisés afin d'éviter une recanalisation. Une série de 36 cas, dont 29 du sexe féminin, opérés en quatre ans à Winnipeg nous est présentée. A part une mortalité chez un bébé prématuré de sept semaines et pesant quatre livres, les résultats furent excellents, et la morbidité à peu près nulle.

HOMOLOGOUS SKIN GRAFTS—FACTORS AFFECTING SURVIVAL AND A REPORT ILLUSTRATING PROLONGED SURVIVAL

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In a previous publication, the successful treatment of an 80% surface area burn was reported.[1] At that time note was made of the prolonged survival of a skin homograft. It is proposed now to review the factors affecting the life-span of such grafts as a whole, with particular and additional reference to the case in point.

Since the initial report, the patient's recovery has continued. He has been gainfully employed now for somewhat over a year and a half.

It has been known for some 30 years that skin homografts will survive permanently if the donor and recipient are identical (monozygous) twins. Good and Varco[2] have demonstrated permanent survival of homotransplanted skin, taken from normal donors, on two recipients with *congenital* agammaglobulinæmia. In all other instances, homologous skin grafts are rejected after a variable and usually brief interval. Theories formulated to explain homograft rejection include:[3] (1) the blood group theory; (2) the cellular theory; (3) the active immunity theory. The last-named indicates the present concept, that rejection of homografted skin is a systemic immunological reaction: i.e., antigens present in the skin of the donor incite antibody formation by the host. Thus the homograft is cast off.

The exact nature of skin antigens and their relationship to blood and tissue antigens and to other genetic factors is obscure. This lack of definite knowledge persists despite a vast amount of animal research and investigation. However, data concerning man's reactions have also been accumulating.

Converse and Rapaport[4] found, in non-related volunteers whose ABO and Rh blood groups did not necessarily coincide, that the survival time of reciprocal full thickness skin grafts between pairs of subjects was seven to 10 days.

In two non-related individuals whose blood groups' examination was identical for most of the known factors, Woodruff and Allan[5] obtained life-spans of 14 to 21 days following cross-homografting.

Bishop[6] reports a case in which he used skin from one non-identical (heterozygous) twin to homograft the other who was severely burned. Their blood groups were closely similar. He noted graft survival times of 23 to 26 days.

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Rogers[7] cross-homografted each pair of two sets of non-identical twins. In one pair, the blood groups were identical in all currently known factors. In the other, only one minor factor differed. He obtained life-spans of 19 to 29 days in the grafts.

Good *et al.*[8] have shown that in patients with *acquired* or *transient* agammaglobulinæmia, homografted skin from normal individuals does not survive permanently but does have an increased life-span.

Dammin, Couch and Murray[9] noted longer duration of skin homografts on recipients suffering from chronic uræmia—32 to 115 days.

Thus it is known that familial relationship, similarity of blood groups, agammaglobulinæmia and uræmia influence favourably the life-span of skin homotransplants. In addition, it is agreed that total body radiation, or the administration of salicylates or antihistaminics,[10] also prolongs homograft survival.

Case Report and Investigation

Consideration of some preliminary and pertinent data relative to the patient in question will facilitate explanation and understanding of the details to follow.

During the first few months of hospitalization, skin was taken from 19 donors to help cover, albeit temporarily, the raw areas which amounted to 60% of the patient's total body surface. The donation from a brother, who was second in the chronological order of donors, survived from early May until late December, a period of almost eight months. This skin was placed on the three separate recipient areas best prepared to receive it, and in each instance its behaviour was identical. Figs. 1 to 5 show two of these areas at the various times stated.

Cortisone had been administered in gradually decreasing dosage during the first six months of treatment. As a factor in promoting the *prolonged* survival of these grafts it was deemed unimportant since many other homografts, from both non-related and related donors, lasted only three to six weeks. Nevertheless, it is likely that the administration of cortisone does increase the survival time of homografts in general.[7, 11, 12] It is also noteworthy that

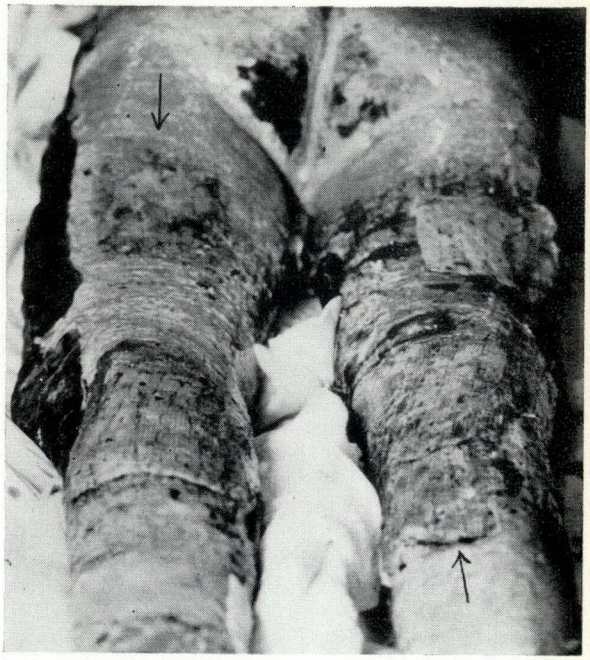


Fig. 1.—Left posterior thigh and right posterior calf, one week after grafting. (The other grafts on right thigh and left calf are from another donor.)

the grafts under discussion were unaffected during a period when the patient showed a marked negative nitrogen balance.

At first it was considered that the homografts had been replaced by a creeping substitution of the patient's own epithelium. However, rejection of the grafts indicated that this was not so (Fig. 5). Investigation was therefore undertaken.

Blood grouping of the patient and donor was carried out in detail. The similarity is striking:

	MNS	*Rh*	*Lu*^{a}	*Kk*	*Le*	*Fy*^{a}
Patient A_1	−+−	cde/cde	−	−+	a−b−	−
Donor A_2	+−+	cde/cde	−	−+	a−b+	−

A reciprocal skin transfer experiment was performed between donor and patient just before the latter was discharged from hospital to return to work.

A recipient area was prepared on the donor's right lower chest by excision of an ellipse of skin and most of the subcutaneous fat. A graft of suitable size and 20/1000 inch thick was taken from an unburned area of the patient's skin, and was sutured in position. A 100% take was

Fig. 2.—Growth of edges of grafts two months after grafting.

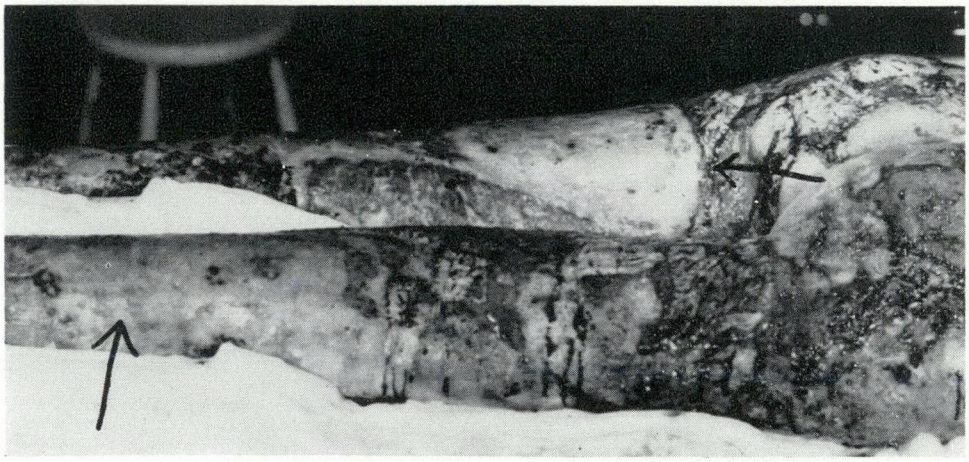


Fig. 3.—Healthy appearance of both grafts three months after grafting.

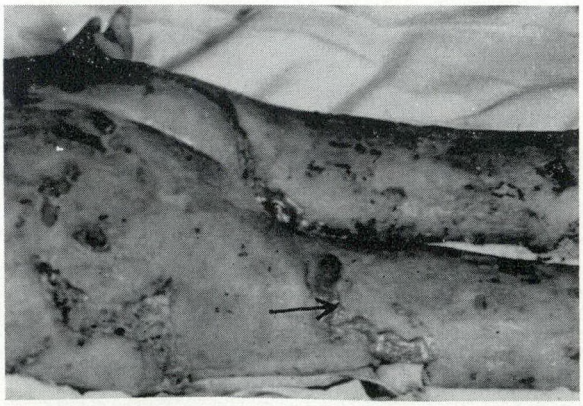


Fig. 4.—Continuity with the patient's skin five and one-half months after grafting.

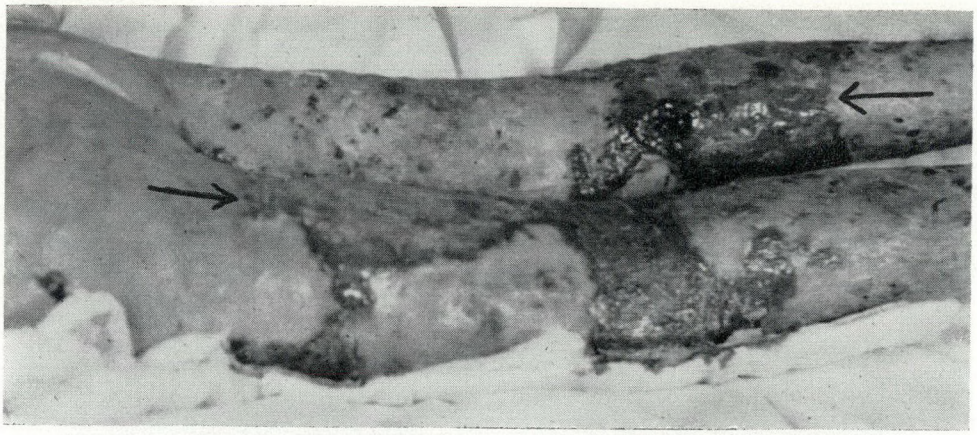
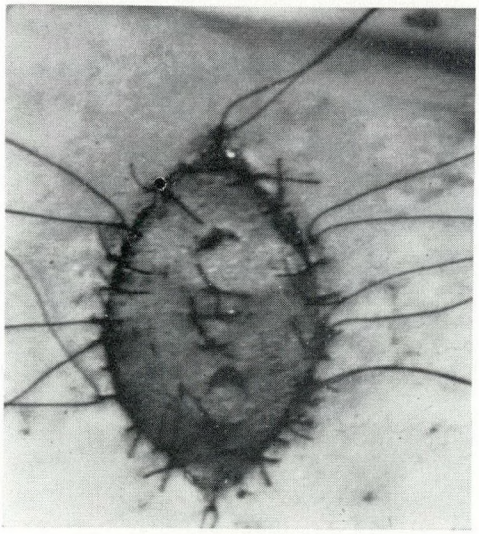


Fig. 5.—Patchy disintegration of the grafts is occurring, eight months after grafting.



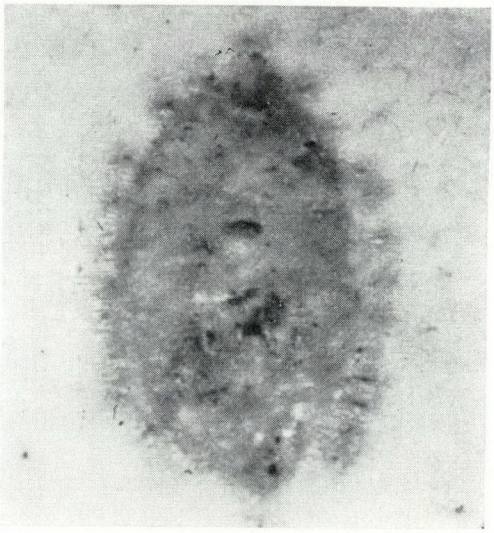
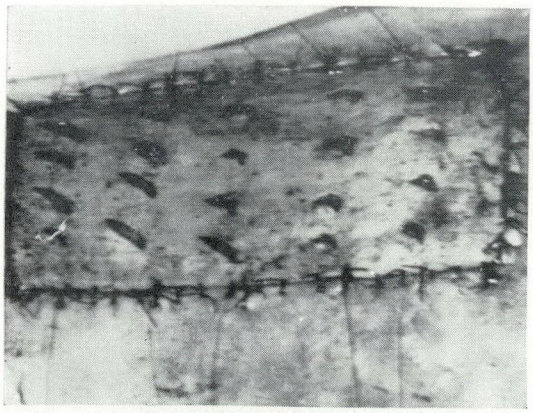


Fig. 6.—Graft from patient to donor, on day of operation. **Fig. 7.**—Graft healthy but slightly "puffy", 19 days after operation.



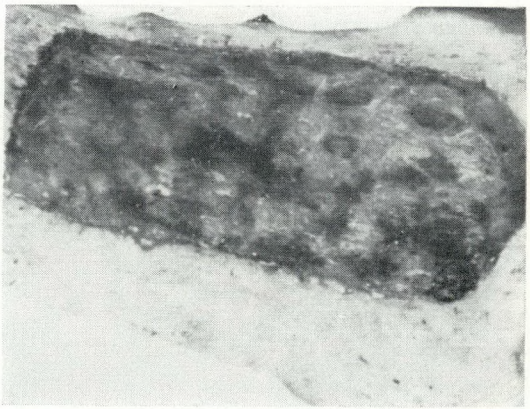


Fig. 8.—Graft from donor to patient on day of operation. **Fig. 9.**—Graft almost completely rejected, 10 days after operation.

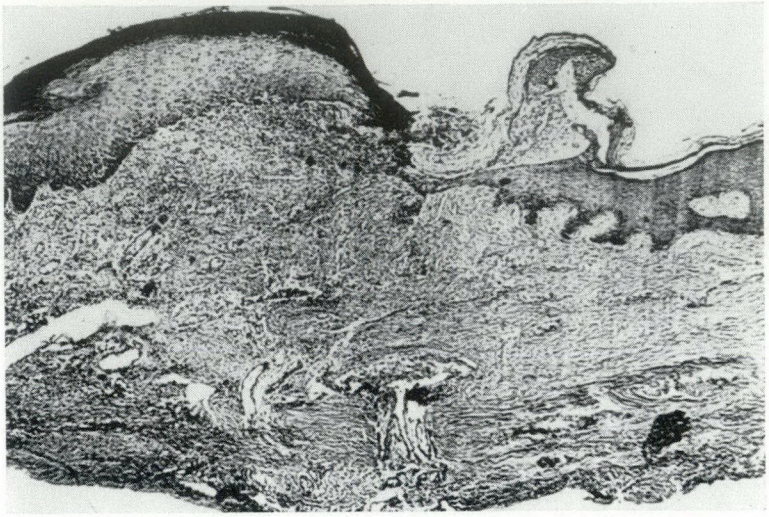


Fig. 10.—Low-power view of junction of graft (on the left) with the patient's skin. A small ulcer is present here. Dense, fibrous tissue underlies the "normal" skin whilst an oedematous, cellular, inflammatory reaction underlies the hyperkeratotic "donor" skin. Healing has occurred and rejection is about to occur.

obtained. Nineteen days after operation the graft was "pneumatic" and slightly cyanosed (Figs. 6 and 7). Two days later it had been replaced by a hard, dark brown eschar.

On two separate occasions skin was transplanted from the donor to the patient. The second procedure was carried out because it was felt that the poor result of the first operation was due to a technical fault. Each time the technique and end results were essentially the same, the second graft lasting perhaps two days less than the first.

A recipient bed was prepared by excision of an area of poor skin and very tough, dense, underlying scar tissue. A split thickness skin graft 20/1000 inch thick and of commensurate size was taken from the donor and sutured in position. The graft took poorly and after only seven days showed well-marked signs of rejection. Unhealthy patches remained for a few days thereafter (Figs. 8 and 9). In view of the long life of the therapeutic grafts this result was disappointing, but probably what should have been expected.

A biopsy of the junction between graft and normal skin was taken on the ninth postoperative day. Continuity of the grafted skin with its bed showed that it had taken, thus eliminating technical error as a cause of failure to survive. However, signs of rejection, viz: œdema and inflammatory reaction, were manifest and indeed in most other areas the graft had already sloughed (Fig. 10).

Electrophoretic studies on patient and donor were carried out, and the estimates are shown in Table I.

The results will not permit conclusions, but certain features are noticeable. Firstly, the consistently elevated readings for gamma globulin shown in the patient's serum. Likely these are due to the long-standing surface infection in the raw areas. Secondly, the markedly elevated level of the same fraction on February 24. This may reflect the additional reaction to two drums of homologous skin grafted five weeks previously. Before this procedure no homografting (or indeed any operation) had been performed for 15 weeks. Thirdly, the small rise in the donor's gamma (and $alpha_2$) globulin levels just over four weeks after the experimental operation. It would be interesting to follow the results of more systematic estimations in burned patients.

Discussion

The *main* factors influencing the survival of homologous skin grafts, apart from technical considerations, are close similarity in blood groups, and genetic relationship.

TABLE I.—The Results of Electrophoretic Studies

	Alb.	*Alpha*$_1$	*Alpha*$_2$	*Beta*	*Gamma*
Patient					
January 18..... 1.	48.5%	5.7%	8.4%	14.0%	24%
2.	48.2%	6.0%	8.4%	15.0%	23.1%
February 24.....	48.6%	7.0%	5.0%	6.1%	33.2%
April 9.....	47.3%	9.4%	13.9%	8.5%	20.6%
Graft experiment					
May 10.....	50.3%	3.8%	11.5%	11.35%	23.3%
Donor					
January 25.....	58%	7.1%	8.3%	11.5%	15.1%
April 9.....	60%	5.8%	8.6%	11.0%	15.4%
Graft experiment					
April 26.....	60.4%	4.9%	8.6%	9.9%	16.0%
May 10.....	53.6%	5.6%	12.4%	10.1%	18.3%
Average Normal					
	55-63%	4-6.8%	7-14%	11-14%	15-20%

These factors are present in this case, and are reflected in the survival time of 19 days obtained when skin was grafted from patient to donor. The failure of the experimental grafts from donor to patient to survive may be explained on the basis of the "second set phenomenon". Gibson and Medawar[13] first noted such an occurrence. Later Medawar[14] used the phrase when he observed in rabbits that a second skin graft from the same donor and applied to the same recipient was rejected after a shorter life-span. In other words, the host has become sensitized to the donor skin. This phenomenon has been confirmed in man by Baxter and Entin.[15]

It was also noted during the treatment of the patient under discussion, when a second set of homografts was taken from a sister. The survival time of the grafts was so shortened as to make the operation hardly worth while, and the benefit to the patient fleeting.

Survival of the therapeutic grafts for almost eight months is not easily explained, even when full allowance is made for the enhancing influence of genetic relationship, blood group similarity and cortisone. None of the other accessory factors was present. There was no evidence to suggest uræmia or hypogammaglobulinæmia.

In addition, an important "control" factor was the survival times of three to six weeks noted in the other homografts. Admittedly these times are longer than might be expected, but it is recognized that in the severely burned, homografts last longer than in the healthy experimental volunteer.

One can theorize on the reasons for survival and also, perhaps more correctly, on the reasons for rejection after such a long time. It is suggested that a skin compatibility or skin antigen similarity must have been present with familial relationship, blood group similarity, and cortisone acting as enhancing factors. This skin affinity may have been so close that a sufficiently strong antibody response could not be invoked until the patient gained better health. In the interim his immunological mechanism was in a state of "near exhaustion" because of the presence of other, more dissimilar homografts and gross infection in the many large raw areas.

There are at least two additional blood antigens for which neither patient nor donor was examined. It seems likely that there are others as yet unknown. Absolute compatibility of the former in all details between donor and recipient might further influence the survival of homografted skin.

It might be argued that if a skin compatibility did exist, one might expect a graft survival time of more than 19 days on transferring skin from patient to donor. However, this may not necessarily be so, since each skin will differ in its degree of antigenicity and each host in his degree of antibody response.

It becomes apparent, therefore, from a practical standpoint, that the following features merit attention when using homo-

logous skin grafts if longer lasting coverage is to be obtained. Of course, if an identical twin exists, then the problem does not arise.

1. The donor should be as closely related to the patient as possible.

2. The donor's blood groups (in detail) should be as similar to the patient's as possible.

3. Cortisone, apart from other considerations, appears to improve the survival time of homografts.

4. The use of "second set" grafts is not recommended.

Summary

Factors promoting prolongation of survival of homologous skin grafts are discussed. Survival of a skin homograft for almost eight months, and the investigation thereof, are described. Explanation of this phenomenon cannot be given, but speculative reasons are advanced. Suggestions are made regarding the best source of homograft skin.

Acknowledgments

I am grateful to the Editor of the *Annals of the New York Academy of Sciences* for permission to reproduce certain material previously published in the Second Tissue Homotransplantation Conference (*Ann. New York Acad. Sc.*, **64:** 767, 1957).

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Finally, I wish to thank Dr. Hamilton Baxter, Royal Victoria Hospital, Montreal, for his ever-present help, guidance and encouragement.

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Résumé

Dans cet article l'auteur se réfère à un cas personnel publié antérieurement pour étudier les facteurs qui entrent en ligne de compte dans le succès des greffes de peau homologues.

Jusqu'à ce jour trois hypothèses ont été avancées pour expliquer le mode d'évolution d'un greffon cutané; (a) l'hypothèse de la compatibilité des groupes sanguins; (b) la théorie cellulaire; (c) la théorie de l'immunité active d'après laquelle des antigènes provenant du greffon déclenchent chez le receveur la production d'anticorps capables d'entraîner la résorption du transplant. La nature exacte de ces antigènes cutanés reste encore obscure malgré de très nombreuses expériences faites chez l'animal.

Au cours d'une revue de la littérature, l'auteur relève plusieurs cas dans lesquels la durée de la survie du greffon avait été augmentée par la similitude des groupes sanguins du donneur et du receveur. Outre la ressemblance des groupes sanguins, la proximité du degré de parenté, l'agammaglobulinémie et l'urémie chronique augmentent la durée de survie du transplant entre deux individus.

L'auteur a eu l'occasion de traiter un brûlé à 60% par des greffes de peau provenant de 19 donneurs différents, dont l'un était un frère du malade. Les greffons provenant de cet homme survécurent pendant environ huit mois, tandis que ceux des autres donneurs dégénérèrent en trois à six semaines. De la cortisone fut administrée à des doses régulièrement décroissantes pendant une période de six mois. Une étude approfondie des groupes sanguins des deux frères démontra une

très grande ressemblance dans divers systèmes (ABO, Rh, Lu, MN, Kk, La, Fy). A la fin du traitement, on tenta à deux reprises, à titre expérimental, une transplantation de peau croisée entre donneur et receveur: à ce moment les greffons ne survécurent chez le receveur que fort peu de temps.

L'auteur en déduit que la similitude des groupes sanguins est un facteur d'importance primordiale. L'échec des tentatives expérimentales de greffes peut s'expliquer de la façon suivante: la sensibilisation du receveur aux antigènes cutanés du donneur se fait très lentement, car si la ressemblance humorale entre les deux individus est grande elle n'est cependant pas absolue, et la fabrication des anticorps en quantité suffisante pour être cliniquement décelable requiert une longue période de temps.

En conclusion on se rappelera que pour pratiquer des greffes cutanées homologues avec le plus de chances de succès, il faut que le donneur et le receveur soient aussi proches parents que possible; que les groupes sanguins des deux individus soient très semblables; se souvenir que l'on peut être aidé de façon précieuse par l'administration de cortisone et ne jamais greffer en plusieurs temps, à cause des phénomènes de sensibilisation.

CYSTINURIA: REVIEW OF LITERATURE: GENEALOGY AND REPORT OF A CASE WITH RECURRENT UROLITHIASIS*

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CYSTINE is one of the sulphur-containing amino acids which is normally excreted in human urine at the rate of 40 to 80 mg. daily.[1] Cystinuria is a congenital disease in which the excretion of cystine is markedly increased.

INCIDENCE

Cystinuria is more common than is generally appreciated and is usually symptomless. The entity was first investigated in 1810 by Wollaston. It was always considered a rare disorder until 1932 when Lewis[2] investigated over 10,000 students and found cystinuria to be present in one out of every 600. Cystine crystalluria occurs in one out of 15,000 to 20,000 routine hospital urinalyses. Clinical manifestations occur in the 2 to 3% of cystinurics who develop urinary calculi. One to four per cent of all urinary calculi are of the cystine variety.

Males are affected more frequently than females. The defect is probably present from birth. Calculi may occur at any age but are more commonly seen in young adults.

PATHOGENESIS

It is highly probable that cystinuria is due to an inherited renal defect.

Dent and Rose[3] in 1949 used partition paper chromatography to demonstrate that in cystinuria with stone formation, lysine and usually arginine and ornithine were present in abnormal amounts. Since other urinary amino acids were normal and since the plasma levels of all the amino acids in these patients were normal, they postulated that the condition represented an inherent defect in the enzyme system in the renal tubular cells involved in the reabsorption of amino acids of related structural type. In the past few years considerable evidence has accumulated to support the renal hypothesis.[4]

Cystine is a relatively insoluble amino acid, and high urinary concentration accounts for precipitation and clinical manifestations of urolithiasis.

GENETICS AND CLASSIFICATION

Dent and Harris[5] in 1951 reviewed the pedigrees of 11 new cases of cystinuria.

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Six of these patients had presented with symptoms of urinary calculi subsequently proved to be composed of cystine. One patient was symptomless and cystinuria was discovered by chance. There were three cases of Fanconi syndrome and one example of hepato-lenticular degeneration or Wilson's disease. A large number of relatives were examined and a further 11 cases discovered. On the basis of clinical, biochemical and familial findings, these authors suggested the following classification of the genetically determined "cystinurias";

1. *Classical cystinuria.*—Patients usually enjoy good health but occasionally form cystine stones in the urinary tract. The urine always contains large quantities of cystine and lysine and, usually, arginine and ornithine. An identical condition is frequently found in close relatives. Recent studies by Harris and Robson[4] indicate the genetic complexity of classical cystinuria; but it is possible to divide the families into two main groups:

(a) Recessive cystinuria. The familial distribution is typical of a Mendelian recessive character. Usually the abnormality occurs in a single sibling in each family who is likely to have recurrent calculi.

(b) Incompletely recessive cystinuria. Most members of the families excrete large amounts of the four amino acids but usually remain symptom free. Stone formation will occur if cystine excretion is high enough.

2. *Fanconi syndrome.* — This condition and its variants may occur in very similar forms in children or adults. The syndrome comprises resistant rickets (or osteomalacia), chronic acidosis, hypophosphatæmia, renal glycosuria, and a large excretion of many amino acids. The condition is familial and Mendelian recessive.

3. *Hepato - lenticular degeneration or Wilson's disease.*—This is associated with a large excretion of many amino acids including cystine. It is regarded as being recessively inherited.

Hepatic cystinuria.—In addition to the familial types of cystinuria, generalized excretion of amino acids including cystine may occur in acute and chronic liver disease.

Clinical Features

The loss of the four amino acids in cystinuria does not lead to nutritional disturbances under normal dietary conditions. The clinical features are all related to recurrent urinary calculi.

The signs and symptoms of cystine urolithiasis do not differ greatly from those which accompany calculi of other composition. The calculi are usually unilateral initially with a tendency to recur, particularly on the same side. Staghorn calculi are rare. Infection, if present on the same side, can be regarded as secondary.

Diagnosis

I. *Urine*

(a) The alkaline cyanide—nitroprusside test of Brand, Harris and Biloon[6] is a useful screening test for urine, but frequently the colour which develops in this reaction is difficult to interpret.

(b) One-dimensional chromatography on filter paper using butanol: acetic acid: water (4:1:5) as a solvent and developing the paper strip with 0.2% alcoholic ninhydrin solution and heat is a more definitive method for detecting cystinuria (Fig. 1).

II. *Renal Calculi*

1. *Macroscopic appearance.*—The typical cystine calculus is brownish in colour, and on section the cut surface presents radiating crystals.

2. *Chemical analysis.*—

(a) The calculus is dissolved in hot dilute hydrochloric acid and the solution neutralized with hot sodium acetate solution, then allowed to cool slowly; the precipitate is examined microscopically for the typical hexagonal crystals of cystine.

(b) Chromatographic analysis of a solution of the calculus in hydrochloric acid is carried out

3. *Examination of powdered calculus material by polarized light with a petrographic microscope.*[7]

4. *Study by x-ray analysis.*[8]

5. *Infrared spectroscopy.*[9]

TREATMENT

The general principles for treatment of cystine urolithiasis and accompanying complications are the same as those applied to calculi of other compositions. However surgery should be planned with the thought that recurrence is almost inevitable. Prophylactic measures against recurrence are particularly important in this entity.

1. *Forced Fluid Intake and pH of Urine*

At a pH between 5 and 7, only 300 to 400 mg. of cystine per litre can be kept in solution. A patient with cystinuria may excrete up to 1000 mg. daily, so that the concentration may frequently reach saturation level, particularly at night. Forced fluid intake around the clock is obviously important. It has been recommended that at least two glasses of water should be taken at bedtime and again during the night when up to micturate.

Cystine is more soluble in alkali than acid, but it has been shown that a large increase in cystine solubility does not occur until the urinary pH is over 7.6. This requires continuous high dosage of alkali, which may not be practical for long term therapy.

2. *Diet*

Omission of sulphur-containing protein from the diet has been recommended in the past. Only severe restriction of protein causes an appreciable reduction of cystine excretion. Methionine, which is a precursor of cystine, is an essential amino acid which should not be eliminated from the diet. It has been pointed out that there is danger of negative nitrogen balance if protein is restricted to the point that it reduces cystine excretion.

3. *Vitamin C*

Ascorbic acid therapy has been suggested by Levine, as reported by Rolnick.[10] Ascorbic acid is a strong reducing agent which will theoretically favour the synthesis of the more soluble amino acid cysteine in preference to cystine. However, it has not generally been shown to accomplish this.

4. *Cortisone and ACTH*

These hormones are known to increase the excretion of nitrogenous wastes. Weinberg and Tabenkin[11] have studied the effect of cortisone in a cystinuric and found that the excretion of cystine was increased.

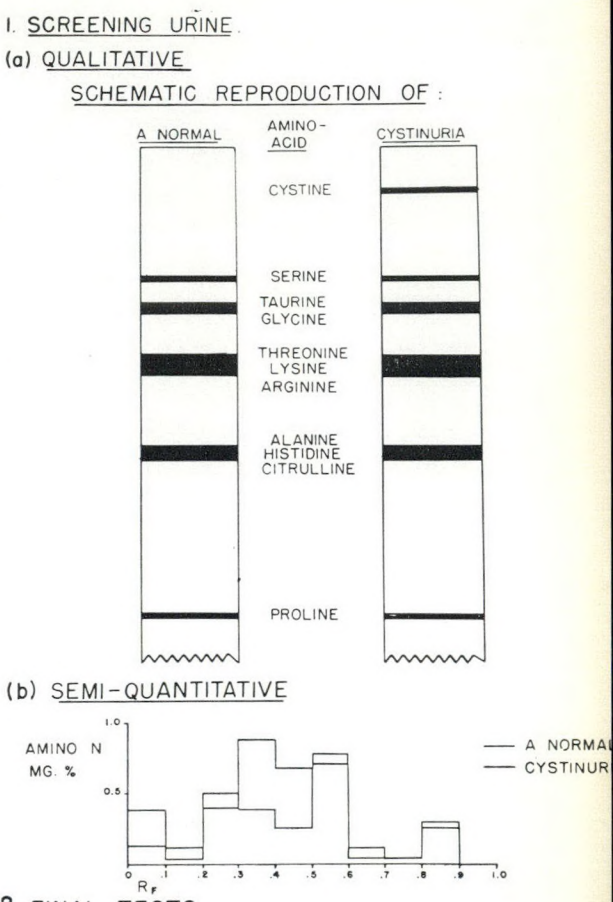

Fig. 1.—Chromatography

5. *Choline*

Hottinger[12] in 1942 first reported that choline would reduce cystinuria. Zinsser[13] in 1950 was also successful in reducing cystine excretion in two patients using choline therapy. Feeding cystine to a cystinuric does not increase its excretion, but feeding the cystine precursors methionine and cysteine does increase cystine excretion. Methionine acts as a donor for methylation in metabolic processes and is subsequently converted to cysteine and cystine. Choline is also a methyl group donor and the rationale for its use is based on the theory that

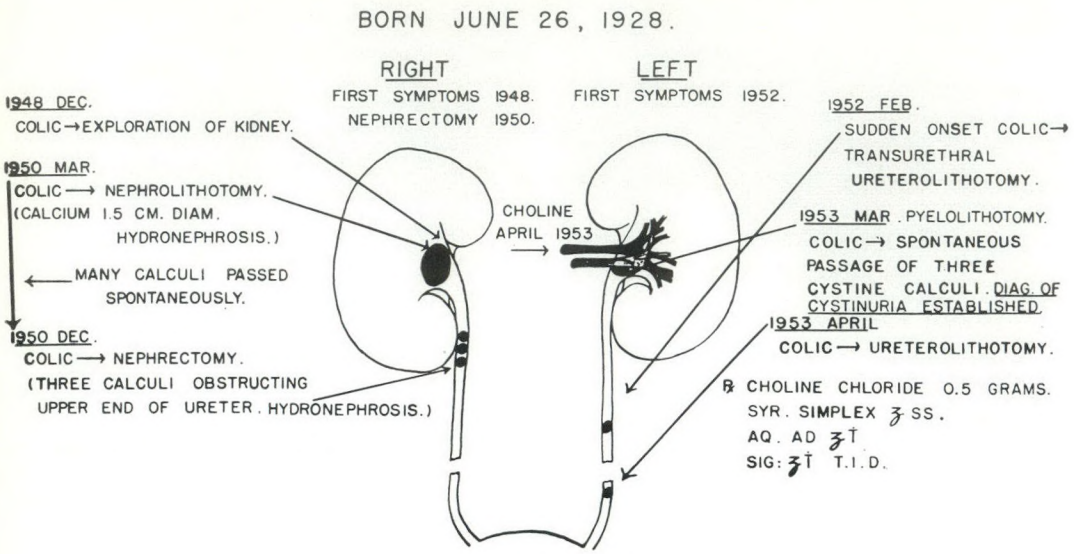

Fig. 2.—Urological history.

by supplying methyl groups it lowers the demand for methionine breakdown and subsequent cystine formation.

Weinberg and Tabenkin[10] were unable to reduce the excretion of cystine in their patient by the administration of choline. In 1954 Coxon and Kolb[14] carefully studied the effects of choline administration in three cystinurics in dosages of 3 to 8 g. daily. They found that choline did not change the amount of urinary cystine excreted. They concluded that the conversion of methionine to cystine in the cystinuric is not influenced by the availability of labile methyl groups under normal nutritional conditions.

Case History

The urological history of C.H.(Jr.) is shown in Fig. 2. From 1948 until 1953, this young male had multiple attacks of renal colic. Six surgical procedures, including a right nephrectomy, were required. Many calculi were spontaneously passed and always described as being light brown in colour. Routine laboratory analysis had always reported the calculi to consist mainly of cholesterol with traces of carbonate, but calcium was never found. Calcium and phosphorus studies were done. The only period in which serum calcium was lowered and serum phosphorus was elevated was in March 1953, when the non-protein nitrogen was elevated and the patient acidotic.

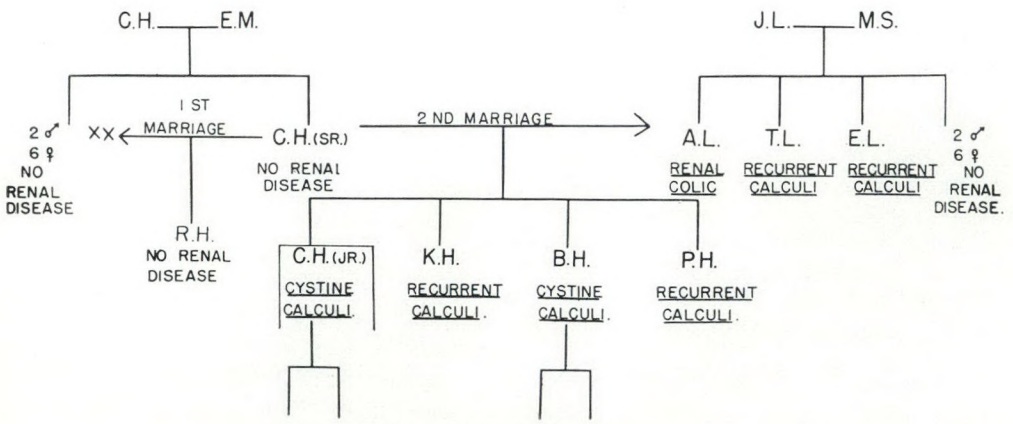

Fig. 3.—Genealogical tree.

When obstruction to the remaining kidney was relieved, blood chemistry reverted to normal.

The diagnosis of cystinuria was established in March 1953, when a calculus removed by pyelolithotomy was found to be composed of almost pure cystine. The following month a pure cystine stone was removed by left ureterolithotomy. In addition to general measures choline* therapy was instituted. The patient has been on oral choline since that time (0.5 gram t.i.d. in simple syrup solution). He has been entirely asymptomatic, and repeated pyelograms have shown no recurrent calculi. It should be emphasized that this patient had recurrent calculi on the right side originally; after nephrectomy, episodes of left renal colic began. This is quite a typical clinical course for a cystinuric.

Unfortunately the urine was not quantitatively examined for cystine before choline was prescribed. In February 1958, the 24 hour excretion of cystine was found to be 228 mg. This is well above the normal but considerably less than the quantity reported to be excreted by clinically manifest cystinurics. These facts, combined with the clinical course over the past five years, give strong support to the view that choline reduced cystine excretion in this case.

This patient's genealogical tree makes a fascinating study of the familial aspects of cystinuria (Fig. 3).

There is no paternal history of renal calculi. The father (C.H., Sr.) and one sibling from a first marriage had no renal disease. However, the second marriage was to a woman (A.L.) who had a strong family history of urinary calculi. All of the four siblings from this marriage, including the patient, have had recurrent renal calculi now proven to be cystine.

The patient now has four children under seven years of age. Recently, cystine urinary excretion studies of the four children were done. Values ranged from a negligible amount to 14.2 mg. cystine per 24 hours. Although these values are within normal limits, it is known that clinical manifestations will be unlikely before early adult life. It should be of value to establish a baseline of cystine urinary excretion in childhood where a known familial tendency exists.

Summary

Cystinuria is a congenital disease in which an excessive quantity of the amino acid cystine is excreted in the urine, along with amino acids of related structural type. The most plausible theory states that the cause is an inherited renal defect in tubular reabsorption of these amino acids. Cystine is relatively insoluble, and 2 to 3% of cystinurics will develop clinical manifestations of urinary calculi.

The entity is more common than generally realized, and careful calculus analysis for cystine should be a routine part of laboratory investigation. A strong familial history of recurrent urinary calculi is often present.

Cystine is more soluble in alkali than in acid, and as a prophylactic measure the urine should be kept alkaline by drug therapy and alkaline ash diet combined with forced fluid intake. Choline does not consistently reduce cystine excretion, and there is no general agreement in the literature regarding the efficacy of choline therapy. However, some patients have shown dramatic benefit from its use, and a trial of therapy would appear to be indicated. Cystine urinary excretion studies before and after therapy should be a valuable measure of assessment.

*Supplied in crystalline form by British Drug Houses.

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Résumé

La cystine, aminoacide soufré, est normalement excrétée dans les urines au taux journalier de 40 à 80 mg. Si ces chiffres sont nettement augmentés, il y a cystinurie. Cette affection est plus fréquente qu'on ne le croit généralement, car elle provoque peu de manifestations cliniques. La proportion des analyses d'urine de routine faites dans les hôpitaux montrant des cristaux de cystine est de 1 à 15,000 ou de 1 à 20,000. Sur ce chiffre de cystinuries, seulement 2% à 3% sont accompagnés de symptômes. Les hommes sont plus souvent atteints que les femmes. La maladie est très probablement causée par un trouble fonctionnel rénal héréditaire. Lorsque les troubles de lithiase sont présents, la cystinurie est souvent accompagnée d'excrétion anormale de lysine, d'arginine et d'ornithine.

En 1951, deux auteurs, Dent et Harris, ont procédé à l'examen très détaillé, aux points de vue clinique, biochimique et héréditaire de 11 cas de cette affection, qui, selon eux, peut se rencontrer dans les trois syndromes suivants: (a) la cystinurie banale, dans laquelle le patient jouissant habituellement d'une bonne santé, élabore de temps en temps des calculs de cystine dans ses voies urinaires; le plus souvent, la distribution familiale de la maladie est celle d'un caractère héréditaire mendélien récéssif; (b) le syndrome de Fanconi, également héréditaire récessif; (c) la maladie de Wilson, dans laquelle il existe une excrétion anormale de nombreux acides aminés. Le diagnostic peut être fait dans l'urine par le test de Brand ou mieux par la chromatographie. Les calculs sont caractéristiques et doivent être analysés.

En ce qui concerne le traitement, on trouve dans la littérature des considérations diverses sur les points suivants: l'abondance des boissons et l'importance de maintenir les urines alcalines; le régime pauvre en soufre; l'administration de vitamine C qui favoriserait peut-être la formation de cystéine à la place de cystine dans le métabolisme général; l'augmentation de l'excrétion de cystine provoquée par la cortisone et l'ACTH; la possibilité théorique, non retrouvée en clinique, de diminuer la formation de la cystine par la choline en jouant sur les processus de méthylation.

Les auteurs rapportent alors un cas nouveau. C'est celui d'un jeune homme qui avait souffert de 1948 à 1953 de nombreuses crises de coliques néphrétiques et avait subi six interventions chirurgicales dont une néphrectomie droite. Le diagnostic ne fut cependant posé qu'en mars 1953, lorsqu'on put lui extraire un calcul composé de cystine pure. Outre le traitement général, il fut alors prescrit, afin d'éviter les récidives, de la choline à la dose orale de 0.5 g. t.i.d. Depuis lors ce malade n'a plus présenté d'épisodes lithiasiques. Il est regrettable qu'un dosage de la cystine urinaire n'ait pas été pratiqué avant l'instauration du traitement à la choline; à l'heure actuelle, le taux de cystine excrétée est de 228 mg. par 24 heures, ce qui est élevé, mais beaucoup plus bas que les chiffres généralement trouvées chez les cystinuriques calculeux. Il est intéressant de noter que la mère et certains collatéraux du patient sont également atteints de ce trouble.

BRITISH ASSOCIATION OF PLASTIC SURGEONS

The British Association of Plastic Surgeons is holding an International Congress in London from July 11-17, 1959, under the Presidency of Mr. Rainsford Mowlem. The Secretary and Treasurer is Mr. David Matthews, and the address of his Secretariat to which enquiries should be addressed is:

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CANCER OF THE THYROID: UNDIFFERENTIATED AND MISCELLANEOUS CARCINOMAS*

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ONE HUNDRED and five thyroid cancers encountered at the Vancouver General Hospital during a 10 year period (1947 to 1956 inclusive) have been recently reviewed with particular regard to their pathology and natural history. The 31 undifferentiated and 74 differentiated cancers were so different that they will be the subject of separate reports. Only the distinction between poorly differentiated follicular and some small cell carcinoma created difficulty in separating these groups. It is the purpose of this paper to report on the undifferentiated group which constituted 30% of the total, a larger than usual proportion.[1]

Undifferentiated lesions of the thyroid are of several pathological types. Proper classification is desirable because it is apparently our most important determinant of the natural history of the disease. Unfortunately this is often difficult for the pathologist, particularly as regards allocation of small cell carcinoma, lymphosarcoma, and reticulum cell sarcoma. The classification used follows:

Undifferentiated Carcinoma
Giant cell — 17cases
Small cell — 8 cases
Miscellaneous Carcinoma
Squamous cell — 2 cases
Lymphosarcoma — 2 cases
Reticulum cell sarcoma — 2 cases

Each of the above types will be reviewed briefly with reference to pathology and clinical features.

GIANT CELL CARCINOMA (17 cases)

Pathologic observations: On the whole this group was distinguished without difficulty. These lesions presented a heterogeneous histologic appearance. Cell type varied in different tumours from those with large polyhedral cells (Fig. 1), sometimes with bizarre multinucleated cells, to spindle cell lesions simulating sarcoma (Fig. 2). All spindle cell lesions were placed in this group despite the inability to show definite origin from epithelial elements in several of them.

Clinical observations: Sixteen cases were followed up. These were:

(a) of equal sex incidence;

(b) in patients 50 years of age or over.

Only one person lived more than one and a half years after diagnosis, and died, like the others, of locally invasive disease at 30 months. The mean survival time was five months. The treatment, generally by combined surgery and irradiation, had no apparent effect on the course of the disease.

SMALL CELL CARCINOMA (8 cases)

Pathologic observations: This was a less distinct group than the cases of giant cell carcinoma. The histologic appearance was that of a highly cellular proliferation of uniformly small cells. Often no organoid pattern was present, and the appearance may be impossible to distinguish from malignant lymphoma (Fig. 3). In most instances, however, where sufficient sections were cut, foci bearing some semblance to solid alveolar or even acinar structures could be found, and this established the diagnosis with certainty (Fig. 4). We did not find the study of the reticulum pattern to be of great value. In one of the patients who died five years after diagnosis of intercurrent disease with no autopsy, diagnosis was equivocal since malignant lymphoma could not be ruled out histologically.

Clinical observations: All eight cases were followed up. These were:

(a) predominantly in females (six of eight);

(b) again in the older age group. The youngest patient was 46 and five out of nine patients were 70 years of age or older.

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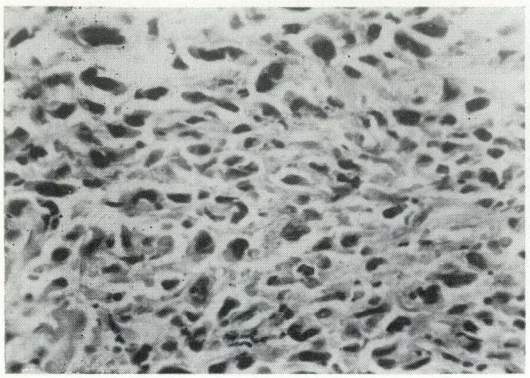

Fig. 1.

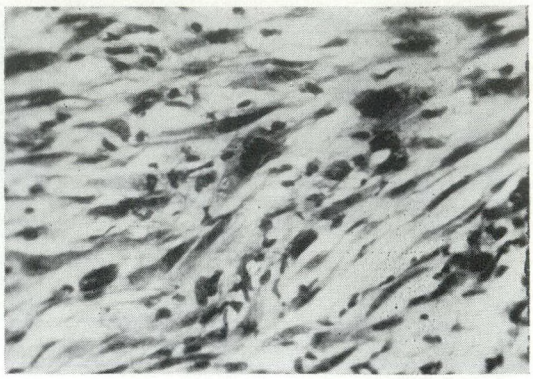

Fig. 2.

Fig. 1.—Giant cell carcinoma of thyroid, pleomorphic cell type (x375). **Fig 2.**—Giant cell carcinoma, spindle cell type (x375).

In contrast to the giant cell lesions, this group showed marked variability. Only three were dead in less than a year, another two lived one to two years, and three lived five years or more. Of the three long-term survivors, one died at five years and three months of other causes (cerebral hæmorrhage), another is alive and well at five years, and the last is alive with disease at 12 years.

The treatment applied was again surgical excision of as much involved tissue as possible, with subsequent external irradiation. Judged by immediate response and the 30% five year survival, irradiation significantly affected the natural course of some. A more guarded prognosis than in giant cell carcinoma is indicated.

SQUAMOUS CELL CARCINOMA (2 cases)

Pathologic observations: There would appear to be two types of squamous cell carcinoma of the thyroid, one a pure squamous carcinoma (Fig. 5), the other an adenocarcinoma of the thyroid with associated squamous carcinoma (adeno-acanthoma). Both are readily identified. Where the changes of squamous carcinoma are frank and fairly extensive, the prognosis would seem to be that of the squamous rather than the adeno-carcinoma.

Clinical observations: Both patients were older women (45 and 80 years) and succumbed to their disease at three and fourteen months respectively. Though susceptible to x-ray in other sites the squamous cell carcinoma of the thyroid, in neither of the present examples, showed any response.

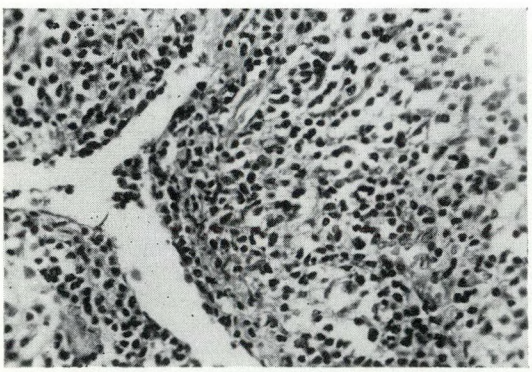

Fig. 3.

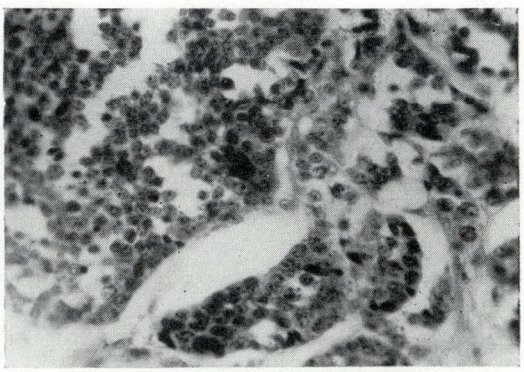

Fig. 4.

Fig. 3.—Small cell carcinoma of thyroid resembling lymphosarcoma and showing infiltration of a vein wall (x375). **Fig. 4.**—Small cell carcinoma of thyroid showing focus of organoid pattern (x375).

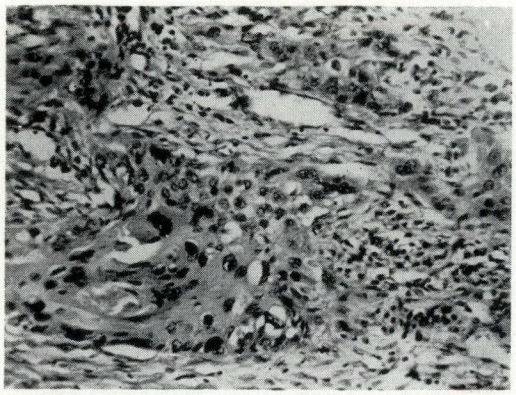

Fig. 5.—Squamous cell carcinoma of thyroid (x150).

LYMPHOSARCOMA (2 cases)

Pathologic observations: These cases are often difficult to distinguish when:

(a) poorly differentiated, from small cell carcinoma (see above);

(b) well differentiated, from Hashimoto's disease.

The present two cases lend point to the latter difficulty.

In Case 1, the original tissue (Fig. 6) did not have all the features of Hashimoto's disease, in that Hürthle cell proliferation and lymphoid follicles were absent, but the lymphocytes appeared mature. Opinions from the Canadian Tumour Registry and Armed Forces Institute of Pathology favoured Hashimoto's disease but the possibility of lymphosarcoma was also suggested. The recurrent lesion (Fig. 7) was a poorly differentiated lymphoblastic lymphosarcoma and there was no doubt about the diagnosis.

The biopsy from the second case resembled the original biopsy from the case above. Although lymphocytes were well differentiated, we believe that the almost complete replacement of thyroid parenchyma with lymphocytes in the absence of lymphoid follicles, plasma cells, and Hürthle cell proliferation are criteria sufficient to differentiate the lesion from Hashimoto's disease. Other helpful features include the presence of mitoses and infiltration beyond the thyroid capsule. The problem is not clear-cut, however, since there are well documented cases of Hashimoto's disease in which lymphosarcoma eventually developed.

Clinical observations: The first case was in a man of 74 who died two months after a firm diagnosis of lymphosarcoma. Three years earlier Hashimoto's disease had been diagnosed by a biopsy.

The second case is very recent—in a 62 year old woman who remains alive and well five months after a biopsy and irradiation. No conclusions are merited about the effectivenesss of treatment from this small experience.

RETICULUM CELL SARCOMA (2 cases)

Pathologic observations: A distinction between reticulum cell sarcoma and lymphosarcoma on the basis of cellular morphology and reticulum formation is by no means sharp, and possibly no useful purpose is served by making it. The premise that reticulum cell sarcoma or struma reticulosa is unique in its frequent metastases to the gastrointestinal tract remains to be proven. Furthermore, Winship's observation that American pathologists generally interpret these lesions as undifferentiated carcinomata, whereas in England there is a

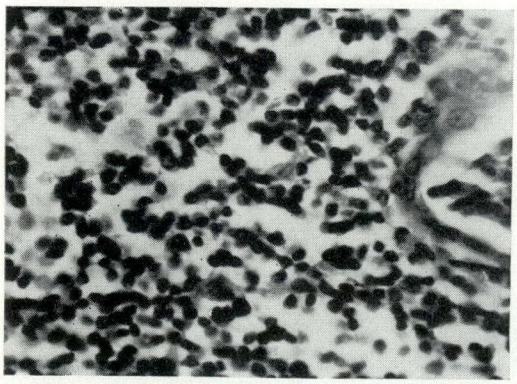

Fig. 6.

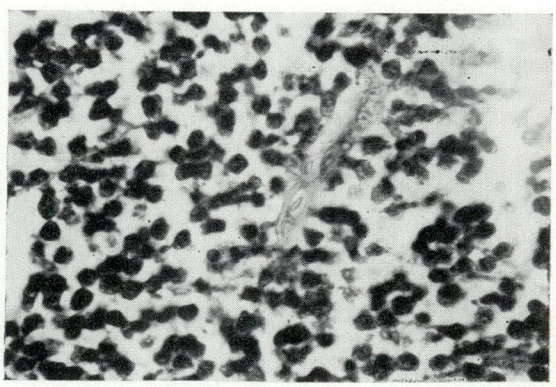

Fig. 7.

Fig. 6.—Questionable Hashimoto's disease of thyroid showing infiltration with mature lymphocytes (x500). **Fig. 7.**—Lymphoblastic lymphosarcoma of thyroid. Same case as Fig. 6, showing transition to lymphoblastic lymphosarcoma after three years (x500).

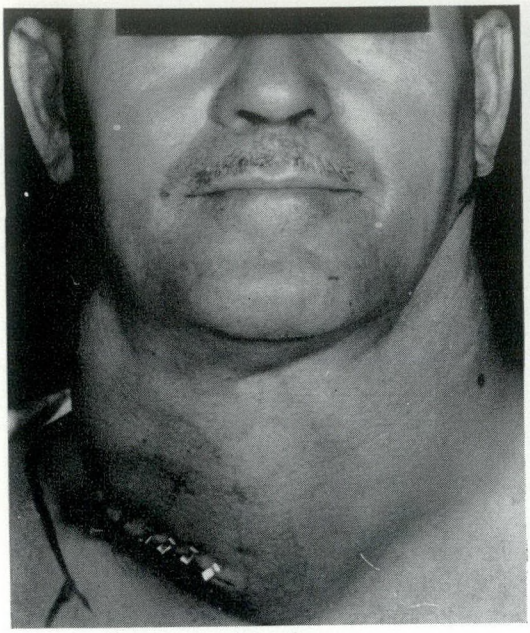

Fig. 8.

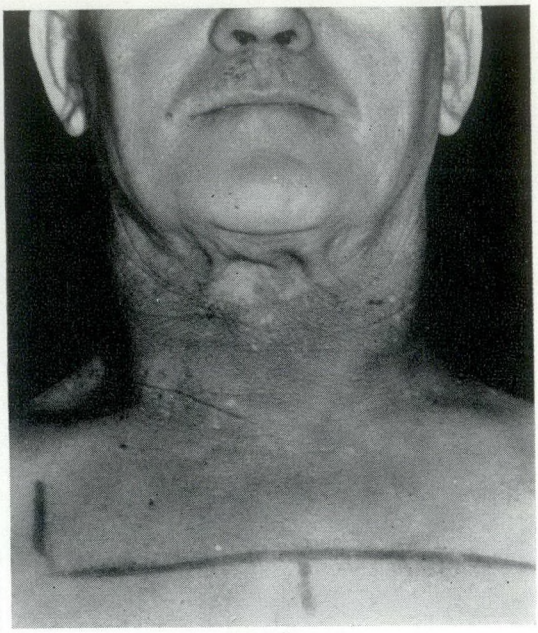

Fig. 9.

Fig. 8.—Reticulum cell sarcoma (Case 2) before radiation treatment. **Fig. 9.**—Case 2 after radiation treatment.

distinct tendency to regard them all as of reticulum cell origin points to difficulties in diagnosis by purely histo-pathological means.

Clinical observations: As these are rather unusual and controversial lesions, brief summaries of the two cases are presented.

Case 1.— This woman, aged 69, was seen in April 1954, with a right thyroid lump of six weeks' duration. This adherent lobe was removed and surgery was followed by regional irradiation (Co^{60}—6300 r in 31 days). Recurrence in the neck in August 1954, required further irradiation (6000 r). She died on January 22, 1955, the immediate cause being respiratory obstruction caused by laryngeal œdema. At autopsy the neck was found to be clear but two visceral metastases were present in the stomach and right kidney respectively. Review of the original and autopsy slides led to a revision of the initial diagnosis from small cell carcinoma to reticulum cell sarcoma.

Case 2.—A man, aged 53, presented in August 1955, with marked swelling of the neck which had progressed for the previous eight months. There was associated hoarseness and dizziness. The lesion was biopsied and considered to be a very undifferentiated small cell carcinoma of the thyroid (Fig. 8). This was treated by Co^{60} irradiation (5815 r t.d.) resulting in rapid dissolution of the mass and improvement of symptoms (Fig. 9). In December 1955, he complained of indigestion. Barium meal examination showed an infiltrating lesion in the stomach. Gastroscopic biopsies were inconclusive as to the nature of the growth. In September 1956, with progression of symptoms and hæmorrhage, he was treated by epigastric irradiation with some symptomatic improvement. He finally died in December 1956, 16 months after diagnosis and 24 months after the onset of symptoms. Autopsy revealed tumour infiltration in the thyroid and stomach and their immediate vicinities. Review of the original slides from the thyroid (Fig. 10) and

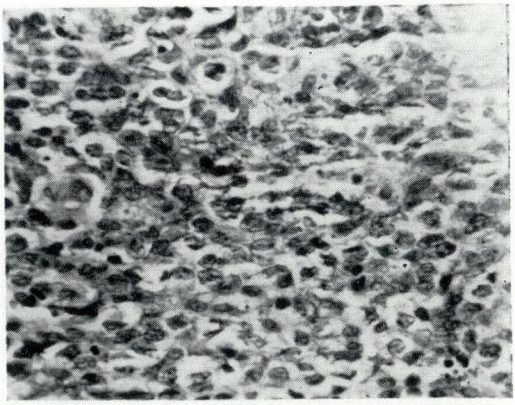

Fig. 10.—Reticulum cell sarcoma of thyroid (x500).

the autopsy slides led to the diagnosis being changed from small cell carcinoma to reticulum cell sarcoma.

Both these cases proved quite sensitive to irradiation. Were it not for distant spread a better prognosis might pertain in these cases.

Summary

Thirty-one cases of undifferentiated and miscellaneous neoplasms occurring in a total series of 105 thyroid tumours have been reviewed.

1. Giant cell carcinoma (17 cases) was confidently diagnosed by the pathologist. Of equal sex incidence, it occurred in the older age group (mean 65 years). The prognosis was invariably poor, the mean survival being only five months and the longest survival two and a half years. Treatment had no apparent effect on the course of the disease.

2. Small cell carcinoma (eight cases) could be less confidently classified by the pathologist. There was a marked preponderance of females—six out of eight. One-third of the cases showed a surprising survival of five years or more. Radiation was the apparently effective agent in these long-term survivals.

3. Squamous cell carcinoma (two cases). This was susceptible of a positive pathologic diagnosis and carried a prognosis comparable to the giant cell lesion.

4. Lymphosarcoma (two cases). Differential diagnosis from struma lymphomatosa was a problem. No conclusions could be reached with respect to prognosis and effectiveness of treatment.

5. Reticulum cell sarcoma (two cases). This is an equivocal entity. Both the cases reported carried a poor prognosis despite good resolution of tumour locally with irradiation.

Acknowledgment

We wish to acknowledge the considerable assistance provided by the B.C. Cancer Institute.

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Résumé

La matière de cet article a été fournie par l'examen de 31 cas de cancers thyroïdiens non différenciés observés au Vancouver General Hospital. Leur classification n'est pas facile, mais on se propose de les étudier en les rassemblant dans les groupes suivants: (a) carcinomes indifférenciés à cellules géantes (17 cas); (b) carcinomes indifférenciés à petites cellules (8 cas); (c) cancers divers, à cellules squameuses (2 cas); (d) à cellules réticulaires (2 cas); et (e) lymphosarcomes (2 cas).

Les *cancers à cellules géantes* sont d'un diagnostic anatomopathologique facile du fait de l'irrégularité des formes cellulaires (grandes cellules polyédriques à côté de cellules plurinucléées et de cellules fusiformes). Cliniquement, ce type de lésion se rencontre de façon à peu près égale chez les deux sexes vers la cinquantaine. La survie moyenne est de cinq mois environ. Le traitement, combinant la chirurgie et la radiothérapie, semble inefficace.

Les *carcinomes à petites cellules* sont constitués microscopiquement par des amas de petites cellules proliférant très activement dans une anarchie architecturale très marquée: ce n'est seulement que sur une grande série de coupes que l'on parvient à retrouver çà et là des formations qui ressemblent vaguement à des acinus. Du point de vue clinique, cette forme prédomine chez les femmes de 50 ans ou plus. La durée de survie varie d'un à douze ans. Le pronostic est donc meilleur que dans le groupe précédent. Le traitement consiste également en l'association de la chirurgie et de la radiothérapie; d'après l'évolution, il semble que cette dernière soit utile.

Cancer à cellules squameuses.—Histologiquement il s'agit soit d'un carcinome squameux pur, soit d'un carcinome squameux associé à un adénocarcinome. Cliniquement, les deux malades appartenant à ce groupe étaient des femmes âgées de 45 et 80 ans, qui moururent toutes deux. Bien que dans d'autres localisations la radiothérapie soit efficace sur l'adénocarcinome, elle semble sans action ici.

Le diagnostic anatomo-pathologique du *lymphosarcome* est délicat. La confusion est possible avec le carcinome indifférencié à petites cellules. Les deux cas traités dans ce service—un homme de 74 ans et une femme de 62 ans—ne permettent de tirer aucune conclusion d'ensemble.

Le diagnostic histologique entre le lymphosarcome et le *sarcome à cellules réticulaires* est difficile; à tel point que des divergences de vue existent entre les écoles américaine et anglaise. Le premier cas présenté—une femme de 69 ans opérée et irradiée qui mourut 6 mois plus tard—et le second—un homme de 53 ans traité seulement par irradiation qui décéda 18 mois plus tard—présentèrent tous deux des métastases au niveau de l'estomac. Le pronostic est donc très mauvais, bien que la tumeur primitive se fût montrée très sensible à l'irradiation.

THE PRESENT STATUS OF EXTRACORPOREAL CIRCULATION*

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It is five years since the first successful open intracardiac operation was performed, a mechanical pump oxygenator being used to maintain cardiorespiratory function while the heart was incised and corrective surgery performed.[5] Since that time the technique has spread to many medical centres, and as experience has been gained, the risk of extracorporeal circulation has diminished to the point where the indications for its use have broadened to include lesions previously operated upon by other techniques, and lesions producing only mild symptoms. Extracorporeal circulation has come into its own as the surest method for performing deliberate corrective intracardiac surgery. In considering the present status of pump oxygenators it must be remembered that there are several different types of apparatus that work well, although not all types work well for everyone. Often overlooked is the importance of team-work, first in the experimental surgical laboratory and later in the operating-room. A good team with poor equipment may well surpass a poor team with good equipment.

A concept of the current status of extracorporeal circulation might perhaps be obtained by considering some of the technical problems that have been overcome.

Anticoagulation

Pump oxygenators are composed of plastic tubing through which the blood is detoured to chambers of plastic, pyrex or stainless steel containing varying amounts of stainless steel or plastic within them. Heparin has been used to prevent any blood clotting in the extracorporeal circuit. When experience has been gained, operations may be safely performed on heparinized patients, although occasionally bleeding from the chest wall may begin after the heparin is given. Such bleeding is not a generalized uncontrollable ooze but rather a flow from one or more small vessels which may be clamped and ligated in the conventional way. There seems little point in reducing the heparin dose to the absolute minimum, for clotting is then a danger. We have given 2.5 mg. per kg. to the patient and have added 20 mg. to each 500 c.c. of donor blood. That heparin could be neutralized by protamine sulfate was shown by Jorpes and his colleagues,[7] and much work on the interaction of heparin and protamine has been done by Jaques.[6] The dosage of protamine currently being given following bypass varies but is usually close to the dosage of heparin. We have given a dose to equal that of the heparin but, if clots were not seen in the wound before closure, a second dose equal to half the first dose has been given. It is important that the protamine be given slowly for it may cause a transitory hypotension. We have given it in a dilute solution over a period of several minutes.

The Pumps

The pumps in general use today have no moving parts in contact with the blood, propulsion being achieved by the rhythmic external compression of flexible tubing. In this way the plasma hæmoglobin concentration, which is used as an indicator of red cell destruction, can be kept at a low level. Hæmolysis may also result from turbulent flow at a point of constriction in the extracorporeal system or from poorly machined connectors between plastic tubing. The connectors now available are mirror-polished internally, and the internal diameter of the connector is equal to that of the plastic tube which must be stretched over it. In this way constrictions and eddy currents are avoided.

Although some pumps in the past were designed to produce a pulsatile flow, this has not been found necessary and none of the pumps in common use produce a pulse pressure in the normal range.

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Drainage of venous blood from the venæ cavæ is best achieved by gravity. The veins are cannulated by large bore catheters that lead to a chamber open to the atmosphere placed at a level about 60 cm. below the right atrium. In this way the venous blood is drained by a siphon system. Drainage is more satisfactory than when the system is closed, with a pump sucking blood from the cavæ and pumping it to the oxygenator, for here there is a tendency for the vein wall to collapse around the catheter. Having drained the blood into the venous chamber, one pump is used to pump it to the oxygenator and another to pump the arterial blood from the oxygenator to the patient.

The Oxygenator

Oxygenators in use today are of three basic types: (1) Film type,[10] (2) Bubble type,[4] (3) Membrane type.[3, 8] In the film type a thin layer of venous blood is exposed to a constant flow of oxygen; oxygen is taken up and carbon dioxide given off by virtue of the gradient in the partial pressures of these gases in the blood and in the gas flowing over it. The film may be produced by pumping the blood over stationary vertical wire mesh screens or by slowly rotating a series of parallel discs in a shallow trough of blood. In the bubble oxygenator the oxygen is simply bubbled through the column of blood. This is a perfectly satisfactory way to oxygenate but it introduces the problem of defoaming, for the blood is stirred into a froth in the oxygenating process. Defoaming is done with commercial antifoam, a thick paste containing silicone, to which the blood is exposed in a settling chamber. There are experimental and theoretical objections to the bubble oxygenator based on the possibility of embolism of gas or of antifoam. We have raised these objections based on our own experience, but we recognize that the bubble oxygenator has performed magnificently for Lillehei and his associates in Minneapolis and for Cooley in Houston. In Canada, Callaghan has used this type of oxygenator with success. In our hands the margin of safety has been much narrower with the bubble oxygenator than with the film type.

The membrane oxygenator has been developed mainly by Clowes[3] of Cleveland and by Kolff[8] of the same city, who observed the incidental oxygenation that took place in his artificial kidney. Here a very thin membrane (formerly of polyethylene but currently of teflon) is interposed between blood and gas as a sort of synthetic alveolar wall. The transfer of gases takes place through this membrane. The avoidance of a blood-gas interface is looked on as an improvement but, although it has been used successfully for clinical cases, the membrane oxygenator is not yet in widespread use.

Sterilization

Many pump oxygenators include parts made of lucite, which is non-autoclavable. This plastic has been used because of its transparency, there being a general reluctance to have any glass in contact with the blood. The equipment was formerly cold sterilized according to accepted techniques using a bactericidal solution, but there has been dissatisfaction with such methods as occasional positive blood cultures have been obtained. Ethylene oxide sterilizers are effective, but these sterilizers are not yet standard hospital equipment. We have used a chlorine-liberating substance "Warexin".* which is claimed to be bactericidal, sporicidal and fungicidal and which has the added advantage that it breaks down into a non-toxic end product, thus requiring less rinsing than the sterilizing agents formerly used. Pump oxygenators containing only stainless steel, malleable plastic or pyrex are completely autoclavable.

Temperature

Body temperature will drift down during cardiopulmonary by-pass unless there is a system of warming the blood in the pump oxygenator. Not all machines have this equipment, nor is it always effective. Some machines have an electrical heating unit buried in the wall of the oxygenator, which seems to be the tidiest system. Use of a water bath is more clumsy, as is the tech-

*Guardian Chemical Company, Long Island City, N.Y.

nique of playing heat lamps on the oxygenator. A degree of temperature regulation can be obtained by warming the patient on a heating mattress, but normal body temperature cannot be maintained by this method alone, and in infants the body temperature may drop below 30° C., despite the warming machine. The larger the patient the easier it is to prevent hypothermia by using the warming mattress alone.

A slight drop in temperature may do no harm and in fact may add a margin of safety to the operation, for the tissue oxygen requirements are diminished. However, temperatures below 30° C. are undesirable because of increased myocardial irritability, and with physiological perfusion at a normal flow rate there is no need for the benefits of hypothermia. It seems preferable to us to eliminate this variable entirely by incorporating a satisfactory heating unit in the apparatus.

Blood Requirement

Most pump oxygenators require from 2000 to 3000 c.c. of donor blood for priming before by-pass. In addition to this heparinized blood which is drawn the morning of operation, two or three pints must be drawn to replace possible blood loss during by-pass. The procurement of these eight odd pints of heparinized blood imposes a severe administrative problem, for the prospective donors must be contacted and present themselves for cross-matching some time before giving the blood. When they have been satisfactorily matched against the patient, arrangements are made for the donors to return on the morning of operation to give blood. The difficulty in arranging for sufficient fresh blood for a patient of a rare blood group can easily be imagined. We have been fortunate in having the complete cooperation of the Canadian Red Cross. In some areas the problem has been reduced by enlisting convicts as donors.

Blood Balance

The maintenance of a normal blood volume requires special attention in extracorporeal procedures, for in these operations a large transsternal incision is made, the patient is heparinized and during the period of cardiopulmonary by-pass changes may occur not only in the patient's blood volume but in the blood volume of the apparatus. The avoidance of hypervolæmia or hypovolæmia is most critical in patients weighing less than 10 kg., for small variations may seriously deplete or flood their vascular system. In some pump oxygenators it is possible to maintain constant the volume of blood in the apparatus. This is one of the virtues of the screen oxygenator that we have employed.* The maintenance of blood balance then becomes a matter of making accurate measurements of blood loss and replacing the loss by blood transfusion in the conventional manner.

An illustration of recordings in a clinical case at The Montreal Children's Hospital is shown in Fig. 1. The table form is modified from that used by Theye and Kirklin at the Mayo Clinic.[11]

Our system of recording blood outlet and intake is as follows:

1. Sponges and drapes are weighed before operation and soaked sponges are weighed as discarded to indicate blood loss from the operative field.

2. Immediately after the chest has been entered, the hard rubber catheters to be used for postoperative drainage are placed in each thoracic cavity through stab wounds and connected to gentle wall suction through a measuring chamber. Thus, pooling of blood in the thorax is prevented. The standard operating aspirator is also led out to an accurately calibrated chamber.

3. Allowances are made in advance for certain steps which, in our experience, have caused blood loss, for example, the insertion of caval cannulas.

4. Blood removed as samples is accurately measured and replaced. At intervals throughout the procedure the loss accumulated in each of the above categories is recorded as in Fig. 1.

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*The Mark Company, Randolph, Mass.

Time and remarks		Weighed loss	Chest suction	Wall suction	Visual and misc.	Samples and tubing	Gross out	Table saline	Net out	Net in	Cit. blood	Hep. blood	Saline
	10:10	50	25	25	50	15	165	—	165	50	50	—	
	10:20	50	25	25	75	35 100	310	—	310	200	200	—	
	10:22	70	25	25	125	35 100	380	—	380	250	200	50	
	10:28	70	10	10	175	35 100	405	—	405	350	200	150	
	10:33	80	25	50	175	35 100	465	—	465	500	200	300	
	10:40	100	25	90	200	35 100	550	—	550	620	200	420	
	10:45	100	50	200	200	35 100	685	—	685	670	200	470	
Preperf.	10:50	135	50	300	200	35 100	820	—	820	720	200	520	
Perfus.	11:05	140	50	320	250	35 100	895	—	895	920	200	720	
Postperf.	11:30	190	50	450	250	35 100	1075	—	1075	1010	250	760	
	11:45	205	50	500	300	55 100	1210	—	1210	1085	325	760	
	12:00	312	70	500	250	100 70	1297	—	1297	1260	500	760	
Final	12:30	312	70	500	250	100 100	1330	—	1330	1330	575	760	
Date: Dec. 1957													
Name V.C.													
Number CASE 5													
Date MITRAL INSUFF.													

Fig. 1.—Sample blood balance record.

A Dry Field

Although the objective has always been to perform definitive open-heart surgery within a dry surgical field, this has not always been possible. The cannulas divert all caval venous blood to the pump oxygenator, but the coronary venous blood empties directly into the right atrium by way of the coronary sinus. In addition to this flow, which must persist as long as the coronary arteries are perfused, there is a flow of blood into the left atrium by way of the pulmonary veins. This blood will flood into the surgical field whenever the surgeon is operating within the left side of the heart, or if he is operating in the right side and a septal defect exists. A moment might be spent in considering this pulmonary venous blood. With the right heart widely open, there is no flow through the pulmonary artery, and the pulmonary venous blood must therefore come from the bronchial arteries. This is blood that is injected into the aorta by the heart-lung apparatus and, entering the intercostal arteries, flows through the bronchial arteries to the pulmonary veins.

There is thus a varying flow into both the right and left sides of the heart during total cardiopulmonary by-pass. This blood must be aspirated from the surgical field and led back to the venous side of the heart-lung machine. A few years ago, when some operations were done with a blood flow much below normal, the flow back to the open heart was much reduced and this blood was simply aspirated and discarded. Today, however, perfusions are being carried out at physiological flow rates and the volume of intracardiac blood is too great to permit its discard. Coronary venous blood alone is estimated to equal about 7% of caval venous return.[1] In the event of elective cardiac arrest during cardiopul-

monary by-pass, coronary venous flow is eliminated.

Air Embolism

Systemic air embolism is a danger whenever the left side of the heart is open to the atmosphere. This situation exists when the left heart is opened, as in the performance of mitral annuloplasty, or when the right side of the heart is opened and a septal defect exists. If the heart has been arrested, no air will be ejected into the aorta by the left ventricle and the problem is one of filling the chambers of the heart completely with blood before the heart is restarted. If the heart has not been arrested, the left ventricle is still unable to eject air or blood into the aorta when that chamber is open to the atmosphere. Thus, with the right ventricle widely incised for the repair of an interventricular septal defect the contents of the left ventricle simply flood into the right ventricle during systole, and it is only when the defect has been closed that the ventricle is capable of ejecting its contents into the aorta against the normal blood pressure that exists in the aorta during by-pass. Similarly, in mitral insufficiency the contents of the left ventricle simply flow back into the left atrium until the insufficiency has been corrected and the interventricular pressure can reach the level required to open the aortic valve. The avoidance of air emboli in these conditions has not been difficult. We have attempted to increase the margin of safety by not emptying the left side of the heart during defect closure. Following mitral annuloplasty through a left atrial approach, we have carefully filled the left ventricle with blood and massaged the aortic leaflet of the mitral valve against the anterior wall of the left ventricle to prevent trapping of air in this pocket.

Not aspirating on the left side of the septum is probably more important during closure of an atrial than a ventricular septal defect, for here, the mitral valve and ventricular septum being normal, any air finding its way into the left ventricle may be ejected into the aorta on ventricular systole.

Acid-base Balance

The various methods of achieving exchange of oxygen and carbon dioxide in the artificial lungs have been discussed above. Serial observations of blood pH, plasma CO_2 tension and bicarbonate level in our laboratory and in clinical cases have shown that the following five facets of these procedures are important:

1. The effects of thoracotomy and of artificial respiration by the anæsthesiologist.
2. The state of the donor blood.
3. The gaseous environment and efficiency of the oxygenating system.
4. The flow rate and blood pressure during perfusion.
5. The early postoperative period.

The pH of the blood will remain within roughly normal limits if the ratio $\frac{BHCO_3}{H_2CO_3}$ remains at about 20 to 1.[14] To simplify: the denominator of carbonic acid content is a function of respiration, while the bicarbonate content or numerator gives the value of the buffer reserve and, if depressed, reflects loss of the ability to buffer acid products of metabolism.

It has been noted here and elsewhere that vigorous ventilation of the patient with a thoracotomy, particularly if young or in the supine position, will lead to a depression of pCO_2. In addition, because of this change and by the very nature of the operative circumstances, there will be some depression of bicarbonate values. Thus, the pH will remain normal with maintenance of the ratio at 20 to 1 and a state of compensated respiratory alkalosis.

To this relatively simple state is then added the complicating factor of mixture of blood from the pump oxygenator which, in fact, may be several times the volume of the patient. In our observations in the laboratory the pH, pCO_2 and CO_2 combining power of donor blood are relatively normal; however in clinical cases where venous blood is withdrawn using a tourniquet on the arm, there has been a uniform drop in pH of donor blood to about 7.2 with accompanying depression of bicarbonate.

Before the by-pass this donor blood is used to fill the pump oxygenator and it is recirculated through the oxygenator prior to the attachment of the apparatus to the patient. In this process the carbon dioxide is blown off and the pH rises although the bicarbonate remains depressed (Fig. 2). Thus, perfusion is begun in a patient with a normal pH but depressed bicarbonate content and carbon dioxide tension, using blood which has a normal pH but again some depression in both the numerator and denominator of the Henderson-Hasselbach ratio, which then remains near 20 to 1.

After a typical perfusion, pH is still within reasonably normal limits, as in Fig. 3, with depression in both carbon dioxide tension and bicarbonate content, as explained above. As the operation is completed and the patient breathes on his own, carbon dioxide will be accumulated and the metabolic acidosis previously masked by the low carbon dioxide tension will be revealed. If necessary, this is easily treated by administering sodium bicarbonate, and preferably this is begun immediately after perfusion when the depressed blood bicarbonate value, despite normal pH, is recorded.

The above comments are based on our clinical experience. We have had no problem with management. It would, of course, be desirable to collect donor blood with a normal bicarbonate and pH. We do not feel that perfusion *per se* will be the cause of much depression of bicarbonate as long as normal cardiac output is maintained. We are at present investigating in our laboratory various methods of blood collection for these procedures.

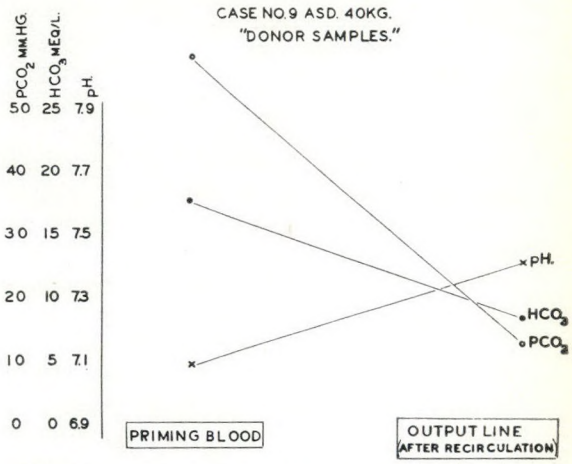

Fig. 2.—Acid-base changes in donor blood before and after filming oxygenator.

Elective Cardiac Arrest

There are obvious technical advantages in having a motionless heart. Over the past three years cardiac arrest[9] has become increasingly popular and some centres make almost routine use of the method. There are two cardioplegic agents in use—potassium citrate and acetylcholine. Whichever is used is injected into the base of the aorta proximal to a clamp in such a way that the drug perfuses the coronary arterial system. We have used a solution of 2.5% potassium citrate in oxygenated blood. Arrest occurs immediately, usually requiring less than 50 c.c. Normal action is returned by removing the aortic clamp and allowing coronary flow to recommence.

Potassium blocks reception of stimuli by the heart muscle and complete arrest is obtained. Oxygen consumption is reduced to 5% of normal.[13] On the other hand, return of heart beat may be delayed after restoration of coronary perfusion.

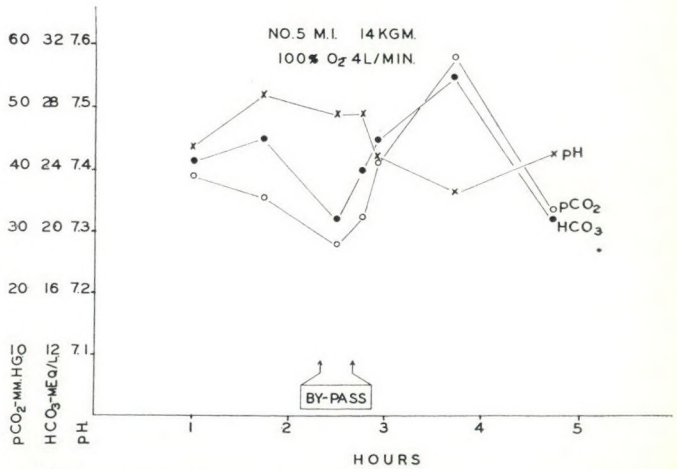

Fig. 3.—Serial acid-base changes of arterial blood during operation and in early postoperative period.

Acetylcholine gives functional but not complete electrocardiographic arrest and, since there is merely a block in transmission, stimuli to the muscle will cause isolated ventricular beats. Cardiac oxygen consumption is reduced to 30% of that in the normal beating heart.[13] It is said that normal function returns more quickly with this method.

Advantages of arrest include technical convenience, reduced risk of air embolism, and reduced blood return to the heart via the coronary sinus. In some cases the nature of the lesion may make it preferable to have a beating heart so as to better gauge the efficiency of repair. Thus, in the repair of mitral insufficiency, continuance of the beat allows one to gauge when insufficiency has been satisfactorily repaired.

The indications for intentional cardiac arrest vary from centre to centre. At The Montreal Children's Hospital it is used in all cases at the moment except for atrial septal defects and mitral insufficiency.

Indications

In our opinion there are two steps to be achieved in any centre beginning to use the pump oxygenator. First of all, the surgical team must prepare itself in the laboratory so that cardiotomy may safely be carried out on animals. The operations must be done methodically in an atmosphere of confidence. When these goals have been attained, operations may be performed on patients with a limited life expectancy having lesions not correctable by other means. This does not mean that very seriously ill cases should be treated exclusively, since the failure rate in this type of patient would be very high anywhere and discouragement might lead to cessation of attempts in this field. Nor, on the other hand, do we feel that it is justified to begin with cases which may be operated on with less risk using hypothermia, such as cases of isolated valvular pulmonary stenosis.

Secondly, once confidence in clinical application has been achieved, elective surgery may begin. Mortality in this phase must be evaluated according to the lesion attacked; all cases should not be lumped together, regardless of type. Operation is not suggested for completely asymptomatic patients as it is in cases of patent ductus arteriosus, but it is reserved for patients with hæmodynamically significant lesions that have produced symptoms. The symptoms may be mild such as failure of normal development, increased fatigability or mild exertional dyspnœa, but in the face of a significant hæmodynamic lesion, demonstrated by careful and thorough cardiac catheterization, operation is advised. If deterioration is not too rapid, operation should be deferred at least until a child has reached a weight of 20 lb. In cases of left to right shunt with greatly increased pulmonary blood flow, operation should not be delayed once any deterioration has begun, for not only will a failing heart increase the operative risk but pulmonary arteriolar changes may progress to the point where corrective surgery is impossible.

Extracorporeal circulation using a pump oxygenator is accepted as the method of choice for dealing with interventricular septal defects, interatrial septal defects of the ostium primum type, and arterioventricularis communis. Isolated pulmonic stenosis of the infundibular type lends itself well to this technique. As experience is gained, it is likely that the simpler atrial septal defects of the secundum type will be repaired in this way for, although hypothermia has been generally satisfactory, the surgeon may be pressed for time when the defect is large or anomalous pulmonary venous drainage is present. We have had uniform success with both techniques in a small series of patients.

In acquired heart disease, extracorporeal circulation has permitted the excision of aneurysms of the ascending aorta. The technique is also under evaluation in other types of heart disease, notably mitral insufficiency, in which the reports to date have been encouraging. Acquired aortic stenosis represents an anatomical derangement that may be impossible to correct despite one's ability to see the valve. Congenital aortic stenosis on the other hand is well suited to open surgery using the pump oxygenator.

We have not had experience with open-heart surgery for tetralogy of Fallot. Here opinion is divided, although the dividing line may be shifting. The systemic-pulmonary anastomosis of Potts or Blalock has provided satisfactory results in many cases, despite the fact that anatomical correction of the various anomalies has not been carried on. As an alternative operation, open-heart surgery now offers the possibility of complete anatomical correction. This carries with it a mortality somewhat greater than the systemic-pulmonary shunt. The approach to this condition has varied from centre to centre depending mainly on the degree of satisfaction with the extracardiac shunt.

There are other conditions for which extracorporeal circulation may provide an effective operation. Hope for complete physiological correction of transposition of the great vessels lies in a technique of intra-atrial venous transposition whereby pulmonary venous blood is directed to the tricuspid valve and systemic venous blood is directed to the mitral valve. In acquired lesions, should satisfactory valve prostheses become available, aortic stenosis and insufficiency might be corrected. The possibility of using this technique for coronary artery disease is an exciting one. Not only might the diseased coronary arteries be dealt with directly, but also a patient after severe infarction might be supported temporarily by an extracorporeal pump oxygenator. Success in just such a case has been reported by Stuckey *et al.*[12]

Extracorporeal Circulation in the Laboratory

In order to operate successfully on animals, the same methodical attention to detail must be given in the laboratory as is given in the hospital operating-room. There are a few basic differences in dog work, which it may be wise to mention. Dogs do not withstand bilateral thoracotomy well. Cardiac arrest is very poorly tolerated in the dog, and very few have been able to attain more than the occasional survival after cardiotomy and arrest, although the individual procedures may be easily withstood.

Research may now proceed along several lines. First of all, basic research on refinement of the pump oxygenator may be carried out; no one presumes that the final or best method has been achieved and more will be said about this later. Secondly, the ability to exclude the heart from the circulation permits study of cardiac metabolism with measurements of arteriovenous differences of various substances. Study of the cardiac conduction system is also possible, as is dynamic study of myocardial circulation and valve function. Study of differential myocardial cooling is possible. Thirdly, extracorporeal circulation can be used to perfuse organs selectively. Thus, the liver of a dog in shock can be perfused at normal blood pressure. Fourthly, at the moment perhaps most work is being done on refinement of surgical technique, particularly valvular reconstruction and development of valve prostheses.

The Ideal Oxygenator

We may conclude with some speculation on the ideal features of a pump oxygenator. Certainly we have not achieved the final apparatus as yet. Furthermore, it is conceivable that different types may be indicated for various cases, for example, supportive care as opposed to open-heart surgery. Also, combination with hypothermia may yet be found to be worth while, although at the moment prevention of significant hypothermia seems important.

Experience would indicate the following ideal qualities:

1. *Low blood volume.*—With increasing use of these procedures, the drain on blood banks will become severe unless the amount of donor blood needed to prepare the machine for perfusion is reduced.

2. *Simplicity.*—The complexity of some of the present systems makes the team required to perform such operations often cumbersome and expensive.

3. *Proof against error.*—In addition to simplicity, the removal of risks such as are involved in electrical power failure would be of value.

4. *Ready maintenance of constant machine blood volume.*—Allowance for this is not made in all pump oxygenators, and in

those where it is present improvement can still be made.

5. *Ease of cleaning and sterilization.*— If not disposable, the pump oxygenator should be readily cleanable and able to withstand autoclaving, which is superior to common methods of cold sterilization both in speed and simplicity.

6. *Absence of the gas-blood interface.*— On theoretical grounds the physiochemical changes which may occur at a gas-blood interface are disturbing. The membrane oxygenator of Clowes[3] interposes a plastic "alveolar membrane" between gas and blood.

7. *Efficient oxygen saturation at high flow rates.*—Full oxygen saturation, of course, is necessary from any artificial oxygenator, and we feel that it should be able to provide this level at high flow rates so as to simulate normal cardiac output. This means a capacity of 6000 c.c. per minute.

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Résumé

Les problèmes de la circulation extracorporelle prennent de plus en plus d'importance à l'heure actuelle avec le développement de la chirurgie cardiaque. Dans des centres toujours plus nombreux, on forme des équipes et l'on expérimente des appareillages de types divers, en vue de la mise au point de cette nouvelle méthode. Celle-ci soulève de nombreux points problématiques que nous allons passer en revue, en essayant de nous rendre compte comment il est possible d'en triompher.

Lutte contre la coagulation sanguine. — Les pompes oxygénatrices sont construites avec les matériaux suivants: pyrex, plastique et acier inoxydable. Le sang qui y circule contient de l'héparine, et le patient lui-même devra être préparé avec cette drogue, par l'administration de 2.5 mg./kg. avant l'intervention. L'héparine peut être neutralisée en cas de besoin par le sulfate de protamine injecté en solution diluée.

Problème du pompage.—Il faut éviter tout contact direct du sang avec des parties mécaniques en mouvement; c'est pourquoi les pompes modernes agissent par écrasement latéral d'un tube élastique. La surface interne de tous les conduits et raccords métalliques devra être polie. Le drainage du sang du malade se fait par de gros cathéters introduits dans les veines caves, par simple gravité, dans un récipient collecteur ouvert à la pression atmosphérique, placé à 60 cm. en dessous de l'oreillette droite; de là, il est aspiré dans l'oxygénateur et retourné au patient. L'absence de succion au niveau des veines caves prévient leur affaissement.

Technique de l'oxygénation. — Les appareils oxygénateurs dont le principe repose sur le barbotage de l'oxygène dans le sang permettent un excellent échange des gaz, mais créent de graves risques d'embolies. Actuellement, on étudie des appareils dans lesquels une fine membrane plastique interposée entre le sang et le gaz joue le rôle de la paroi alvéolaire.

Méthodes de stérilisation.—Différentes méthodes sont décrites; elles devront varier selon les matériaux utilisés dans la construction de l'appareil.

Contrôle de la température.—Lorsque le circuit est en marche, la déperdition calorique est toujours assez importante. Une légère hypothermie n'est pas nuisible; elle augmente même la marge de sécurité de l'intervention en réduisant le métabolisme des tissus. Cependant il est bon de prévoir un système réchauffeur.

Récolte du sang.—L'ensemble du circuit requiert environ trois litres de sang. On conçoit que la récolte d'une telle quantité—surtout s'il s'agit d'un groupe rare—puisse poser des problèmes administratifs. Cependant, les donneurs doivent être rassemblés à temps et les épreuves de compatibilité soigneusement effectuées.

Conservation du volume sanguin.—Le volume sanguin en circulation peut varier, par suite notamment d'hémorragies ou de fuites dans l'appareil. Les précautions nécessaires devront être prises à cet effet, et on devra disposer de flacons de sang de réserve. Dans certaines interventions, une perte importante peut provenir des retours veineux coronaires ou pulmonaires, qui, contrairement à ce qui est pour les retours caves, ne sont pas drainés dans l'appareil. Il faut alors aspirer ce sang et le remettre dans le circuit.

Lutte contre les risques d'embolies.—L'embolie gazeuse est un danger constant lorsqu'on opère sur le cœur gauche, ou sur le cœur droit avec une cloison incomplètement obturée. Ce danger n'existe cependant qu'au moment de la fermeture du cœur, et sera évité par le remplissage soigneux des cavités.

Contrôle de l'équilibre acidobasique.—Le pH sanguin dépend principalement de la relation $BHCO^3/H^2CO^3$, qui est à maintenir dans un rapport de 20/1. Au commencement de l'intervention, le sang des donneurs, prélevé par ponction veineuse sous garrot, présente une légère diminution de la concentration des bicarbonates; après en avoir rempli l'appareil, il faut le faire circuler avant de connecter le malade au circuit; de cette façon, bien que le taux des bicarbonates reste inférieur à la normale, on rétablit un pH correct en diminuant la concentration du gaz carbonique. Mais, après l'opération, il faudra guetter l'apparition de l'acidose et l'enrayer par administration de soluté bicarbonaté.

Arrêt du cœur.—L'obtention d'une immobilité complète du cœur est techniquement très avantageuse. On utilise à cette fin la perfusion du système coronaire par le citrate de potassium ou l'acétylcholine.

La technique de la circulation extracorporelle est la méthode de choix dans les interventions sur les défauts de la paroi interventriculaire, les communications auriculo-ventriculaires et les sténoses pulmonaires. D'autres indications viendront s'ajouter à celles-là lorsque l'expérience dans ce domaine augmentera. Cette technique, appliquée à l'animal, se révèle fondamentale dans le travail de recherche. Les auteurs concluent en énumérant les qualités que devrait posséder l'appareil parfait.

OPTIMUM FLOW RATE WITH EXTRACORPOREAL CIRCULATION

Andersen of Buffalo (*Surgery*, 43: 1021, 1958) discusses the optimum flow rate when extracorporeal circulation is being used and warns against low flow rates in the following terms:

"Although it is known that patients may tolerate a certain duration of shock and yet survive, no one would argue that it is a desirable state or one to be deliberately encouraged. It is more reasonable to suppose that extracorporeal circulation with a subnormal flow rate is desirable except from the standpoint of increasing the ease of technical performance and permitting the use of less-than-adequate pump-oxygenators. When low flow rates are used it should be with the realization that the factor of time is of great importance, that the tolerance is limited, and that physiologic abnormalities are being created which subsequently must be corrected. The only possible justification for their use must lie in the possibility of a protective redistribution of blood flow at low perfusion rates which could maintain adequate blood flow to the vital organs at the expense of the less vital. Further studies of this subject and of the actual tolerance to various levels of circulatory rate are in progress; until these factors are better understood, we must conclude that the safest course to follow is the maintenance of a 'high flow'."

CASE REPORTS

CHOLEDOCHUS CYST WITH ASSOCIATED CARCINOMA*

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ABOUT 200 cases of choledochus cyst have been described in the literature. Many reports have been of one or two cases, exceptions being a particularly fine report of six cases by Walton[3] and a large series, now more than 52 cases, in children, collected by Gross.[1] Only one instance of choledochus cyst and carcinoma has come to our attention, a squamous cell carcinoma reported by Irwin and Morison in 1944.[2] It was thought that a recent experience with choledochus cyst and associated carcinoma should therefore be recorded.

CASE REPORT

A 25 year old woman had perfectly good health until May 1957, when she was delivered at term of a normal child. After this, she had recurrent bouts of right upper quadrant pain. She was admitted to hospital in July 1957, and these complaints were investigated with barium meal, intravenous pyelography and gall-bladder radiography. Only the latter proved abnormal, the oral dye producing no shadow. When the examination was repeated with intravenous dye, a normal gall-bladder was outlined but the biliary tree was not visualized. Her complaints subsided within a few days and she was discharged from hospital. She was readmitted three months later on October 27, 1957, when she stated that her attacks of pain had persisted and had been accompanied by slight icterus. Just before this admission she had a very severe attack with fever and definite jaundice. She had been nauseated and had vomited five or six times. Physical examination: temperature 98.3° F., pulse 100, blood pressure 120/80 mm. Hg. She was an asthenic, slight woman, who appeared ill. The abdomen was tender in the right upper quadrant, with some increased muscle resistance. Laboratory examination showed a white blood cell count of 13,700 (75% polymorphonuclear leukocytes, 20% lymphocytes, 5% monocytes), serum bilirubin 3.3 mg. %, alkaline phosphatase 55 King Armstrong units. Observed for 24 hours, her local findings increased and the patient was taken to the operating-room with a preoperative diagnosis of acute cholecystitis. At operation on October 28, 1957, the diagnosis was confirmed. A tense, distended gall-bladder with a regional inflammatory mass about it was noted. The gall-bladder was removed from the fundus down to the cystic duct which communicated with a large structure in the portal region. The gall-bladder was removed by dividing the cystic duct and this structure, on exploration, was found to comprise a large cavity filled with quantities of brown bile. Neither of the hepatic radicles nor the lower end of the common bile duct could be demonstrated satisfactorily with the probes. The duodenum was therefore opened and the ampulla probed with little success, as no entry to this large cavity was obtained. The cavity was therefore drained by means of a T-tube and the abdomen closed.

The pathological report read as follows: "The specimen was a gall-bladder, 10 x 3.0 cm., which had a markedly thickened wall. No stones were found. Microscopically it showed typical changes of acute superimposed on chronic cholecystitis."

After operation the patient had quite a stormy postoperative course but settled down in about a week. She had been marginally icteric preoperatively. This condition persisted and gradually progressed, the serum bilirubin reaching 6.8 mg. % on November 19. The alkaline phosphatase also progressed to a level of 80 King Armstrong units. Meanwhile, she continued to drain quantities up to 1000 c.c. of thin bile a day from her T-tube. Her stool was very light in colour. X-ray examination of her biliary system was attempted through the T-tube and revealed only a very large cystic space which had no demonstrable communication with either the intestine or the hepatic radicles, though some dye passed into the duodenum. Further information was sought by a coincident barium meal examination and cholangiogram, and this showed the large cystic space to lie in part behind the duodenum (Fig. 1).

In view of the persistent and slightly progressive jaundice, and with the diagnosis of a choledochus cyst, a second operation was undertaken on November 26, 1957. The intent

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was to improve drainage of the choledochus cyst to the intestinal tract by anastomosing either the cyst to the duodenum or an isolated Roux-Y loop of jejunum. This operation demonstrated a great deal of inflammation and adherence of all adjacent structures to the undersurface of the liver in the region of the gall-bladder bed. The previously inserted T-tube was followed into the large globular structure which proved to be a cystic space some 12 to 15 cm. in length and from 8 to 10 cm. in width, which ran from the portal area of the liver to the region of the lower portion of the duodenum, in fact coming close to the ligament of Treitz. The lining was smooth and soft with the exception of the antero-lateral portion above the duodenum where there was induration and roughening of the lining of the cyst. The interior of the cavity was inspected with a Cameron light. No aperture was found inferiorly. At the upper extremity a small slit-like aperture was noted. Introduction of a catheter into it and dye injection followed by x-ray examination showed the left hepatic duct to be communicating through this aperture. There was no evidence of the right hepatic duct. Exploration revealed the right hepatic duct occluded in cicatrix. Proximal to the cicatrix a dilated duct was mobilized. The left hepatic duct and right hepatic duct were then brought together, and an isolated Roux-Y loop was brought up and anastomosed mucosa-to-mucosa to the approximated right and left hepatic ducts. The large cystic space was then drained into the duodenum and the aperture used for exploration closed with some loose catgut sutures. A portion of the thickened wall was taken to facilitate closure and serve as a biopsy specimen. This was a somewhat lengthy operative procedure and the patient, who at best was an asthenic, frail person, responded very poorly. Blood pressure was low and it was deemed necessary to administer hydrocortisone and support her during the postoperative course with corticoid substances. This was done with a satisfactory response.

Pathological examination of the removed tissue showed a dense infiltration by an adenocarcinoma that was fairly well differentiated but nevertheless contained numerous mitotic figures. There were a few foci suggestive of rather primitive squamous metaplasia. A review of the earlier gall-bladder specimen by further sections revealed a small focus of adenocarcinoma histologically identical with the above tumour, located at one end of the specimen.

The patient's postoperative course continued to be difficult and was further complicated by a suppurative parotitis of fairly severe degree. This did not respond to therapy, the patient's condition worsened, and she died 10 days after operation.

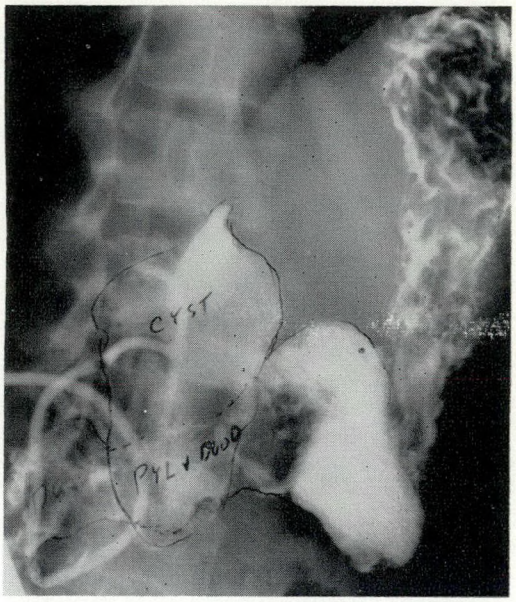

Fig. 1.—Barium meal and Diodrast injection of T-tube reveal a large cyst, partially retroduodenal. Stub at upper end of cyst represents left hepatic duct.

An autopsy was performed and the following findings were recorded:

Abdominal Findings

The peritoneal cavity contained 100 c.c. of green-brown fluid pocketed in the right upper quadrant by the hepatic flexure and transverse colon. It was continuous with a 3 cm. rent in the wall of a cyst in the porta hepatis. There were many peritoneal adhesions, especially about the hepatic flexure. A defunctioning Roux-Y loop of jejunum originated 24 cm. from the ligament of Treitz. It lay anterior to the porta hepatis, and into it was surgically anastomosed a common hepatic duct made by suturing the right and left hepatic ducts together.

Beneath this surgical reconstruction of the biliary tree there was a 10 x 5 x 5 cm. cyst, the wall varying in thickness from 15 to 7 mm., that lay anterior to the portal vein and behind the second part of the duodenum and pancreas. It had a smooth shiny surface. It did not appear to erode into the duodenum, though the thick wall of the cyst and the serosal surface of the duodenum could not be separated. A 1 cm. surgical anastomosis joined the cyst to the second part of the

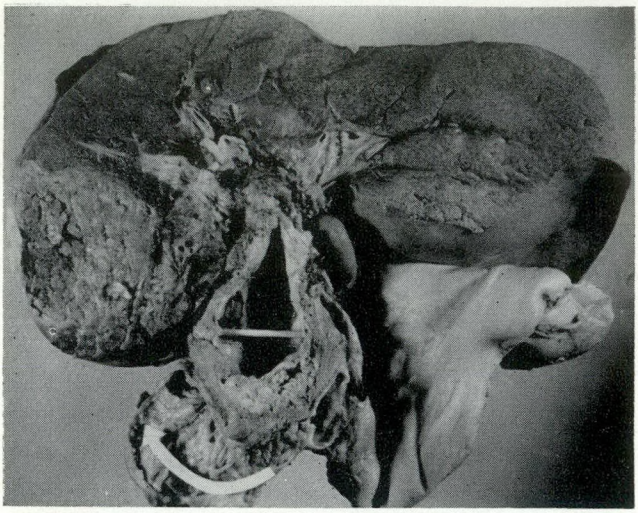

Fig. 2.—Autopsy specimen with thick-walled cyst apparent. Partial necrosis of right lobe of liver resulted from thrombosis of right hepatic artery and partial occlusion of right branch of portal vein.

duodenum. On the inner aspect of the left wall of the cyst near the duodenum was a small pin-point opening through which a probe could be passed for 2 cm. This probably represented the exit of the common bile duct, though continuity could not be established with the ampulla of Vater (Figs. 2 and 3).

The right upper wall of the cyst was firm, scirrhous and white. This fibrous material spread out to involve the gall-bladder bed. The same fibrous material surrounded the right hepatic duct and extended along it to a depth of 4.5 cm. into the liver tissue. In the liver substance immediately adjacent there was a firm 0.5 cm. hæmorrhagic metastatic nodule.

The left hepatic artery was normal, but the right was completely thrombosed. The portal vein was intact and the left branch was normal. The right branch 1 cm. from the bifurcation was completely obstructed by white, firm tissue adjacent to the tissue lining the gall-bladder bed, and by a suture which transfixed it.

The liver was intensely green with the lobular pattern prominent. In the right lobe there was an area of yellow-green soft necrotic material 8 cm. in diameter, and the surrounding liver tissue was suffused and dark.

The pancreas was unremarkable, though the head was splayed out over the cyst as the latter descended behind the second part of the duodenum.

The remainder of the gross autopsy examination was negative.

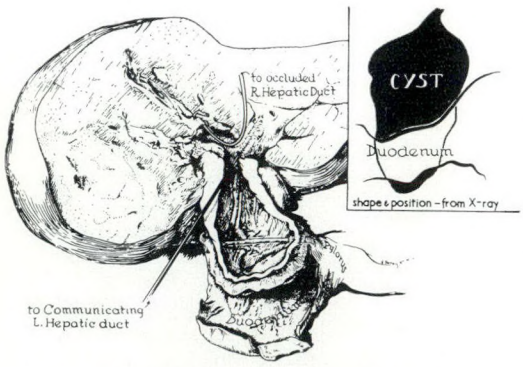

Fig. 3.—Correlation of radiographs and gross autopsy findings.

Microscopic Examination

The cyst wall consisted of a dense submucosa of collagen tissue and few fibroblasts. In one area near the duodenum, there was an epithelium of high columnar cells which were occasionally thrown up over club-shaped areas of fibrous tissue and chronic inflammatory cells. There was no muscle coat to the wall.

Scattered throughout the submucosa was a patchy infiltration of a poorly differentiated adenocarcinoma with many mitotic figures. It tended to form glands, and in some areas was undergoing degeneration (Fig. 4). It did not appear to be producing mucus. This tumour was identified in all parts of the wall of the cyst, as determined by multiple sections. Several sections below the gall-bladder bed revealed the tumour arising directly from the mucosal surface of the cyst. The tumour was seen to invade perineural lymphatics, nerve bundles, lymphatics and neighbouring lymph nodes and perivascular areas. Tumour thrombi were identified in several small arteries. There was, however, no invasion of the pancreas or duodenum. The appearance was that of a carcinoma rising from the mucosa of the cyst and spreading via the lymphatics and contiguously to involve the entire cyst wall. There was direct invasion into the gall-bladder bed and along the right hepatic duct into the liver substance. A small metastasis was identified in the liver, as noted on the gross inspection.

The right lobe of the liver had undergone complete coagulation necrosis with a polymorphonuclear and mononuclear leukocytic

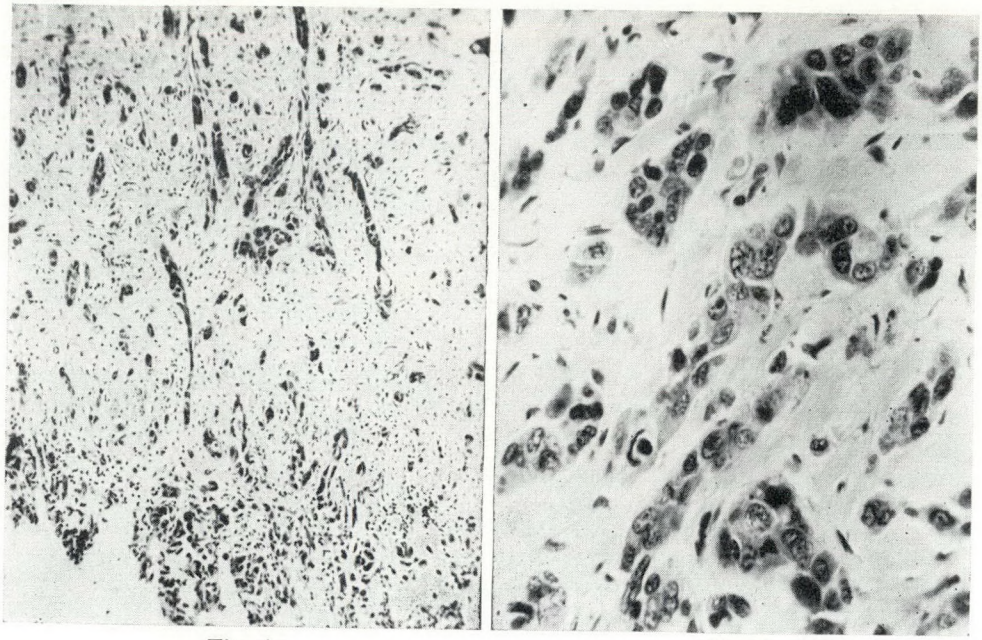

Fig. 4a. Fig. 4b.

Figs. 4a and 4b.—Low and high power sections of cyst wall showing poorly differentiated adenocarcinoma.

infiltration typical of an infected abscess. The remainder of the liver showed intense centrilobular bile staining and bile plugs in the small canaliculi. There was a very slight increase in the portal connective tissue.

Comment

A choledochus cyst, termed by Gross "idiopathic dilatation of the common bile duct", has been considered by that author as probably the result of a congenital weakness of the wall associated with secondary obstruction, though he further records seven possible etiological factors.

Choledochus cyst is commonly considered to be a disease of children and infants. This, however, is not the case, as is demonstrated by this report and review of the reported cases in the literature. For example, the six patients whose cases were recorded by Walton were aged 16, 34, 25, 39, 43 years, and one month, respectively. This is confirmed by Gross's review of cases; he showed that 44 occurred from birth to 10 years, 31 from 11 to 20 years, 32 from 21 to 30 years, 11 from 31 to 40 years, and 10 over 40 years.

The above case records an unusual combination of events: a congenital lesion—a choledochus cyst; an acute inflammatory process – acute suppurative cholecystitis; and neoplasia—an adenocarcinoma.

There was considerable evidence at post-mortem examination to clearly identify the origin of the adenocarcinoma from the mucosa of the choledochus cyst. The mucosa of the cyst was a tall columnar glandular epithelium, where it was not denuded. Further, the tumour was identified in all sections and could be seen arising from the actual inner surface of the cyst. The age of the patient and lack of cholelithiasis make the site of origin in the gall-bladder further unlikely.

The failure to make the diagnosis of the choledochus cyst preoperatively is not unusual. This patient had two of the three diagnostic criteria—pain and jaundice—but the important third—a palpable mass—was not found. It was thought before the second operation that the hepatic ducts might have been damaged at the time of the acute gall-bladder surgery. In retrospect this seems unlikely, for the right hepatic duct and cystic duct were involved by tumour, and this probably accounted for the acute inflammatory gall-bladder episode. The filiform tortuous common duct leaving the

cyst is characteristic and accounts for the failure to identify this duct surgically, though it was undoubtedly patent, as indicated by the passage of radio-opaque dye into the duodenum.

This case serves to underline the importance of the variability of biliary duct anatomy. The occurrence of the neoplasm with the congenital and inflammatory elements in this case makes a most extraordinary combination. One can only theorize about the possible inter-relationship of these three factors.

SUMMARY

A case is reported of a 25 year old woman with a choledochus cyst complicated by adenocarcinoma developing in its wall, and acute cholecystitis.

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RÉSUMÉ

Il a été publié dans la littérature environ 200 cas de kystes du cholédoque, dont un seul cependant était associé au cancer. Les auteurs présentent dans cet article un second cas original. Il s'agissait d'une jeune femme de 25 ans, admise à l'Hôpital général de Vancouver pour des douleurs de l'hypocondre droit et un ictère léger datant de deux mois. A l'examen physique, on note une légère contracture musculaire abdominale, de la maigreur et de l'asthénie. La malade fut gardée en observation pendant 24 heures, mais le tableau clinique s'aggravant, on soupçonna une crise de cholécystite aiguë et l'on décida d'opérer. La laparotomie fit découvrir une vésicule distendue noyée dans un paquet d'adhérences inflammatoires. On pratiqua une cholécystectomie directe et lors de la section du cystique on se trouva en présence d'une vaste formation kystique remplie de bile noire. Le cathétérisme du canal hépatique ou du cholédoque se révéla impossible. On put sonder l'ampoule par duodénotomie, mais cette manœuvre ne détecta aucune communication avec le kyste en question dans lequel un drain fut posé. L'examen anatomo-pathologique de la vésicule amputée confirma le diagnostic de cholécystite chronique non lithiasique en poussée aiguë.

Les suites opératoires furent médiocres: non seulement l'ictère ne disparut pas, mais il augmenta même légèrement. Les selles étaient décolorées. On pratiqua une injection de liquide opaque aux rayons X par le drain: ceci montra une large cavité kystique sans communication avec l'arbre biliaire. La jaunisse devenant de plus en plus intense, on décida de réopérer la patiente dans l'intention de drainer le kyste par anastomose sur l'intestin. A l'intervention, on trouva, engaînée dans de nombreuses adhérences, cette poche située entre le hile du foie et la portion inférieure du duodénum; elle fut ouverte et l'on découvrit dans la partie supérieure de la face interne de sa paroi un petit pertuis qui communiquait avec le canal hépatique gauche; le canal hépatique droit était étranglé par une formation cicatricielle. Les deux canaux furent libérés et anastomosés à une anse grêle. Quant au kyste, il fut abouché au duodénum pour drainage, et une biopsie de sa paroi fut pratiquée. Les suites opératoires furent mauvaises et compliquées d'une parotidite suppurée; la patiente mourut 10 jours plus tard.

A l'autopsie on trouva, outre de nombreuses adhérences péritonéales, une formation kystique de 10 cm. x 5 cm. x 5 cm. collée au duodénum. Sa paroi supérieure se continuait directement par une masse dure qui englobait le lit vésiculaire et le canal hépatique droit et pénétrait même dans le parenchyme du foie. Ce dernier était ictérique, d'une couleur verte intense. Histologiquement, la paroi du kyste était faite d'un épithélium prismatique élevé reposant sur un chorion inflammatoire envahi par des infiltrations adéno-carcinomateuses; celles-ci montraient de nombreuses mitoses, présentaient une nette tendance à s'arranger en formations glandulaires et pénétraient dans les vaisseaux, les lymphatiques et les filets nerveux. Il s'agissait sans aucun doute d'un cancer dont l'origine était la muqueuse kystique.

En fin d'article, les auteurs rappellent et discutent les théories qui ont été émises sur la pathogénie de cette affection.

SOLITARY PRIMARY LEIOMYOMA OF THE LUNG*

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PRIMARY LEIOMYOMA of the lung is a rare lesion, since only six authentic cases have been recorded in the available literature[1-6] (Table I). It is probable that the lesion is more common than this, as the condition is mentioned in most large series of pulmonary "coin" lesions. We have not included tumours mentioned as myofibromas, etc., in the absence of precise histological proof. The following case is of interest because of the associated finger clubbing which led to its discovery, and because the patient was the youngest in whom a pulmonary leiomyoma has been recorded and successfully removed at thoracotomy.

TABLE I.—RECORDED CASES*

Author	*Sex*	*Age*	*Location and size of tumour*	*Symptoms*	*Operation*
Förkel[1]	F	63	Parenchymal; left upper lobe; "lemon" size.	None	Autopsy finding
Franco[2]	F	56	Parenchymal; right upper lobe; 13 x 9 cm.	?	Autopsy finding
Brahdy[3]	F	18	Parenchymal; right lower lobe; 2.5 cm.	None	Right lower lobectomy
Williams and Daniel[4]	F	8	Parenchymal; left lower lobe; 10 cm.	Productive cough	Left pneumonectomy
Freireich, Bloomberg and Langs[5]	M	61	Intrabronchial; right upper lobe; 1 cm.	None	Right upper lobectomy
Pierce, Alznauer and Rolle[6]	M	24	Parenchymal; right middle lobe; 3 cm.	None	Right middle lobectomy
Lynn and MacFadyen	F	5	Parenchymal; left upper lobe; 4 cm.	None (finger clubbing)	Left upper lobectomy

*Modified from Pierce, Alznauer and Rolle.[6]

CASE REPORT

G.L., a five year old girl, was sent to her doctor by a public health nurse who noticed that the child's fingers were clubbed. The parents stated that the ends of the child's fingers had been swollen for about one and a half years, but they had paid no attention to the condition since the child had no complaints. On the advice of the nurse, however, they had gone to their doctor who could find no abnormality on history or physical examination. A chest radiograph was taken and this showed a mass in the upper left chest.

The patient was a healthy, slightly pale girl in no distress. Her measurements were proportionate and average for her age. Examination of the head and neck was negative. The chest was clear to percussion and auscultation. Heart size and sounds were normal. Spleen and liver were palpable, but there were no abnormal masses or tenderness on abdominal examination. Genitals were normal. The extremities were not cyanosed but there was quite distinct clubbing of the toes and fingers.

Urinalysis was normal. Hæmoglobin value was 10.7 g. %; W.B.C. 7500 with a normal differential count. The erythrocyte sedimentation rate was 88 mm. in one hour. Mantoux test was positive.

Radiographs of the chest showed a large, oval mass lying posteriorly in the left upper chest (Figs. 1a and 1b). There was no gross abnormality in the cervical or dorsal spine, and there was no evidence of erosion of ribs. A tentative diagnosis of a posterior mediastinal neurogenic tumour was made.

Progress.—Left thoracotomy revealed a solid tumour in the apico-posterior segments of the left upper lobe. There were several enlarged hilar lymph nodes. These were normal on frozen section, and accordingly a left upper lobectomy was performed. On frozen section of the lesion after removal of the lobe a tentative diagnosis of neurofibroma was made. The postoperative course was uneventful and the child was discharged home on the 10th postoperative day. Follow-up 10 months later showed the child to be well. Physical examina-

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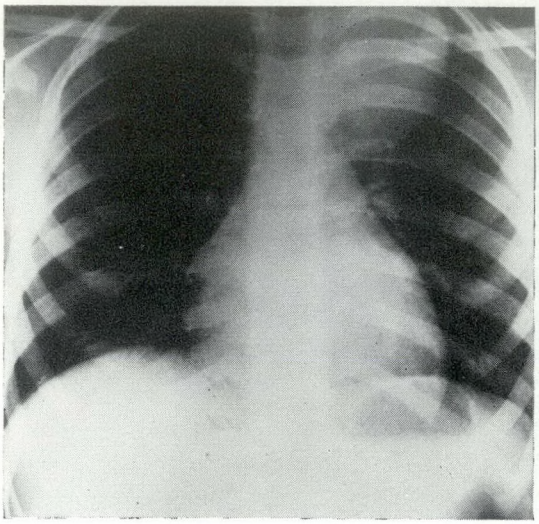

Fig. 1a.

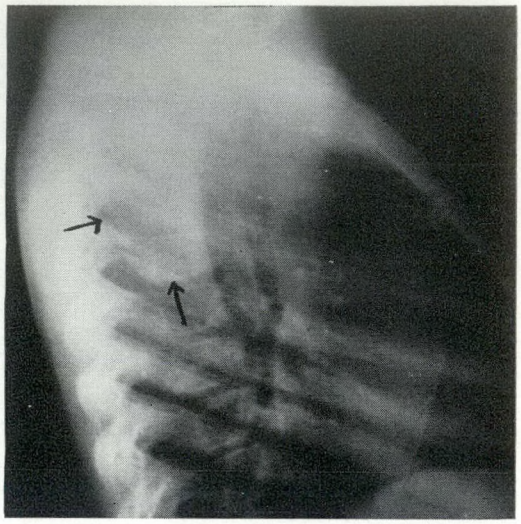

Fig. 1b.

tion was negative. X-ray examination of the chest was negative and the finger clubbing was regressing.

Pathology (Dr. D. J. Moore).—There was a spherical, well demarcated tumour, 4 cm. in diameter, embedded in lung tissue. The specimen weighed 92 grams. It was composed of firm, but rubbery, yellowish grey tissue which was streaked by numerous fine lines of brighter yellow or greyish white tissue (Fig. 2).

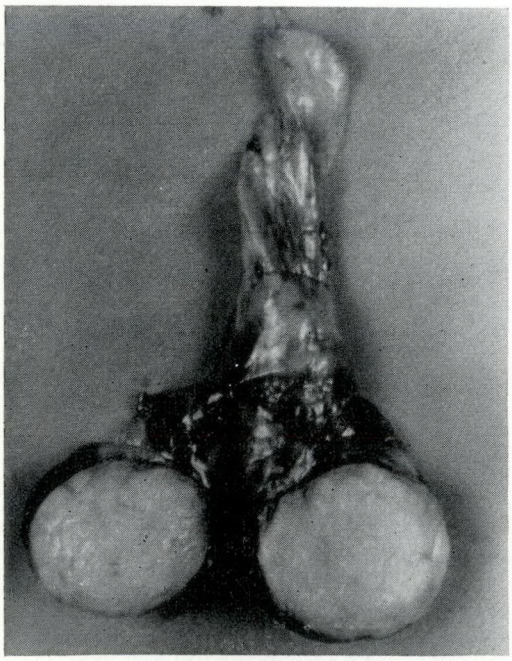

Fig. 2.

The microscopical examination showed a tumour composed of interlacing bundles of elongated or spindle shaped cells. The cytoplasm was indistinct but the cells assumed the characteristic colour of smooth muscle on special staining (Masson and Lillie trichrome and H.P.S.). Their nuclei were generally large, pale and ovoid, possessing a scanty fine chromatin structure. Palisading was not seen. Much of the neoplasm was obscured by a dense, wide-spread infiltration of plasma cells and lymphocytes. Collections of fat droplets and calcium granules were also scattered about. A diagnosis of leiomyoma of the lung was made (Figs. 3a and 3b). The mediastinal lymph nodes and adjacent lung tissue showed no histological abnormality.

Discussion

This case presents several interesting features. As with most similar lesions, the child was asymptomatic but attention was directed to the chest by the presence of finger and toe clubbing. The association of digital clubbing with benign intrathoracic tumours is rare. That the association in this patient was valid was verified by the improvement of the clubbing within three months of operation. Secondly, this is the youngest patient recorded as having a leiomyoma of the lung removed surgically. Thirdly, as is so often the case in these tumours, a tentative diagnosis of intrapulmonary neurofibroma was made before special staining confirmed the true nature of the spindle cells. Both smooth muscle

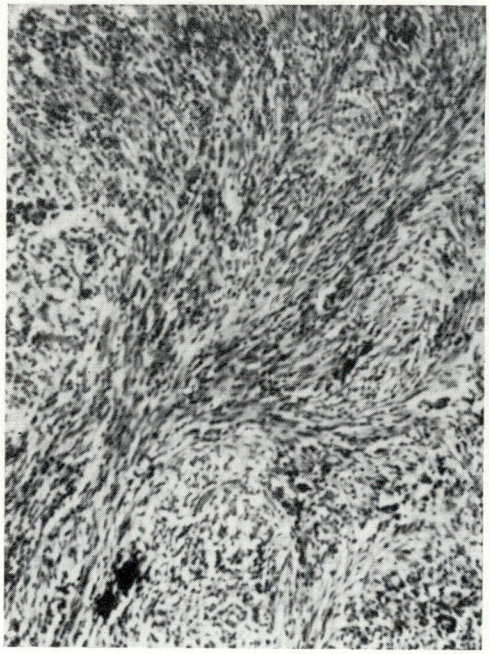

Fig. 3a.

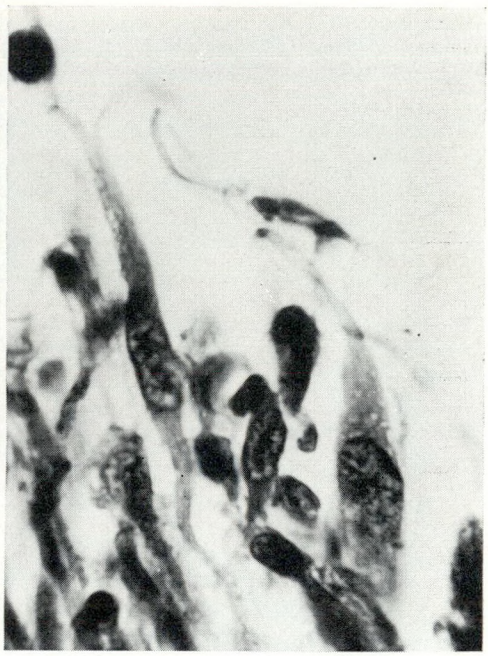

Fig. 3b.

and neurogenic tumours may show similar features such as palisading, which was not present in this tumour, and whorling of spindle cells. Thus special stains, i.e. Masson and Lillie trichrome or van Gieson's acid fuchsin, must be used to avoid errors in diagnosis.

Although asymptomatic, most solitary lesions of this nature are now removed because of the impossibility of otherwise establishing a diagnosis. It is well known that leiomyomas of the uterus may undergo malignant degeneration and there is no reason to exclude the development of a leiomyosarcoma in a benign leiomyoma of the lung. For this reason alone, resection was mandatory. The fact that clubbing of the digits had developed also suggests that the neoplasm in this patient was having some general effect. Thoracotomy is now little more dangerous than laparotomy, so that all such unexplained intrathoracic lesions must be given the benefit of surgery. Primary sources for such tumours, chiefly in the genital tract of females, however, must be excluded before operation is undertaken. No primary tumour was detectable in this girl at the time of thoracotomy, and physical examination and chest radiograph remain negative more than a year after surgery, so that we conclude that this tumour is a benign primary leiomyoma of pulmonary origin.

Summary

The sixth and youngest case of benign solitary leiomyoma of the lung is recorded. The presenting complaint was clubbing of the fingers and toes. Some of the diagnostic features of these tumours are re-emphasized. Thoracotomy is indicated in all such solitary intrathoracic masses.

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Résumé

Le léiomyome du poumon est considéré comme une lésion rarement rencontrée en clinique, puisque la littérature n'en dénombre que six cas authentiques. Les auteurs estiment cependant que cette affection est plus fréquente qu'on ne le croit généralement et en donnent une observation personnelle.

Il s'agit d'une petite fille de cinq ans adressée au médecin par une infirmière de la Santé Publique pour la seule raison qu'elle présentait des doigts en "baguette de tambour". Ce phénomène existait depuis environ un an et demi, mais personne ne s'en était inquiété jusque là. Il n'y avait d'ailleurs rien à signaler dans l'anamnèse de cette enfant. Par contre, la radiographie des poumons permit de découvrir une masse sombre dans la région supérieure gauche. La petite malade était en excellent état général. L'auscultation était tout à fait normale, la vitesse de sédimentation à 88 et le Mantoux positif. De nouvelles radiographies pulmonaires confirmèrent l'existence d'une tumeur ovalaire située dans la région postérieure du sommet pulmonaire gauche.

Une thoracotomie fut alors pratiquée, qui fit découvrir la masse radiologiquement décelée; de plus, les ganglions lymphatiques hilaires étaient hypertrophiés, mais ne présentaient rien de malin à l'examen histologique extemporané. On exécuta une lobectomie supérieure gauche. Les suites opératoires furent sans complication; l'enfant quitta l'hôpital le dixième jour. Un examen général de contrôle, dix mois plus tard, ne révéla rien d'anormal. L'hippocratisme digital était en régression.

Examen anatomo-pathologique: tumeur sphérique bien limitée, d'un diamètre de 4 cm., incluse dans le parenchyme pulmonaire; elle est microscopiquement constituée de cellules fusiformes présentant les caractères histologiques de colorabilité du muscle lisse, envahies de plasmocytes et de lymphocytes. Rien à signaler dans les ganglions lymphatiques adjacents. Diagnostic: léiomyome pulmonaire.

Ce cas présente plusieurs particularités intéressantes: l'hippocratisme digital comme seul symptôme—l'âge de la patiente—l'emploi de colorations histologiques spéciales. En conclusion, la thoracotomie, à peine plus dangereuse maintenant que la laparotomie, doit toujours être pratiquée dans des cas de ce genre.

STENOSIS OF SMALL INTESTINE DUE TO ISCHÆMIA FOLLOWING MASSIVE RESECTION*

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THERE HAVE BEEN a number of reported cases of fibrous stenosis of the small bowel at the constricting rings after the reduction of strangulated herniæ. Intestinal obstruction due to stricture formation has followed the healing of inflammatory lesions such as regional ileitis and tuberculous enteritis. Reports of only four other cases were found in which mesenteric vascular occlusion was followed by fibrous stenosis; in three of these cases a bowel obstruction was produced. The case to be reported is of further interest in that all but 15 inches (38 cm.) of jejunum and ileum was resected 30 months ago, with survival in continuing good health.

Case Report

Mr. H.L., a 42 year old Polish labourer, was treated in the Toronto General Hospital in April 1952, for superficial thrombophlebitis of the veins of right thigh. He was given anticoagulant therapy as an outpatient but he co-operated poorly and was readmitted in June 1952, for treatment of thrombophlebitis of the superficial veins of the abdominal wall. He was thought to have suffered a thrombosis of the inferior vena cava which caused these superficial dilated veins. He was again given anticoagulants on leaving hospital but stopped taking the drug after several months. He was readmitted for the third time in March 1953, with thrombophlebitis involving the right circumflex iliac vein. He was discharged on anticoagulant therapy with a final diagnosis of migrating thrombophlebitis.

He was admitted to St. Michael's Hospital on January 18, 1956, complaining of vomiting and severe abdominal pain. Ten days before admission he was awakened one morning with crampy abdominal pain which seemed to encircle his waist. The cramps were severe and persistent and finally required a hypodermic injection for relief. By the seventh day before admission the cramps had subsided but he began to feel a steady severe abdominal pain; at first this was all over the abdomen but within a few hours it settled in the right upper quadrant. He lost his appetite and four days before admission began to vomit all foods.

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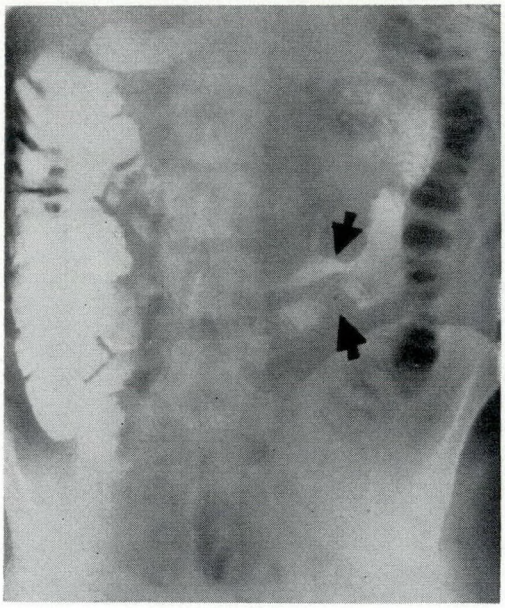

Fig. 1.—The ischæmic segment of jejunum (lower arrow) and the leakage of barium (upper arrow).

The vomitus was green and bitter and he soon became very thirsty. He noticed his urine was dark in colour, but said that the last bowel movement he had a week before admission was normal. He said his abdomen had been enlarging in the last three days. There was no history of indigestion or food intolerance. The only previous illness was a migratory thrombophlebitis of the superficial veins of his right leg and of the abdominal wall.

He was a well nourished man in moderate distress from abdominal pain, and with no physical abnormalities except in the abdomen. Blood pressure was 150/100 mm. Hg, pulse rate 100, and temperature 99.4° F. There was no evidence of recent or old thrombophlebitis. There was moderate dehydration. The abdomen was tender in all quadrants but there was more tenderness in the right upper quadrant, especially on deep breathing. The gall-bladder could not be felt and the liver was not enlarged. No masses were found and only very few bowel sounds were heard. There was no rebound tenderness or guarding. Rectal examination was negative and no stool was obtained for examination.

The urine was clear but concentrated. The hæmoglobin value was 103% and the leukocyte count 7500 with a normal differential count. An electrocardiogram showed a complete right bundle branch block. A radiograph of the abdomen showed moderate distension of both small and large intestines. Because of the right upper quadrant tenderness it was felt that he had paralytic ileus due to acute cholecystitis. The patient said that the right upper quadrant pain was less severe and he appeared to improve during the first four days in hospital.

He complained of increasing pain on the evening of the fourth day in hospital and shortly thereafter was found in shock. His

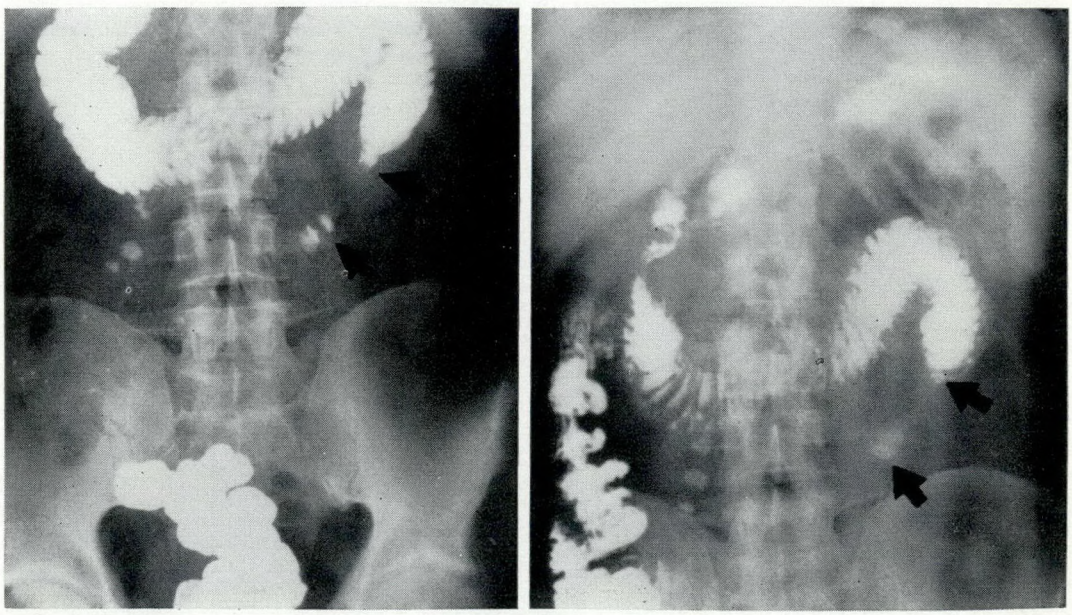

Fig. 2.—Incomplete obstruction due to stenosis of ischæmic segment of jejunum.

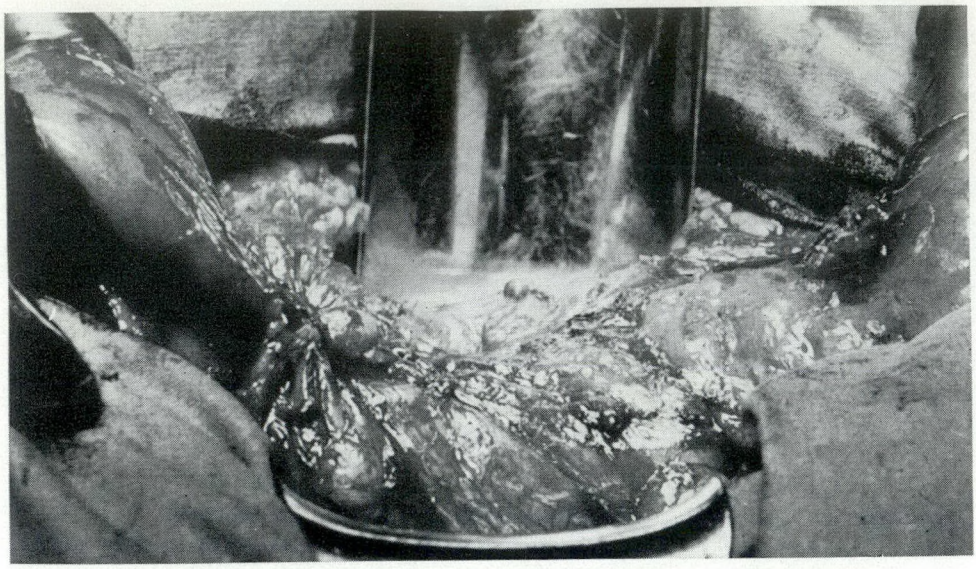

Fig. 3.—The stenosed segment of jejunum at operation.

pulse could not be felt, and with great difficulty a low blood pressure reading was obtained. It was felt that although he was *in extremis,* the only hope lay in emergency laparotomy.

At operation on January 22, a very large segment of necrotic small bowel was found. No time was spent in examining the mesentery to determine whether the infarction was due to mesenteric artery thrombosis or embolism or venous thrombosis. The gangrenous small bowel was quickly resected, leaving about seven inches of jejunum and nine inches of terminal ileum. The mesentery was divided two or three inches from the bowel and no bleeding occurred from the divided mesentery except at the upper and lower limits of the resection. An end-to-end anastomosis was made in two layers, using continuous catgut sutures. The abdomen was rapidly closed and the postoperative resuscitative measures were surprisingly successful. The postoperative course was very satisfying considering the nature of the operation. Fluid and electrolyte balance was easily maintained and he was able to eat on the third day.

The patient had 12 or 14 bowel movements for the first few days but after the fourth day he had only six or seven movements daily. By the time of discharge six weeks later he had only three or four semi-solid movements daily. His weight dropped from 224 lb. to 175 lb. during the four weeks after operation. The surgical specimen was 14 ft. (4.2 m.) in length. There was a hæmorrhagic infarction of all but the proximal 12 inches (30 cm.). No arterial occlusion was demonstrated but venous thrombi were seen in the mesentery.

Metabolic studies were performed during the fourth and fifth weeks after operation. Over a five-day period, only 30% of ingested fat was absorbed. Nitrogen balance was barely positive at only 0.9 g. per day. Sodium intake and excretion were both low and large quantities of potassium were lost in the fluid bowel movements.

A barium x-ray examination on February 8, 1956, showed a very short small bowel with rapid emptying as the barium reached the hepatic flexure 15 minutes after ingestion. Just proximal to the site of the small bowel anastomosis there was an area about an inch in length lacking mucosal pattern, and there appeared to be a leakage of barium outside the bowel at this level (Fig. 1).

The patient suffered chest pain and hæmoptysis believed to be due to a small pulmonary embolus on January 28, the sixth postoperative day. Anticoagulant therapy was started and by the time of discharge on February 22 he was taking 50 mg. of dicoumarol daily, which was found to keep his prothrombin time at 28 sec.

The patient was readmitted on February 28, 1956, just six days later, complaining of vomiting for three days. His condition was good although he weighed only 163 lb. The patient was thoroughly investigated during the following three weeks and it was decided that he had an almost complete obstruction of the

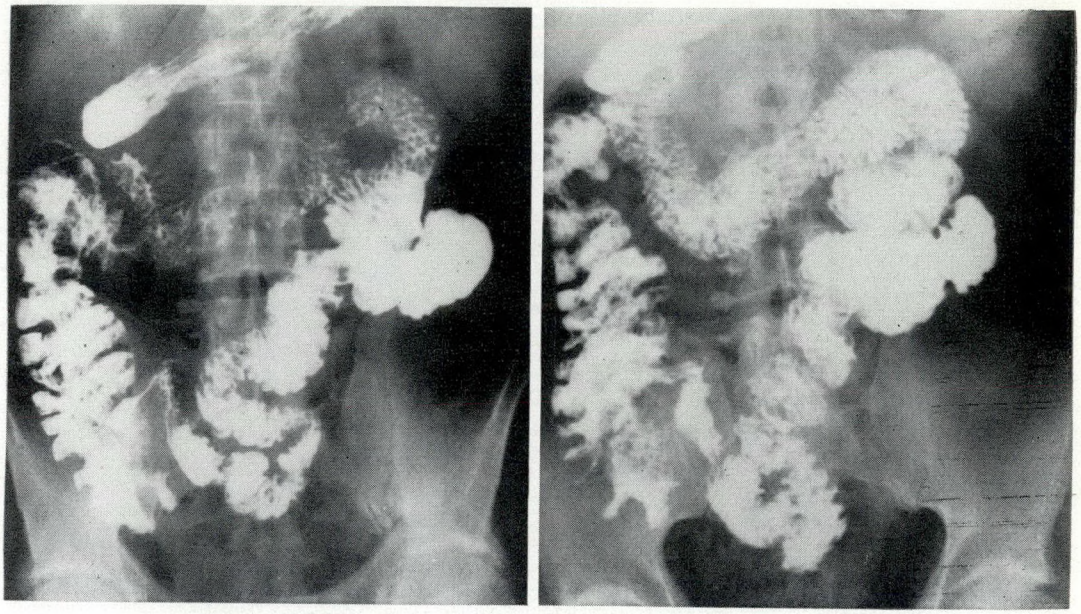

Fig. 4.—Barium radiographs following the side-to-side anastomosis.

jejunum just proximal to the previous anastomosis (Fig. 2). Twenty-four hours later the duodenum and upper jejunum were still grossly distended by barium.

On March 23, 1956, laparotomy was carried out and a 1.75 inch (4.3 cm.) length of stenosed jejunum was found (Fig. 3). This segment was tough and firm and its widest diameter was 0.4 inch (1.0 cm.). The duodenum and jejunum were grossly dilated and their walls were thickened. The jejunum measured two inches in diameter (5 cm.). The terminal ileum was normal and a little less than an inch in diameter (2.0 cm.). The bowel was carefully measured along its antimesenteric border. The jejunum was 6.5 inches (16.3 cm.) and the ileum was 8.5 inches (21.3 cm.) in length. The gall-bladder was thin-walled and contained no stones. A side-to-side anastomosis was performed rather than a resection of the stricture, as more absorptive area would thus be preserved.

The patient's postoperative recovery was satisfactory although his weight dropped to 148 lb. He was discharged on 50 mg. of dicoumarol daily, taken with a high calorie diet and vitamin supplements.

He has been followed up for 23 months as an outpatient and his weight has stabilized at 164 lb. He feels well. He has three or four bowel movements daily. He has complained occasionally of cramps in his abdomen but these are readily relieved by a little phenobarbital and atropine. A barium series (Fig. 4) in May 1957, shows the length of the small bowel and the side-to-side anastomosis 6.5 inches below the ligament of Treitz and 8.5 inches from the cæcum. The mucosa of the duodenum is hypertrophied and the width is increased. A tape (Fig. 5) was used to measure the length of the small bowel. The level of the anastomosis is indicated by a mark showing in the photograph near the patient's umbilicus.

Discussion

1. *Massive Resections*

Althausen, Uyeyama and Simpson[1] and Wilkie[2] have described resection of all of the small bowel except the duodenum and six inches of jejunum in two patients, with survival for one year and one and a half years respectively. Cogswell[3] and Meyer[4] have reported resections of the whole bowel supplied by the superior mesenteric artery except for the duodenum and upper 14 and 18 inches respectively of jejunum, after acute thrombosis of that vessel; their patients survived for long periods. Certainly the most massive resection was reported by Martin *et al.*[5] Their patient suffered a complete superior mesenteric artery occlusion, and a resection was performed of all the intestine from the third part of the duodenum to the mid-transverse colon because the superior mesenteric

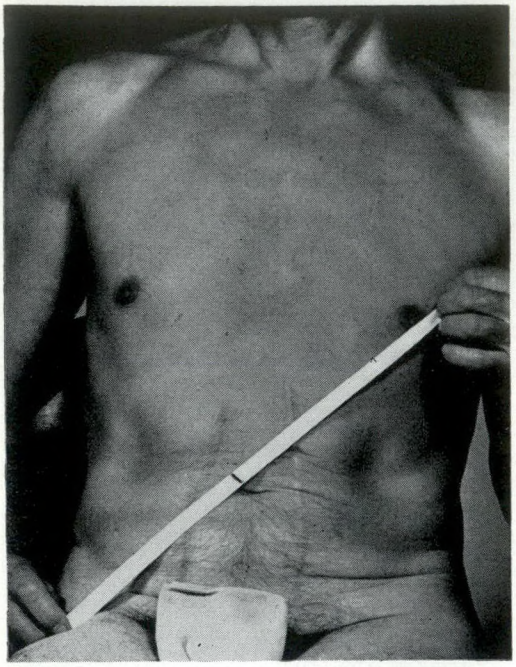

Fig. 5.—The tape showing the length of the small bowel and the mark indicating the level of the anastomosis (May 1957—16 months after the resection).

artery could not be cleared of thrombus. Their patient remained bedridden in hospital for the total survival period of 316 days. He suffered from slow starvation, vitamin deficiencies, and anæmia, and showed marked personality changes in the final months of his life.

After extensive resections of small bowel the absorption of fats and proteins is deficient but carbohydrate absorption is adequate. High doses of vitamin B complex are frequently required for prolonged survival without avitaminosis. Electrolytes generally remain in equilibrium except for calcium. Calcium absorption is decreased, the serum calcium and urinary excretion of calcium are low, and large quantities of calcium are lost in the form of calcium soaps in the stools which contain large amounts of unabsorbed fat. A hypochromic anæmia slowly develops and a high intake of iron is not always successful in preventing anæmia. A high carbohydrate, high protein diet is recommended but fats are reduced because of the danger of osteomalacia. Large doses of all the vitamins and of iron are indicated, and some authors recommend that vitamin B complex be given by injection to prevent pellagra. The general clinical condition and the body weight are most reliable in indicating adequate nourishment. This patient's weight was 224 lb. but now his weight has stabilized at 164 lb. and his hæmoglobin level is 80%. There is no sign of vitamin deficiency clinically or of osteomalacia radiologically.

In all cases, after massive resection the mucosa of the remaining small bowel undergoes tremendous hypertrophy which greatly increases the mucosal surface area.

2. *Fibrous Stenosis of Bowel Following Mesenteric Vascular Occlusion*

Only four reported cases of fibrous stenosis of small bowel following mesenteric vascular occlusion were found. Two patients had suffered numerous coronary occlusions and each suffered infarcts due to arterial emboli in distant organs. In each case the fibrous stenosis followed hæmorrhagic infarction of small bowel due to mesenteric arterial occlusion by emboli. In one case two resections of fibrosed segments were carried out. Both cases were studied at autopsy and the likely site of origin of the emboli was found to be the endocardium underlying myocardial infarctions.

Glaser and Smith[6] reported the case of a 50 year old man who had had at least six and probably 12 myocardial infarctions. Six years after the first coronary occlusion he was operated on for suspected appendicitis. The lowest 10 inches of the terminal ileum was congested and its mesentery had no pulsations; the appendix was removed but the bowel was not resected. Five weeks later he suffered another coronary occlusion and he was admitted to hospital. Because of crampy abdominal pain, a barium x-ray examination was made and a long segment of narrowed terminal ileum was demonstrated. Anæsthesia was induced but because of pulmonary œdema no operation was performed. He suffered a fatal coronary thrombosis a week later, and at autopsy an elongated fibrous stricture was found in the terminal 12 inches of the ileum. The regional branch of the superior mesenteric artery was occluded

and thrombi were found on the endocardium overlying old and new myocardial infarctions.

Rosenman and Gropper[7] reported the case of a 53 year old diabetic man who suffered a coronary infarction complicated by bilateral lower limb thrombophlebitis in 1945. A second coronary attack occurred in October 1951, and this was complicated by a small pulmonary embolus, a splenic infarction, a right femoral occlusion by embolus and severe abdominal pain. He survived on intensive medical therapy and six weeks later had a resection of two inches of jejunum because of fibrous stenosis. Two weeks later he suffered another attack of severe abdominal pain and laparotomy revealed a 30 inch (75 cm.) viable segment of markedly congested jejunum whose mesentery contained no pulsating vessels. No resection was carried out and he survived. Four months later he was readmitted with small bowel obstruction, and laparotomy revealed 30 inches of stenosed jejunum corresponding to the previously congested bowel. A resection was carried out and he survived until three months later when he died with gangrene of both lower limbs. Autopsy showed infarctions due to occluded coronary, common iliac, superior mesenteric, renal and splenic arteries.

Two further case reports are of interest to this problem. Shaw and Rutledge[8] report the case of a 54 year old woman who had a superior mesenteric artery embolus successfully removed and survived without a bowel resection. Approximately eight weeks later barium x-ray examination demonstrated areas of constant narrowing in the jejunum and ileum without clinical obstruction. It is likely that these are areas of fibrous stenosis of small bowel due to regional ischæmia.

Hawkins[9] reported the case of a 64 year old man who developed a mesenteric artery embolism on the 10th day following a coronary thrombosis. Anticoagulants were given and he survived. A month later he developed intermittent jejunal obstruction. This obstruction became complete and at laparotomy, three months after the coronary thrombosis, a two to three inch segment of stenosed jejunum was found and a side-to-side anastomosis was carried out. Although the segment was not excised, it was believed to be an area of fibrotic narrowing after mesenteric arterial embolism.

Our case differed in several respects. The patient had never suffered a clinical coronary occlusion although his electrocardiogram showed a right bundle branch block. He had suffered from migrating thrombophlebitis for four years, and had neglected to continue anticoagulant therapy after leaving hospital. His abdominal pain was not sudden but apparently developed over a period of two weeks. However, these cases are similar, in that each developed a fibrous stricture of the small bowel. In this case the massive resection was presumed to be inadequate; it is assumed that two inches of jejunum above the anastomosis was infarcted and subsequently healed by fibrosis causing stenosis. In order to preserve as much absorptive surface as possible, the area was not resected and no biopsy was taken. We believe that there is often a local leakage through many anastomoses performed in various structures in the body; provided that this leakage remains well localized, no complications ensue.

It appears that in intestinal ischæmia, the mucosa suffers most severely and complete sloughing of the mucosa can occur in cases where the ischæmia is not severe enough to cause necrosis of the muscularis. The submucosa, muscularis and subserosa are often sufficiently resistant to prevent gross perforation when mesenteric vessels become occluded. If gangrene of all coats does not occur and if the ischæmic segment does not become severely infected the bowel may survive and heal by fibrosis. The fibrosis is most marked in the submucosal layer. The mucosa regenerates very poorly and remains thin. The muscularis atrophies. The serosa and subserosal layers also undergo fibrous thickening and the segment of bowel usually becomes adherent to adjacent organs. Resection and anastomosis is in most circumstances the treatment of choice.

SUMMARY

Instances of massive resection of all but 14 inches (35 cm.) of small bowel with prolonged survival have been reported. The greatest metabolic impairment is in fat absorption, followed by impairment of protein assimilation. There is often vitamin B complex deficiency, iron deficiency anæmia and impaired calcium retention. Patients generally stabilize at a lower body weight and have only three or four bowel movements daily. The remaining small bowel mucous membrane undergoes great hypertrophy.

Fibrous stenosis of small bowel following impairment of blood supply is uncommon. The impaired circulation mainly affects the mucous membrane, and if necrosis of the whole wall or massive infection do not occur the fibrous replacement results in a segmental narrowing. This has been noted a number of times after reduction of strangulated herniæ, but only four reported cases have been found after primary disturbance of the mesenteric circulation. These cases were believed to be due to mesenteric arterial embolism or thrombosis, whereas the history suggests that the case reported here was caused by mesenteric venous thrombosis.

The case of a 42 year old man is presented who had suffered from superficial venous thrombosis in the legs and abdominal wall for four years. Two years ago, he suffered a mesenteric venous occlusion and all of the jejunum and ileum except 15 inches was removed. He survived, but two months later he developed an obstruction of the jejunum just proximal to the previous anastomosis. The two inch long segment of stenosed jejunum was believed to be caused by ischæmia due to an inadequate removal of necrotic bowel or to postoperative extension of the venous thrombosis. After a side-to-side anastomosis he recovered and he has continued in good health to the present time, 30 months after the resection.

CONCLUSIONS

Survival in continuing good health is possible after removal of all of the jejunum and ileum except approximately 15 inches. If the circulation to the small intestine is impaired and complete necrosis or massive infection does not occur, healing by fibrous stenosis may occur and an intestinal obstruction may be produced.

Vascular disturbances of the intestinal tract may be a more common cause of abdominal disease in the older age groups than is at present recognized.

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RÉSUMÉ

Quelques cas de résection massive d'intestin grêle avec survie prolongée ont été rapportés. Le dérangement métabolique le plus important qu'engendrent ces interventions réside en l'absorption des graisses, que suit de près la mauvaise assimilation des protides. On a souvent rapporté une déficience du complexe vitaminique B, une anémie ferriprive et une perte de calcium. Les patients se stabilisent à un poids inférieur et ne passent guère plus de trois ou quatre selles quotidiennes. La muqueuse de l'intestin grêle restant s'hypertrophie remarquablement.

Un apport sanguin inadéquat cause rarement de sténose fibreuse de l'intestin grêle. La circulation insuffisante touche surtout la muqueuse, et s'il n'existe pas de nécrose de toute la paroi ni d'infection massive, le remplacement fibreux ne produit qu'un rétrécissement segmentaire. Ces faits ont été observés surtout après la réduction

de hernies étranglées, tandis que seulement quatre cas ont été trouvés après des altérations primaires de la circulation mésentérique. Ces cas semblent avoir été causés par des embolies ou des thromboses artérielles, tandis que le cas dont l'histoire est relatée ci-après serait plutôt le résultat d'une thrombose mésentérique veineuse.

Le malade est un homme de 42 ans ayant souffert de thromboses veineuses superficielles des jambes et de la paroi abdominale depuis quatre ans. Il y a deux ans, à la suite d'une occlusion veineuse mésentérique tout le jéjuno-iléon moins 15 pouces (38 cm.) dût être réséqué. Il survécut à l'intervention, mais souffrit deux mois plus tard, d'une occlusion jéjunale immédiatement proximale à l'anastomose. Le segment sténosé, long de deux pouces (5 cm.), semblerait avoir été causé soit par la résection inadéquate d'intestin gangrené, soit par extension thrombotique post-opératoire. Après une anastomose latéro-latérale, le malade se remit et il demeure actuellement en bonne santé 30 mois après la résection.

En guise de conclusion, il semble donc que l'on puisse survivre adéquatement à l'ablation quasi-totale du jéjuno-iléon.

S'il y a entrave à la circulation de l'intestin grêle, sans nécrose complète ou infection massive, la guérison par sténose fibreuse peut s'obtenir et produire une occlusion intestinale. Les dérangements vasculaires de l'intestin pourraient constituer une cause plus fréquente de douleurs abdominales chez les gens âgés, qu'on est actuellement porté à le croire.

MASSIVE UPPER GASTROINTESTINAL BLEEDING FROM SPONTANEOUS LACERATION OF THE LOWER ŒSOPHAGUS (MALLORY-WEISS SYNDROME)

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SPONTANEOUS laceration of the lower œsophagus is recognized infrequently as a source of massive upper gastrointestinal hæmorrhage. In 1929, Mallory and Weiss[5] described the findings at autopsy in four alcoholics who, following episodes of vomiting, had died of bleeding from this source. Subsequent reports from the same authors,[8] and from Chalmers *et al.*[2] Decker, Zamcheck and Mallory,[3] Small and Ellis[6] and Whiting and Barron[9] have described this condition, and it has become known as the Mallory-Weiss syndrome. Violent retching, which ruptures the mucosa and submucosa of the cardia and lower œsophagus, leads to profuse bleeding from submucosal arteries. Many but not all of the patients have been alcoholics.

CASE REPORT

Mr. J.E., age 40, had been an alcoholic for 15 years. For the two years before admission he had consumed a quart of wine and a quart of rubbing alcohol daily. There was no history suggestive of peptic ulceration, or of previous gastrointestinal bleeding.

He was admitted to the Toronto General Hospital on November 7, 1957. The previous evening the patient drank a quart of milk for his supper. Shortly thereafter he vomited the milk, and, after a period of violent retching, 200 c.c. to 300 c.c. of bright red blood. During the night he had several bowel movements consisting of dark blood and clots. At 6 a.m. he fainted in the bathroom, after which he was brought to the hospital.

In the Emergency Department he was pale and sweating, although conscious and rational. His blood pressure was 60/40 mm. Hg, and his pulse rate was 132. The only abnormality on examination of the abdomen was a slight resistance of the upper right rectus muscle. There were no spider nævi, no "liver palms" or "liver flap", and there was no ascites. The remainder of the physical examination and functional enquiry were negative. His hæmoglobin value was 49%; his prothrombin time was normal. During the examination the patient vomited 300 c.c. of bright red blood, and passed a tarry stool.

During resuscitation with intravenous blood transfusions, and on the assumption that he had cirrhosis with œsophageal bleeding, a Blakemore-Sengstaken tube was passed. The œsophageal balloon was inflated to a pressure of 30 mm. Hg. It was thought that if varices were not the cause, and a peptic ulcer was in fact the source of the bleeding, the bleeding would be uncontrolled and this would be easily recognized by aspiration through the central lumen of the tube.

By 6 p.m. on the day of admission the patient's hæmoglobin value had risen to only 45%, in spite of the transfusion of 3000 c.c.

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of blood in eight hours. It had been possible to aspirate only small quantities of blood from the stomach tube, and the patient had not passed further blood per rectum. Significantly, as was realized later, the patient had vomited blood around the œsophageal balloon on several occasions. It was decided to carry out a laparotomy because it was thought that the patient must be continuing to bleed from a gastric or duodenal ulcer.

At operation the gastric balloon of the Blakemore-Sengstaken bag was found on palpation to lie in correct position against the cardia. There was a moderate amount of bright red blood in the stomach, and a large amount of black changed blood in the small intestine. No gastric, duodenal, biliary, or small bowel source of bleeding could be seen or palpated. A generous gastrotomy was performed. By alternately packing the upper and then the lower end of the stomach it was ascertained that the blood was not coming from the stomach, but was running freely into it through the cardia.

The gastrotomy wound was closed. The œsophageal hiatus was exposed by dividing the coronary ligament and reflecting the left lobe of the liver. After mobilization of the œsophagus it was possible to pass a Penrose drain about it, and to deliver about 6 cm. of œsophagus into the abdomen. A vertical incision was made into the lower œsophagus and cardia in the midline anteriorly. In the mid-posterior wall of the œsophagus, extending 2 cm. above the œsophago-gastric junction, was a laceration of the mucosa and submucosa. In the upper end of the laceration was a small vigorously bleeding artery. This was ligated, and the laceration oversewn with continuous chromic catgut. A Levin tube was threaded into the stomach under direct vision, and the incision in the œsophagus and cardia was closed vertically. The left lobe of the liver was sutured in correct position, and the abdomen closed without drainage.

The patient's postoperative course was complicated by an episode of delirium tremens, but was otherwise uneventful. A gastrointestinal series two weeks postoperatively was normal.

Discussion

In their original paper Mallory and Weiss postulated that the lacerations they found in autopsy specimens resulted from high pressure developed in the œsophagus and the cardiac region of the stomach during episodes of violent retching. They and others have shown at post mortem that the œsophagus is weakest in its lower 6 to 10 centimetres. Complete rupture (so-called spontaneous rupture of the œsophagus) probably occurs when the force is greater, or the wall of the œsophagus more easily torn. Alcoholics, who are likely to have œsophagitis and gastritis, are also apt to have episodes of violent incoordinated retching. Cases have been reported, however, in patients who were not alcoholics.

The Mallory-Weiss syndrome should be considered in the differential diagnosis of obscure massive upper gastrointestinal bleeding. A known or presumed diagnosis of cirrhosis does not preclude this source of bleeding. The 30 mm. Hg pressure in the œsophageal balloon of the Blakemore-Sengstaken bag is adequate to control a ruptured venous varix, but not the arterial bleeding that occurs in this condition. Œsophageal laceration should be thought of as the possible source of bleeding in patients in whom no ulcer can be found at laparotomy. Under these circumstances, a generous gastrotomy and careful inspection of the region of the cardia is indicated to rule out bleeding from above. It is possible that this lesion accounts, in some instances, for persistent bleeding after so-called "blind gastrectomy".

Summary

This case is reported to call attention once more to arterial bleeding from a laceration in the lower œsophagus as a source of serious hæmorrhage from the upper gastrointestinal tract. The lesion is produced by violent vomiting and is more likely to occur in alcoholics, though it has occurred apart from this association. A generous gastrotomy is necessary to locate the source of the bleeding.

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Résumé

Il est peu fréquent qu'une hématémèse soit causée par une déchirure spontanée de l'extrémité inférieure de l'œsophage. Cette entité a été décrite pour la première fois par Mallory et Weiss (d'où l'expression de syndrome de Mallory-Weiss), puis par d'autres. Il semble que certains efforts de vomissement particulièrement violents soient capables de provoquer la rupture de la muqueuse et de la sous-muqueuse œsophagienne à la partie basse de cet organe ou au cardia. Les cas que l'on trouve dans la littérature étaient pour la plupart ceux d'alcooliques.

L'histoire clinique qui nous est présentée est celle d'un homme de 40 ans, alcoolique, sans aucun antécédant d'ulcère ou d'hémorragie digestive. Il est admis à l'hôpital pour une hématémèse suivie de vomissements de caillots, survenue brusquement. A l'entrée, le malade est pâle, couvert de sueur, conscient et orienté. Pression à 60/40; pouls à 132, hémoglobine 49%. A l'examen, rien de particulier si ce n'est une légère résistance dans l'hypocondre droit. Aucun signe de maladie hépatique. On procède immédiatement à la réanimation par des transfusions et l'on met en place un ballon de Blakemore-Sengstaken. Un peu plus tard, le taux de l'hémoglobine restant très bas, on décide de faire une exploration.

Au cours de la laparotomie, on ne trouve de prime abord rien de particulier. Une gastrotomie de vérification est pratiquée qui permet de se rendre compte que l'hémorragie persiste et que le sang vient de plus haut que le cardia. L'œsophage est mobilisé et abaissé, puis incisé: sur sa paroi postérieure, au fond d'une déchirure de la muqueuse, une petite artère saigne avec force; cette dernière est pincée et ligaturée. Le tout est suturé; le ventre est refermé sans drainage. Les suites opératoires furent excellentes. Un contrôle radiologique, deux semaines plus tard, ne montre rien d'anormal.

Ce syndrome de Mallory-Weiss pose un problème nouveau dans la diagnostic différentiel des hémorragies digestives. Il se rencontre de préférence chez les alcooliques, qui font souvent de l'œsophagite et de la gastrite. Lorsque les autres étiologies auront été éliminées, il sera utile de penser à la possibilité d'une déchirure spontanée de la muqueuse œsophagienne juxtacardiaque.

MALLORY-WEISS SYNDROME

Shuttleworth and Hatt (*Brit. J. Surg.*, 46: 1, 1958) describe an unusual case of the Mallory-Weiss syndrome in which the patient had the typical "fissure ulcers" around the gastric cardiac opening with their long axis in line with the œsophagus, but there was no previous history of vomiting.

The patient, a woman of 53, had vomited blood clot for half an hour on the day of admission, and six days later had a severe hæmatemesis. Transfusion and high Billroth I gastrectomy followed, but further hæmatemesis made further resection of stomach and œsophago-gastric junction with œsophago-jejunostomy necessary. The patient recovered.

The unusual feature of this case is the complete lack of evidence that vomiting precipitated the very characteristic lesions. The fissure ulcers were associated with a very severe chronic gastritis and it is thought that the gastritis may have predisposed to the typical numerous small ulcers. The precipitating cause of the vascular abnormality which led to bleeding remains a mystery.

CHORDOMA OF THE DORSAL SPINE*

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CHORDOMA is an uncommon neoplasm arising from the embryonic remnants of the spinal cord, the notochord. It may develop at all levels of the vertebral column, but the most usual sites are the cranial and caudal extremities. A localization in the dorsal spine is extremely rare, constituting about 3% of all chordomata. Because of its unusual characteristics the following case is considered worthy of record.

TABLE I.—REPORTED CASES OF DORSAL CHORDOMA

No.	*Year*	*Author*	*Site*	*Sex*	*Age*	*Presenting symptoms*
1	1928	Cappell[2]	D4-5-6	M	53	Paræsthesia and incoordination of legs
2	1935	Mabrey[12]	D7	?	?	?
3	1939	Güthert[8]	D12-L1	M	65	Spinal tumour
4	1941	Hansson[9]	D7	M	45	Zonasthenia; paresis of legs.
5	1948	Willis[14]	D1-2	M	51	Back pain and paraplegia
6	1950	Wood and Himadi[15]	D11-12	M	54	Pain in left hip
7	1951	Crowe and Muldoon[5]	D3-4	M	30	Mediastinal tumour
8	1952	Dahlin and MacCarty[6]	D11	M	Adult	Spinal cord compression
9	1952	Congdon[4]	C7-D1-2	F	18	Chest pain; paralysis of legs
10	1956	Chiasserini and Marchiafava[3]	D4	M	44	Spastic paraparesis
11	1957	Buraczewski and Rudowski[1]	D3-4-5	M	43	Mediastinal tumour
12	1957	*Idem*	D4	M	37	Mediastinal tumour
13	1958	Gueukdjian	D2-3-4-5	M	41	Lipoma-like mass of back

CASE REPORT

B.A., a man aged 41, attended the surgical out-patient department of Mayday Hospital on October 17, 1956, with the complaint of varicose veins in both legs and a swelling in his back. The latter did not particularly inconvenience him and he stated that, were it not for his varicose veins, he would not have come to hospital. Other than the usual symptoms due to varicosities, the patient had no complaints. He did not give any history of spinal injury. He felt fit and worked full time as a works foreman.

On examination, the patient's general condition was very good. He had moderately advanced bilateral varicose veins. On his back, there was a dome-shaped mass, measuring 4 inches (10 cm.) in diameter, situated slightly to the right of the midline, between the levels of the second and fifth dorsal vertebræ. The tumour was regular in outline, slightly fluctuant, but not cystic in consistency. It felt as if attached to the overlying skin but seemed free from underlying structures. In all aspects it appeared to be a simple lipoma, and because of this diagnosis, arrangements were made for its removal while the patient was in hospital for his varicose veins. Nothing abnormal was detected in the central nervous and other systems.

The patient was subsequently admitted to the ward and on November 27, 1956, a bilateral Trendelenburg operation was performed. He was kept in hospital and after normal recovery was operated on again on December 8, 1956, for the tumour of his back. Under general anæsthesia, with the patient in the prone position, a vertical incision was made 1¼ in. (3.2 cm.) to the right of the spine. On incising the skin, the limits between the latter and the subcutaneous tissues could hardly be defined. From the beginning, the tumour did not look like a lipoma. There was, instead, a multilobulated, irregular, shiny, bluish-tinged tumour of a strikingly rich mucoid nature. It had neither a capsule nor well-defined limits. Myxoma, lymphangioma and chondroma were all suspected. The mass was very adherent to the skin and to the underlying fascia, though it separated with less difficulty from the latter than from the dermis, which appeared to be infiltrated. No stalk or extension into deeper structures or to the spine was noted. The growth spread between the levels of the

*This case was seen at the Mayday Hospital, London, England. The author is now at Roswell Park Memorial Institute, Buffalo, New York.

second and fifth dorsal vertebræ, but was not in the midline. To carry out satisfactory excision, the skin incision had to be extended at both ends. Finally a more or less complete removal was obtained, but radical ablation could not be accomplished. The skin was closed with drainage and a pressure dressing was applied.

On section, the tumour was so abundant in intracellular and extracellular mucin as to give the appearance of mucoid syncytium. There were mucin-distended signet cells and small groups of physaliferous cells showing nuclear vacuolation. In spite of the slightly unusual position of the growth, the histological features made it certain that this was a chordoma. Signs of active malignant proliferation were absent (Fig. 1).

Radiological examination of the whole of the spinal column showed no bony or other abnormality.

Postoperatively the patient was kept under antibiotic cover and remained apyrexial. One week after the operation, the suture line was satisfactory, but there was considerable mucinous collection under the skin, with some inflammatory erythema and œdema of the operative site. A drain was re-inserted and 2 c.c. of hyaluronidase (Hyalase) was injected at the periphery of the swelling. The stitches were left in a few days longer than usual. By Christmas Day, the inflammation had subsided and the swelling diminished. There was still some mucinous drainage but this stopped in due course. The patient was discharged on January 3, 1957, with a completely healed wound. Arrangements were made for a course of radiation therapy as an out-patient. In 14 treatments spread over 22 days, the patient received an indirect dose of 4200 r of radioactive cobalt. When he was subsequently seen at the follow-up clinic, he was very well. The wound had healed with a fine scar and there was no evidence of local recurrence. The skin of the operative site was supple and normal except for a slight residual pigmentation from Co^{60} therapy. There were no abnormal neurological signs.

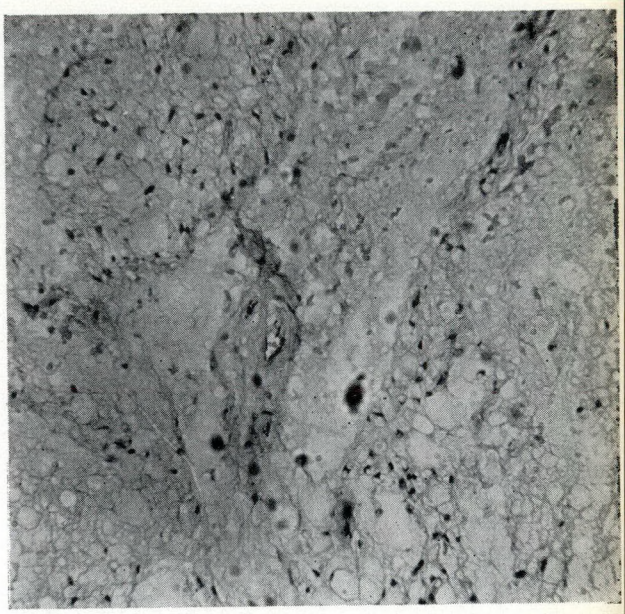

Fig. 1.—Photomicrograph (x 114) of chordoma, showing abundant intracellular and extracellular mucin and typical physaliferous signet cells.

Comment

Chordoma was first reported by von Luschka in 1856.[11] Although the etiology of this, as of other tumours, is not known, trauma seems to be a particularly important factor in chordomata. Ribbert[13] was able to obtain chordoma-like lesions by puncturing the intervertebral disc.

Clinically, these tumours present nothing characteristic. Symptoms arise primarily from compression or involvement of adjacent structures, according to the location. A few of the cases in the dorsal area have presented as mediastinal tumours. Paralytic phenomena are not uncommon.

The course of the disease is progressive. The neoplasm is slow-growing but malignant and invariably fatal; metastases are common. Mabrey[12] estimated that about 27% of these tumours metastasize and, according to his statistics, the average life expectancy is 28½ months. Jackson[10] has seen a case of 30 years' duration.

Treatment is disappointing. Complete surgical removal is almost never possible, both because of the vital structures involved and the non-capsulated, infiltrative nature of the growth. Recurrence is the rule. The tumour is radio-resistant and all forms of therapy can only aim at temporary relief of symptoms. However, even with these limitations, surgery is indicated.

The first record of dorsal chordoma is attributed to Cappell[2] who, in 1928, gave a detailed account of a tumour involving the fifth and sixth dorsal vertebræ. Thereafter sporadic reports have been published and so far I can find only 13 cases of dorsal

chordoma on record (Table I). Goidanich and Battaglia[7] estimate the total number of chordomata of all sites to be about 400. This would bring the proportion of dorsal to all other locations to about 3%.

Besides its unusual location, the present case is also atypical in that it presented as a benign-looking lipoma of the back and that the vertebral structure was not involved.

Summary

Chordoma is a neoplasm of the embryonic remnants of the spinal cord. It is uncommon, and is usually located at the cranial or sacro-coccygeal end of the vertebral column. Only about 3% of these tumours involve the dorsal spine. A case is reported in a man, aged 41, who had an asymptomatic tumour in his back. Clinically this looked like an ordinary lipoma in the region of the second, third, fourth and fifth dorsal vertebræ, but at operation it proved to be a chordoma. Total excision was impossible, but the wound healed without recurrence. Adjuvant radiation therapy was instituted. The 13 cases reported in the literature are briefly tabulated (Table I).

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Résumé

Les chordomes sont des tumeurs peu fréquentes qui naissent des restes embryonnaires de la notocorde. Elles siègent de préférence aux extrémités céphaliques et caudales; leur localisation dans la région dorsale est très rare, à peine 3% de tous les cas connus. L'auteur donne ici l'observation d'un cas de ce genre.

Un homme de 41 ans est admis à l'hôpital pour des varices des deux jambes et une tumeur du dos. Cette dernière le gêne très peu, et le patient ne se plaint que de ses varices; il n'a jamais eu de traumatisme de la colonne vertébrale.

A l'examen: bon état général; varices d'importance moyenne des deux membres inférieurs; dans le dos, sur la ligne médiane, à hauteur D2-D5, présence d'une tumeur ovalaire, lisse, légèrement fluctuante, de 10 cm. de diamètre, semblant adhérente à la peau et mobile sur les plans profonds. Cette tumeur ressemble beaucoup à un lipome et il est décidé de profiter du séjour du malade pour en faire l'ablation. Quelques jours après avoir pratiqué une opération de Trendelenburg bilatérale pour les varices, on procède à l'excision du "lipome". On découvre alors une tumeur très riche en substances mucoïdes, non encapsulée et mal délimitée; cette masse adhère fortement à la peau et aux parties sous-jacentes; elle est enlevée de façon très large, mais non totalement.

Les suites opératoires furent dans l'ensemble satisfaisantes, à part le fait qu'il subsista pendant environ deux semaines un écoulement de substances mucoïdes qui fut drainé et finit par tarir; la cicatrisation ce fit alors parfaitement. Le patient fut renvoyé à domicile et un traitement radiothérapique ambulatoire fut institué: soit 14 séances totalisant 4200 r avec le Cobalt radioactif. A l'heure actuelle, la guérison semble être obtenue. L'examen anatomo-pathologique de la pièce opératoire fait conclure à un chordome sans signes de malignité.

L'étiologie de l'affection n'est pas connue; les traumatismes jouent peut-être un rôle adjuvant. Ces tumeurs ne donnent aucune autre symptomatologie que celle des troubles de compression des organes du voisinage. L'évolution est lentement progressive et avec dégénérescence maligne, fatale; les métastases se font dans 27% des cas. Le traitement est décevant car l'ablation chirurgicale radicale est rarement possible et les récidives sont la règle. Ces néoplasies sont radiorésistantes.

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BOOK REVIEWS

(See also pages 21 and 32)

PEDIATRIC SURGERY: Operative Technics, Surgical Procedures, Management Methods. Orvar Swenson, Boston. 740 pp. Illust. Appleton-Century-Crofts, Inc., New York, 1958. $20.00.

This comprehensive textbook of the surgery of infancy and childhood fills the need for a supplement to standard surgical texts which seldom attempt more than a sketchy reference to pædiatric surgical practice. The difference between pædiatric surgery and adult surgery is just as great as that between pædiatrics and internal medicine. In his foreword, Dr. William E. Ladd points out this fact of modern practice and approves the tendency of some surgeons to concentrate increasingly on the surgery of childhood.

But there are many surgical conditions in children which can well be handled by the general surgeon. Dr. Swenson's book is a good reference work for this, for the writing is clear, precise, and sufficiently detailed. As well as chapters on physical examination, antibiotics, anæsthesia, incisions, surgical technique, each operation description is complete in itself. It is hard to find a branch of surgery in children that is not fully covered: bronchoscopy, deformities of the thorax, bronchiectasis, hiatus hernia, congenital cardiac lesions, undescended testicle, pyloric stenosis, malrotation, meconium ileus, splenectomy, Hirschsprung's disease, urinary tract lesions, embryoma, burns, fractures, hæmangiomas, harelip, parotid tumours—showing a remarkable range of surgical practice. Pædiatric surgery according to this author includes nearly all the specialties in surgery.

This reviewer found this textbook from Boston hard to lay down and recommends it to teachers of surgery, pædiatricians, graduate students and general practitioners as well as to surgeons practising among the very young.

SURGERY IN INFANCY AND CHILDHOOD. M. White and W. M. Dennison. 444 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1958. $7.65.

This is a textbook for medical students from the Royal Hospital for Sick Children, Glasgow. "Pædiatric surgery is not a special branch of surgery but is the whole of surgery applied to a special age group" is the first sentence of the first chapter and in many ways this book is a practical review of the fundamentals of surgical lesions. Concise notes on trauma and infection as modified by infancy and congenital disease such as hæmophilia, and short descriptions of skeletal affections such as fragilitas ossium, rickets, and osteochondritis for example make this a useful small reference source for the general practitioner. The practitioner who does obstetrics will find the chapters on congenital anomalies interesting refresher reading.

Excellent diagrams, good photographs, useful dosage tables and clear writing make "Surgery in Infancy and Childhood" easy to recommend for its purpose. And for protection against the bandying-about of obscure names by the super-specialist (Letterer-Siwe disease, Klippel-Feil syndrome) it provides all most doctors need to know.

A good book not meant for specialists.

OPERATIVE SURGERY: Volume 6. Hand, Amputations, Plastic Surgery, Gynæcology and Obstetrics. Edited by Charles Rob and Rodney Smith. 123 pp. Illust. Butterworth & Co. (Canada) Ltd., Toronto, 1958. $21.50.

This is the sixth in a series of operative surgery manuals and deals with surgery of the hand, amputations in general, plastic surgery, and gynæcology and obstetrics. To combine such a wide field in one volume requires conciseness of description and much organization. This has only been achieved by touching on highlights in some phases. Plastic surgery is condensed to 131 pages and gynæcology and obstetrics to only 123 pages. For this reason the specialist in a limited field will find many aspects of his study dealt with only briefly, if at all, and to such a specialist the volume will have limited appeal.

To the general surgeon, on the other hand, this volume provides ready access to techniques in problems he may encounter and as such it is to be highly recommended.

The format is excellent. The drawings are clear and beautifully executed and writing is reduced to a bare minimum. Along with the five previous volumes, this series offers a wealth of information in operative surgery and will find much use in the general surgeon's library where its excellent binding and presentable appearance will add a justifiable dignity.

TRAUMATISMES ANCIENS: GENERALITES, MEMBRE SUPERIEUR (Old Injuries: General Remarks: Upper Limbs). R. M. d'Aubigné and R. Tubiana. 426 pp. Illust. Masson & Cie, Paris, 1958.

Le Professeur Merle d'Aubigné et ses collaborateurs nous présentent un ouvrage de première valeur, convrant un chapitre important de la chirurgie réparatrice. De cet ouvrage se dégage un enseignement objectif, parce que "basé sur des résultats obtenus". Il est parfaitement illustré, et contient des statistiques personnelles que l'auteur confronte avec des statistiques venant d'autres centres. Ceci confère à ce volume un caractère documentaire peu négligeable. On y traite "essentiellement des séquelles osseuses, articulaires et musculaires, des traumatismes du membre supérieur, moins la main."

La présentation de cet ouvrage est faite dans un ordre didactique tel, qu'elle en fait un traité de base où rien n'est omis tout en laissant place

(Continued on page 112)

(Continued from page 110)

pour une mise au point sur des particularités d'importance.

Au premier chapitre, traitant des "séquelles osseuses des traumatismes anciens" soit troubles de consolidation, altérations biologiques ou infections, les notions de base énoncées constituent un bagage essentiel à la formation théorique et pratique tant pour les spécialistes de la chirurgie osseuse que pour les chirurgiens en général qui s'intéressent aux traumatismes récents.

De ce fait, l'ouvrage du Professeur Merle d'Aubigné présente un intérêt particulier. Pour les infections osseuses, on trouve des notions importantes, qui ne sont pas nouvelles mais qui sont expliquées avec une telle clarté que ces pages constituent une synthèse précieuse du traitement actuel. Il est intéressant de trouver l'expression française de tout un vocabulaire surtout connu dans la littérature anglosaxonne. Avec une insistance nécessaire, les auteurs signalent l'importance d'aborder l'os au travers des parties molles saines, dans le cas des pseudarthroses infectées.

Au chapitre II, "séquelles articulaires des traumatismes anciens", les auteurs soulignent la défense absolue de "mobilisation passive des raideurs articulaires". Ceci peut paraître un anachronisme mais il est nécessaire de le répéter. De même, trouve-t-on cet enseignement précieux à l'article des arthroses; "seule une réduction anatomique à la rotule peut être considérée comme satisfaisante . . . La réduction des fractures bimalléolaires ne doit pas laisser la moindre bascule de l'astragale . . ."

Au sujet des substitutions prosthétiques, même enseignement objectif. On trouve là des détails intéressants sur les greffes articulaires totales.

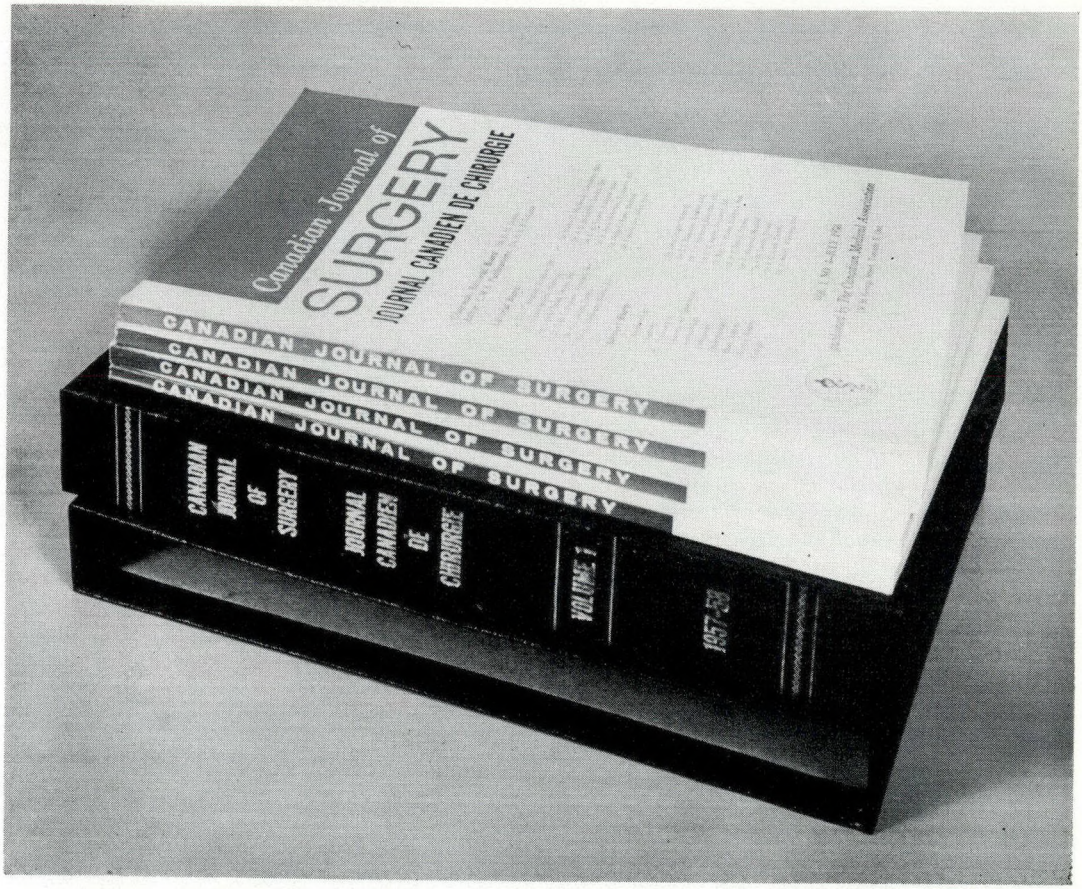
Au chapitre III, richesse de détails tant historiques, histologiques que pathogéniques et techniques, que l'on trouve rarement réunis au sujet des muscles et des tendons.

Le lecteur bénéficiera tout au long de cet ouvrage du fruit d'une recherche exhaustive au travers de la littérature de même que d'une bibliographie aussi complète que possible. Les illustrations dans l'ensemble sont claires et démontratives sauf dans le cas de voies d'approche chirurgicales qui gagneraient à être accompagnées d'une légende plus détaillée.

Pour les traumatismes anciens du coude, on trouve une subdivision intéressante et précieuse pour les indications opératoires. Les séquelles de traumatismes des os de l'avant-bras reçoivent une attention méritée, par une analyse des causes de séquelles. Ici l'on trouve l'expression "traitements orthopédiques insuffisants" par opposition à "traitements chirurgicaux mal conduits"; l'auteur veut sans doute parler de "réductions fermées" par rapport "aux réductions sanglantes".

Les auteurs nous paraissent très prudents lorsqu'ils posent comme limite de temps pour un garrot pneumatique, une heure et quart.—

(Continued on page 116)



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