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This section provides a medium through which Canadian surgeons can declare themselves, briefly and informally, on the day-to-day affairs of surgery.

The Paraduodenal Hernias

In this issue (page 71), Gagic draws attention to a rare type of internal herniation, the right paraduodenal hernia. In the two cases he describes, the diagnosis was made preoperatively because of a high index of suspicion. The most useful investigation was radiologic study of the small intestine with barium contrast medium. Gagic emphasizes the important anatomical relations that must be kept in mind at the time of repair.

Although the term "paraduodenal hernia" is firmly established in the literature, it should not be forgotten that Moynihan[1] recognized two forms of "right paraduodenal hernia". He also described other fossae in the vicinity of the duodenum into which the small intestine could herniate. With this knowledge, it should be obvious that two left-sided and three right-sided internal hernias are possible in the periduodenal area (Fig. 1).

The ability of the surgeon to recognize these fossae after reducing the hernia and to be aware of the anatomical differences needs to be stressed.

Left-Sided Hernias

On the left side, intestine may herniate into either the paraduodenal fossa or the fossa mesocolica.

Paraduodenal Fossa (Fig. 1A)

The paraduodenal fossa is situated to the left of the ascending limb of the duodenum. It is bounded inferiorly by the inferior mesenteric artery or its left colic branch. The inferior mesenteric vein runs along its free margin. The superior end of the fossa is posterior to the duodenojejunal junction. The fundus of the fossa extends to the left, posterior to the descending mesocolon.

Fossa Mesocolica (Fig. 1B)

The entrance to this fossa, situated within the transverse mesocolon on the left side of the abdomen, is directed upwards. Its fundus is cephalad and blends with the posterior and dorsal surfaces of the omental bursa. At the free margin of the aditus are the middle colic artery medially and the marginal artery of Drummond anteriorly. Two minor variations may be noted. In one, the aditus blends with the parietal peritoneum along the inferior border of the pancreas. In the other, part of the fossa extends behind the descending mesocolon and medially to the horizontal limb of the duodenum. In such cases the left colic artery is found along the inferior margin of the aditus but the inferior mesenteric vein and pancreas are covered by the peritoneum forming the posterior wall of the fossa.

Right-Sided Hernias

On the right side, intestine may herniate into the posterior duodenal fossa, the mesentericoparietal fossa or the parajejunal fossa.

Posterior Duodenal Fossa (Fig. 1A)

This fossa always arises from the superior end of the paraduodenal fossa. However, a patient with a paraduodenal fossa does not necessarily

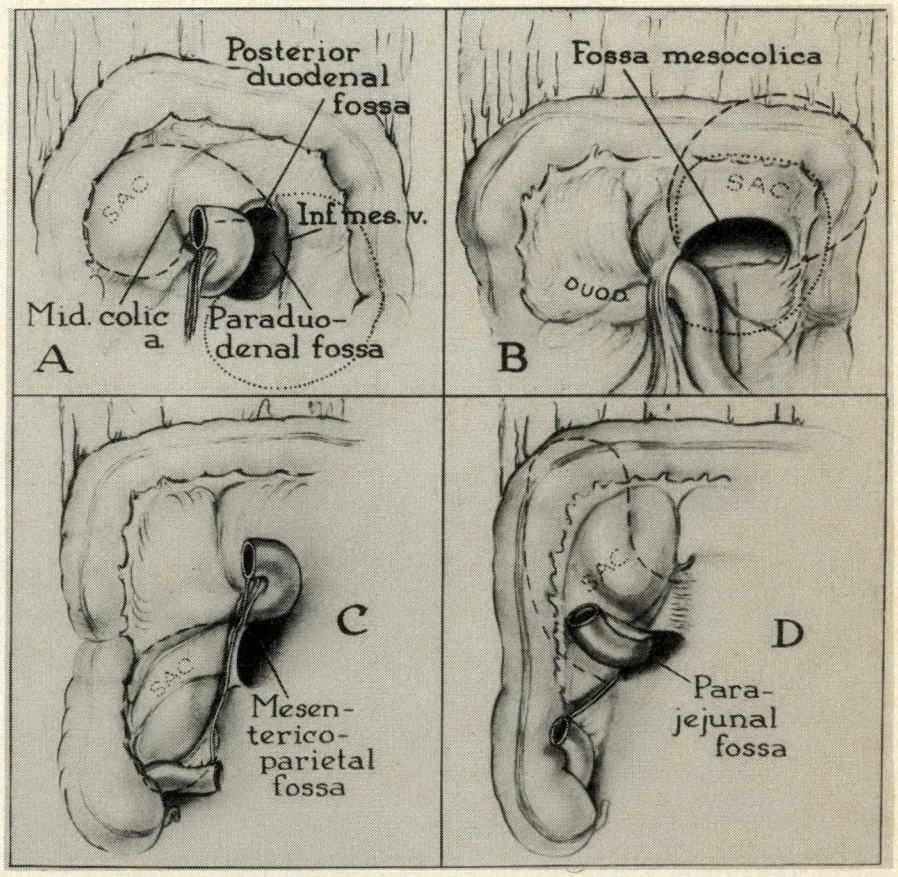

FIG. 1—Periduodenal fossae. Five recesses into which small intestine can herniate as seen when facing subject in supine position: (A) left-sided paraduodenal fossa and right-sided posterior duodenal fossa, (B) fossa mesocolica, (C) mesentericoparietal fossa, (D) parajejunal fossa.

have a posterior duodenal fossa. The aditus is situated behind the duodenojejunal junction to the right of the inferior mesenteric vein. The neck of the fossa extends to the right, the middle colic artery, within the transverse mesocolon, lying anteriorly and the pancreas and superior mesenteric vessels posteriorly. The fundus is downwards, to the right of the middle colic artery and behind the ascending mesocolon.

Mesentericoparietal Fossa (Fig. 1C)

The orifice of this fossa is directed downwards and to the left. The transverse limb of the duodenum forms the superior border. The superior mesenteric artery passes along its free anterior border, formed by the mesojejunum that failed to adhere to the posterior parietal peritoneum. Its fundus is directed downwards and to the right behind the ascending mesocolon.

Parajejunal Fossa (Fig. 1D)

This fossa is situated at the root of the infolded jejunal mesentery, which has adhered along the medial border to the posterior parietal peritoneum covering the great vessels. Its orifice is directed downwards and to the left. The fundus is cephalad, to the right of the second part or descending limb of the duodenum.

It should be remembered that the first few inches of the jejunum are incorporated into the wall of the sac in all these hernias except that into the mesentericoparietal fossa. Only in this hernia are the afferent and efferent limbs of the small intestine seen entering and leaving the hernial sac. Otherwise, only the efferent small intestine is seen emerging from the orifice at the time of recognition.

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Reference

1. MOYNIHAN BGA: *On Retroperitoneal Herma*, Baillière, Tindall & Cox, London, 1899

The Surgeon's Assistant in Canada

Surgeons' assistants have been widely employed in the United States in cardiovascular and thoracic surgical services,[1,2] in community hospitals as employees of individual surgeons or of hospitals and in university services, usually under the aegis of the department of surgery. They are allied health professionals who have completed a 2-year educational program in medical sciences that includes clinical experience. In the US there are many such programs that train both physicians' and surgeons' assistants.

In 1977 a proposal to use surgeons' assistants in the division of thoracic and cardiovascular surgery at the University of Alberta Hospital was made to the department of surgery and to the hospital board. The thrust of this proposal was that there were increasing manpower requirements on the busy cardiovascular and thoracic surgical service and yet, because of restriction in practice opportunities, there was no justification for the training of more housestaff. In view of the American experience with surgeons' assistants, the possibility of hiring such individuals in Canada was entertained.

Both the department of surgery and the hospital board endorsed the proposition and, at that time, the College of Physicians and Surgeons of Alberta was prepared to license such paramedical personnel. The funding was obtained through the Heritage Trust Fund's expansion program in cardiovascular surgery.

Contact was made with the Canadian Medical Protective Association; it had no experience in medicolegal matters relating to surgeons' assistants, so arrangements were made to cover them under the insurance umbrella of the hospital.

A decision was made that such personnel would be hired by the university hospital and would report directly to the director of the division of thoracic and cardiovascular surgery.

In mid-1979 advertising in Canada began; however, after 3 months, no replies were forthcoming, so the position was advertised in the US. There were about 30 applicants, 2 of whom were brought to Edmonton for interviews and 1 was selected.

This man's credentials were then submitted to the College of Physicians and Surgeons, which licensed him to function as a surgeon's assistant within the confines of the University of Alberta Hospital. He began his employ at the University of Alberta Hospital in January 1980. His day-to-day functions were determined by the chief resident in cardiovascular surgery. His function was carefully defined in his job description. This included initial history-taking and physical examination, consultation with the surgeons regarding patient orders, instituting necessary recognized emergency procedures required in life-threatening situations, recording appropriate information on the patient's record and participating in the preoperative and postoperative teaching program for patients and families. In the operating room he assisted the surgeon, either as a first or second assistant in the performance of cardiovascular and thoracic surgical operations.

He functioned extremely well and his interactions with nurses and residents in the operating room, in the cardiac surgical intensive care unit and on the ward were without incident. He functioned essentially as a junior resident on the service in an extremely capable manner.

After 9 months of satisfactory service, he left Canada to return to Florida for personal reasons. Subsequently, a Canadian physician's assistant, trained in the US, was hired.

The licensing of paramedical personnel has been removed from the hands of the College of Physicians and Surgeons of Alberta by the provincial government and a Health Occupations Act (Bill 80) has been passed by the legislature. This effectively puts the responsibility for the licensing of all paramedical personnel into the hands of a bureaucratic agency. Unfortunately the mechanism for licensing has not yet been fully established but will be soon.

It is apparent that surgeons' assistants are going to become an indispensable part of our service. I anticipate that they will be more widely employed in other surgical fields in the future.

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REVIEW ARTICLE

Primary Hyperparathyroidism in Children

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Primary hyperparathyroidism is rare in children. This report describes a 15-year-old boy who had an intrathymic chief cell adenoma. The literature related to this condition in neonates and children is reviewed. Neonatal hyperparathyroidism differs from hyperparathyroidism in children. The severity of symptoms and osseous lesions, genetic inheritance in many, pathological changes in the parathyroid glands and the need for more extensive treatment in neonates and infants indicate that primary hyperparathyroidism in these patients should be considered as a different entity from that occurring in older children.

L'hyperparathyroïdie primaire est une maladie rare chez l'enfant. Les auteurs rapportent un patient de 15 ans chez qui un adénome constitué de cellules principales a été trouvé dans le thymus. La revue de la littérature indique que l'hyperparathyroïdie survenant chez le nouveau-né et le jeune enfant est une maladie différente de l'hyperparathyroïdie survenant chez l'enfant plus âgé. La sévérité des symptômes et des lésions osseuses, le mode de transmission héréditaire chez plusieurs, les différences pathologiques dans les glandes parathyroïdes et la nécessité d'un traitement chirurgical plus précoce et plus étendu chez le nouveau-né et le jeune enfant indiquent que l'hyperparathyroïdie primaire chez ces patients doit être considérée comme une entité différente de l'hyperparathyroïdie primaire survenant chez l'enfant plus âgé.

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Primary hyperparathyroidism seldom occurs in infants and children. Even though the diagnosis has been facilitated by the use of automated biochemical determinations of serum calcium and phosphorus and by the increasing availability of parathormone radioimmunoassay, there are few reports of this condition in children under 16 years of age. Until 1980, only 85 cases had been described in the literature.[1-16] We report the case of a 15-year-old boy with primary hyperparathyroidism caused by an intrathymic chief cell adenoma. When diagnosed early, the disease can be cured by surgical treatment. Because the disease is rare and its manifestations differ somewhat from the adult form, a review of its clinical presentation, pathologic features and treatment is worthwhile.

The first review of primary hyperparathyroidism in children was published in 1960 by Nolan and associates[17] who reported 23 cases. Bjernulf and colleagues[6] reviewed the literature in 1970 and found an additional 20 patients. To these 43 cases, we must add 2 reported by Hillman and colleagues,[1] 2 by Mühlethaler and associates[2] and 3 others reported by Corbeel and associates,[3] Farriaux's group[4] and Verger and colleagues.[5] In 1970, reports of 50 cases had been published. Mannix[7] summarized 14 cases reported from 1971 to 1973 and described 3 of his own. Since then, we have found 18 other cases plus the case reported here bringing the total to 86.

Case Report

A 15-year-old black boy was admitted to the Hôpital Maisonneuve-Rosemont in March 1977 for treatment of anemia and retarded growth. He had not complained of gastrointestinal, urinary, cardiac, pulmonary or neurologic symptoms. Born in Haiti, he had emigrated to Canada in 1976. He was the youngest of three children and had been delivered normally after a normal pregnancy. His mother and father died shortly after his birth. His parents, his 30-year-old sister and his 28-year-old brother were apparently also of short stature. There was no family history of primary hyperparathyroidism.

The boy appeared intelligent. He was 127 cm tall (50th percentile of an 8-year-old boy) and weighed 22 kg (50th percentile of a 7-year-old boy). There was slight truncal obesity without apparent muscle atrophy. Blood pressure was 110/60 mm Hg. No hair growth was noted over the pubic region or in the axillae, and the penis and testes seemed rather small for his age. Physical findings were otherwise normal.

The following laboratory determinations gave normal results: falciform hemoglobin S, electrophoresis of hemoglobin and protein, total serum cholesterol and triglycerides, blood urea nitrogen, glucose tolerance curve, D-xylose test and urinary electrophoresis of amino acids.

Basal pituitary thyroid and adrenal functions were normal. An adequate pituitary response to luteinizing hormone-releasing and thyrotropin-releasing hormones, insulin injection and arginine infusion was demonstrated. The initial prolactin value (8.0 ng/ml) increased to 28 ng/ml after administration of thyrotropin-releasing hormone.

The hemoglobin value was 10.2 g/dl, hematocrit 32.9%, leukocyte count 5×10^9/l, erythrocyte sedimentation rate 9 mm/h and reticulocyte count 3.3% red cells. Mean corpuscular volume was 53 fl (normal 90 ± 9 fl), mean corpuscular hemoglobin 19 pg (normal 29 ± 2 pg), mean corpuscular hemoglobin concentration 31 g/dl (normal 34.5 ± 2 g/dl), serum iron value 40 μg/dl (7.2 μmol/l) and total iron binding capacity 495 g/dl (88.6 μmol/l).

Blood sodium and potassium levels were normal while chloride was slightly elevated (111 mmol/l). Blood pH was 7.35 with a carbon dioxide content of 20 mmol/l.

Serum calcium was elevated on many occasions (11.3 to 11.8 mg/dl [2.8 to 2.9 μmol/l]) and serum phosphorus was always low (2.2 to 2.8 mg/dl [0.7 to

0.9 mmol/l]). Calculated ionized calcium was 5.2 mg/dl (1.3 μmol/l). Urinary calcium and phosphorus were normal on many occasions, values ranging from 78 to 236 mg/d (1.95 to 5.9 mmol/d) and 260 to 492 mg/d (8.4 to 15.9 mmol/d) respectively. Alkaline phosphatase was elevated to 1130 Bodansky units (normal for this age, up to 200 Bodansky units). Two radioimmunoassays for parathormone gave values of 587 pg/ml and 719 pg/ml (normal 163 to 347 pg/ml).

Skull and chest roentgenograms, intravenous pyelogram and upper and lower gastrointestinal films were normal. Roentgenograms of the hands and long bones showed diffuse demineralization with a retarded bone age corresponding to that of an 8-year-old child.

Anemia was easily corrected by oral iron therapy. Because of several increases in the serum calcium values and in parathyroid hormone and serum chloride levels, and the decrease in serum phosphorus and carbon dioxide content, primary hyperparathyroidism was diagnosed.

The parathyroid glands were explored in May 1977. An adenoma 1.5 cm in diameter was found in the right lobe of the thymus after transcervical thymectomy. Another atrophic parathyroid gland was embedded in thymic tissue and removed inadvertently. Two other glands were found to be atrophic. Histologic examination showed thymic tissue containing an adenoma made up mainly of chief cells. After the operation, the patient had symptoms of hypocalcemia and required calcium intravenously for 8 days and oral supplements of calcium for 2 months. Three months after operation, the serum calcium level was 8.6 mg/dl (2.1 μmol/l), phosphorus was 5.3 mg/dl (1.7 mmol/l), alkaline phosphatase was 465 Bodansky units, serum chloride 104 mmol/l and carbon dioxide content 24 mmol/l. When the patient was seen 2½ years after operation, his weight was 50 kg (50th percentile of a 15½-year-old boy) and his height 157 cm (50th percentile of a 14-year-old boy). Serum calcium, phosphorus, chloride and alkaline phosphatase values were normal.

Discussion

Among the 86 patients reported, 17 were neonates and all had parathyroid hyperplasia.[1-4,9,10,14,18-23] Of the remaining 69 patients, 1 was a 12-year-old boy with familial primary hyperparathyroidism without any evidence of associated endocrine disturbance.[16] In this condition, hyperplasia of the four parathyroid glands is usually found, but this child and his mother had a single adenoma, which is the usual finding in children. The 68 other cases did not have known genetic inheritance and the parathyroid condition was adenoma in 54, hyperplasia in 3 and unknown in 11 patients (Table I).

In neonatal primary hyperparathyroidism there is no sex predominance (8 boys and 9 girls have been described in the literature) while in children, 40 boys and 29 girls have been reported. Among adults, primary hyperparathyroidism occurs two to three times more frequently in women than in men.[24]

Symptoms and Signs

Neonates and infants with primary hyperparathyroidism have symptoms such as lethargy, hypotonia, poor feeding ability, failure to thrive, dehydration, diarrhea or constipation and respiratory distress. These symptoms may appear as early as a few days or weeks after birth. The patients are frequently very ill and this diagnosis is usually not considered. Serum calcium levels are always extremely high. Most infants have serum calcium levels greater than 15 mg/dl (3.7 μmol/l), and even above 20 mg/dl (5.0 μmol/l). One infant's serum calcium level was 30.5 mg/dl (7.6 μmol/l).[10] The finding of hypercalcemia, obviously, helps establish the diagnosis. A single determination, however, is not sufficient as in several patients the serum calcium levels initially were normal and then rose rapidly over several days. Since neonatal primary hyperparathyroidism may occur in the setting of familial hyperparathyroidism[1,22] with autosomal dominant inheritance,[14,25] neonates and infants with such symptoms, and affected family members, should be tested early in life and periodically thereafter.

During childhood, the clinical picture of the condition is often nonspecific and inconspicuous. Trivial signs and symptoms such as fatigue, nausea, vomiting, constipation, weakness, anorexia, dizziness, weight loss, failure to thrive and personality changes are common. They are due to the hypercalcemia which is often higher than in adults with primary hyperparathyroidism. It is obvious that this diagnosis may not even be considered in many and it is suggested that serum calcium determinations be made in children with such symptoms.

Infants and children with primary hyperparathyroidism have a high frequency of detectable bone diseases.[14,26] Twenty-five of 43 pediatric patients reported by Bjernulf and colleagues[6] had skeletal changes demonstrated radiologically while overt skeletal changes are identified in only approximately 10% of the adults with primary hyperparathyroidism.[24,27] The basic radiologic bone changes are similar to those in adults: demineralization, subperiosteal bone resorption and pathologic fracture. However, there are substantial differences in neonates and infants: all those reported in the literature had significant diffuse demineralization with severe bone resorption; subperiosteal bone resorption involves the long bones rather than the phalanges and pathologic fracture of the extremities or ribs is common.[28]

Renal lesions have not been described in neonates and infants and seem to be less common in children than in adults, probably because of the shorter duration of the disease. Only 25% of the cases reviewed by Bjernulf and associates[6] had renal calculi compared with 30% to 70% of adult patients treated surgically for this disease. Nevertheless in some series, urologic complications are frequent; 78% of the patients with prov-

Table I—Primary Hyperparathyroidism in Children

Authors	No. of cases	Sex		Pathological findings		
		M	F	Adenoma	Hyperplasia	Unknown
Hillman and associates, 1964[1]	2	2	0	0	2	0
Mühlethaler and associates, 1967[2]	2	0	2	0	2	0
Corbeel and associates, 1968[3]	1	0	1	0	1	0
Farriaux and associates, 1968[4]	1	0	1	0	1	0
Verger and associates, 1970[5]	1	1	0	1	0	0
Bjernulf and associates, 1970[6]	43	25	18	35	7	1
Ahuja and Rao, 1973[8]	1	1	0	1	0	0
Garcia-Bunuel and associates, 1974[9]	1	0	1	0	1	0
Mannix, 1975[7]	17	8	9	14	3	0
Rhone, 1975[10]	1	0	1	0	1	0
Malek and Kelalis, 1976[11]	9	4	5	0	0	9
Gluckman and associates, 1977[12]	1	1	0	1	0	0
Behera and associates, 1978[13]	1	1	0	0	0	1
Thompson and associates, 1978[14]	2	2	0	0	2	0
Mejlhede, 1979[15]	1	1	0	1	0	0
Sandler and Moncrieff, 1980[16]	1	1	0	1	0	0
Present report	1	1	0	1	0	0
Total	86	48	38	55	20	11

en primary hyperparathyroidism reported by Malek and Kelalis[11] had such complications.

Pathological Features

All the reported neonates with primary hyperparathyroidism had parathyroid hyperplasia. Most pathologists and surgeons do not have experience with gross and microscopic evaluation of infantile parathyroid glands, which may be difficult to interpret. The size, weight and microscopic appearance differ considerably from those in the adult.[29] Their size ranges from 1 to 3 mm diameter and their average weight is 2.9 mg (range from 0.9 to 4.8 mg) in infants 5 to 7 months of age.[30] Rhone[10] found the average total weight of infantile parathyroid glands to be 8.8 mg. A normal parathyroid gland (diameter 0.5 to 0.8 cm) in an adult weighs 30 mg, more than 10 times that of an infant's gland. The histology of neonatal parathyroid glands must be interpreted with caution. After studying the morphology and development of the parathyroid glands during the first 30 days of life, Kaplan[29] found enlarged glands with hyperplastic changes in infants 3 to 10 days old. Garcia-Bunuel and colleagues[9] found that, except for a greater content of cytoplasmic glycogen and a less conspicuous Golgi apparatus, abnormal cells from neonates with hyperparathyroidism closely resembled the adult light chief cells.

Most of the children with primary hyperparathyroidism had parathyroid adenoma. Among 69 such patients, 55 had adenomas, 3 had hyperplastic glands and in 11 the pathological findings were unknown. So far, no parathyroid cancer has been described in infants or children.

Treatment

Neonatal primary hyperparathyroidism is a surgical emergency requiring immediate parathyroidectomy. These patients usually present the "failure to thrive" syndrome and parathyroidectomy must be done early to be effective.[1,22,23] Moreover, parathyroidectomy may be unsuccessful if it is delayed until irreversible metastatic calcifications develop in the lungs, heart or kidney.[3,10,14] Eight of 17 infants died before they could be operated on.[1,2,4,18-20,23] Six infants who underwent parathyroidectomy survived[1,9,14,21,22] and three others died postoperatively.[3,10,14] Five of the six survivors required re-exploration after initial subtotal parathyroidectomy failed to correct hypercalcemia. Only one infant remained well after removal of 3½ glands.[1] In spite of early diagnosis and recognition of the urgent need to operate, failure results if insufficient parathyroid tissue is removed. The minimal operation for neonatal hyperparathyroidism is excision of 3½ glands but total parathyroidectomy is the treatment of choice to control the disease. Immediate autotransplantation of parathyroid tissue in an accessible area of the neck or forearm or freezing of parathyroid tissue for future autotransplantation in an aparathyroid patient should be considered after total parathyroidectomy.

In children, surgical removal of a parathyroid adenoma or hyperplastic glands is adequate treatment and the majority were cured by removing only the enlarged adenomatous gland. Subtotal parathyroidectomy cured the three patients with hyperplasia. Transitory hypocalcemia often follows the successful removal of an adenomatous gland as it is known that functional adenoma leads to atrophy of the remaining glands. After a few days or weeks, residual parathyroid glands regain normal function and calcium therapy can be stopped.

Parathyroid adenoma can be found in supernumerary or ectopic glands including those in the mediastinal thymus.[31] In children only three cases (including ours) of ectopic adenoma have been described.[8,32] All were found in the anterosuperior mediastinum and two of them were in the thymus.

Although this report emphasizes that primary hyperparathyroidism is a cause of moderate hypercalcemia in children, other diagnoses, such as transient hyperparathyroidism in a neonate secondary to maternal hypoparathyroidism, idiopathic hypercalcemia and hypercalciuria, hypervitaminosis D, sarcoidosis, hyperparathyroidism and malignant disease, should be considered. Determination of serum parathormone levels in relation to serum calcium and phosphorous concentrations permits accurate diagnosis of the condition.

Conclusions

Primary hyperparathyroidism in patients under 16 years of age is rare. Among the 86 reported patients, two types are recognized, one occurring in neonates and infants and the other during childhood. Neonatal hyperparathyroidism is often genetically transmitted as an autosomal dominant trait and is fatal unless recognized and treated early. The characteristic pathological change is chief cell hyperplasia of the parathyroid glands. Near-total parathyroidectomy is the minimal operation required to control the disease. The prognosis following surgery is good, providing a delay in diagnosis has not resulted in irreversible changes. In children the condition does not have known genetic inheritance and may be an early onset of adult acquired primary hyperparathyroidism. It is more frequent in boys than in girls and osseous lesions are more common than in adults. Prognosis is good if appropriate surgery is performed. Excision of the adenomatous gland or subtotal parathyroidectomy for those with hyperplastic parathyroid glands is indicated.

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continued on page 32

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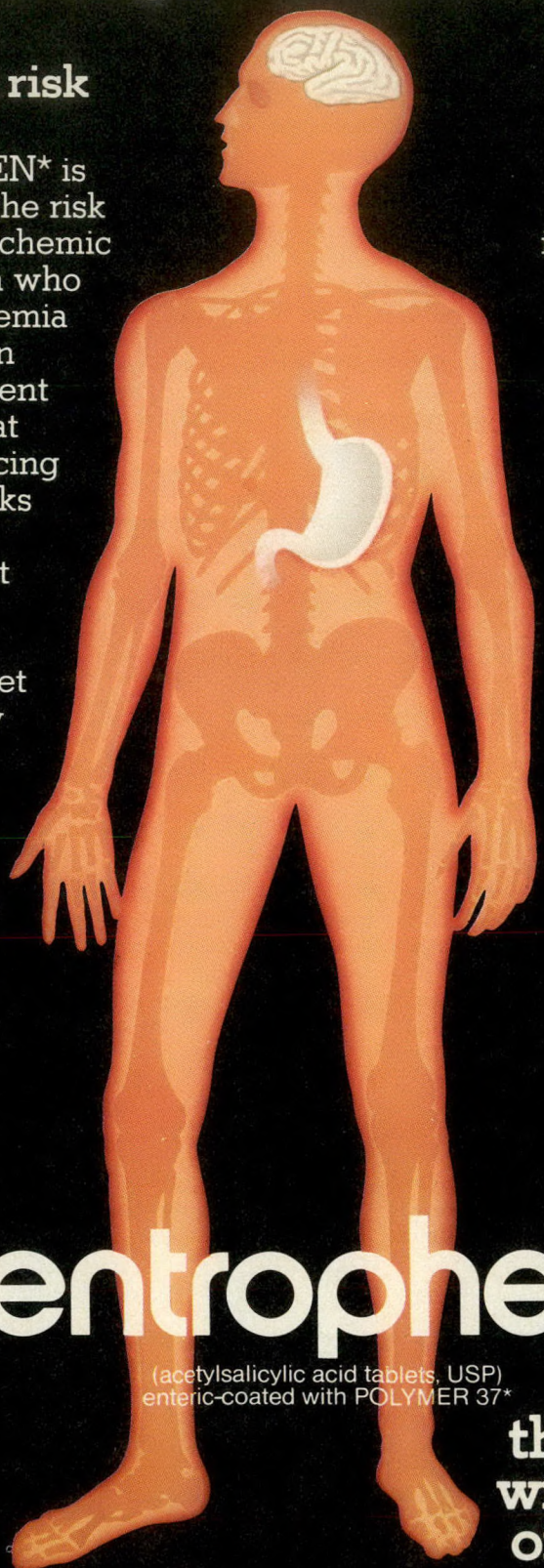

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1. Ali, M. et al.: Plasma acetylsalicylate and salicylate and platelet cyclooxygenase activity following plain and enteric-coated aspirin. Stroke *11(1)*:9-13, Jan/Feb 1980.

TABLETS

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DESCRIPTION

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INDICATIONS

ENTROPHEN* is indicated whenever gastric intolerance to ASA is of concern.

ENTROPHEN* is indicated for the relief of signs and symptoms of the following:

Osteoarthritis
Rheumatoid arthritis
Spondylitis
Bursitis
and other forms of rheumatism
Musculoskeletal disorders

Rheumatic fever, however, penicillin and other appropriate therapy should be administered concomitantly.

ASA is generally considered to be the primary therapy for most forms of arthritis.

ENTROPHEN* is also indicated for reducing the risk of recurrent transient ischemic attacks or stroke in men who have had transient ischemia of the brain due to fibrin platelet emboli. At present there is no evidence that ASA is effective in reducing transient ischemic attacks in women, or is of benefit in the treatment of completed strokes in men or women.

CONTRAINDICATIONS

Sensitivity to the ingredients
Active peptic ulcer

Patients who had a bronchospastic reaction to ASA or non-steroidal anti-inflammatory drugs.

WARNINGS

ASA is one of the most frequent causes of accidental poisoning in toddlers and infants. ENTROPHEN* should, therefore, be kept well out of the reach of all children.

PRECAUTIONS

Salicylates should be administered with caution to patients with asthma and other allergic conditions, with a history of gastrointestinal ulcerations, with bleeding tendencies, with significant anemia or with hypoprothrombinemia.

Salicylates can produce changes in thyroid function tests.

Acute hepatitis has been reported rarely in patients with systemic lupus erythematosus and juvenile rheumatoid arthritis with plasma salicylate concentrations above 25 mg/100 mL. Patients have recovered upon cessation of therapy.

Use in Pregnancy

ASA does not appear to have any teratogenic effects. ASA has been found to delay parturition in rats. This effect has also been described with non-steroidal anti-inflammatory agents which inhibit prostaglandin synthesis.

High doses (3 g daily) of ASA during pregnancy may lengthen the gestation and parturition time.

Because of possible adverse effects on the neonate and the potential for increased maternal blood loss, ASA should be avoided during the last three months of pregnancy.

Drug Interactions

Caution is necessary when ENTROPHEN* and anticoagulants are prescribed concurrently, as ASA may potentiate the action of anticoagulants.

Salicylates may potentiate sulfonylurea hypoglycemic agents. Large doses of salicylates may have a hypoglycemic action, and thus, affect the insulin requirements of diabetics.

Although salicylates in large doses are uricosuric agents, smaller amounts may depress uric acid clearance and thus decrease the uricosuric effects of probenecid, sulfinpyrazone and phenylbutazone.

Sodium excretion produced by spironolactone may be decreased in the presence of salicylates.

Salicylates also retard the renal elimination of methotrexate.

ADVERSE REACTIONS

Gastrointestinal reactions: nausea, vomiting, diarrhea, gastrointestinal bleeding and/or ulceration. Ear reactions: tinnitus, vertigo, hearing loss. Hematologic reactions: leukopenia, thrombocytopenia, purpura. Dermatologic and Hypersensitivity reactions: urticaria, angioedema, pruritus, various skin eruptions, asthma and anaphylaxis. Miscellaneous reactions: acute reversible hepatotoxicity, mental confusion, drowsiness, sweating and thirst.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms

In mild overdosage these may include rapid and deep breathing, nausea, vomiting (leading to alkalosis), hyperpnea, vertigo, tinnitus, flushing, sweating, thirst and tachycardia. (High blood levels of ASA lead to acidosis.) Severe cases may show fever, hemorrhage, excitement, confusion, convulsions or coma, and respiratory failure.

Treatment

Treatment is essentially symptomatic and supportive. Administer water, universal antidote and remove by gastric lavage or emesis. Force fluids (e.g., salty broth) to replace sodium loss. If the patient is unable to retain fluids orally, the alkalosis can be treated by hypertonic saline intravenously. If salicylism acidosis is present, sodium bicarbonate intravenously is preferred because it increases the renal excretion of salicylates. Vitamin K is indicated if there is evidence of hemorrhage. Hemodialysis has been used with success.

Respiratory depression may require artificial ventilation with oxygen. Convulsions may best be treated by the administration of succinylcholine and artificial ventilation with oxygen. Central nervous system depressant agents should not be used.

Hyperthermia and dehydration are immediate threats to life and initial therapy must be directed to their correction and to the maintenance of adequate renal function. External cooling with cool water or alcohol should be provided quickly to any child who has a rectal temperature over 104°F.

DOSAGE AND ADMINISTRATION

Analgesic; antipyretic

Up to 2.925 g daily as necessary.

Anti-inflammatory

Because the suppression of inflammation increases with the dose of salicylate even beyond the point of toxicity, the therapeutic objective is to employ as large a dose as possible short of toxicity. Most patients will tolerate blood salicylate levels in the range of 20 to 25 mg per cent. The most common reason for failing to obtain a therapeutic response to ASA is the administration of inadequate doses.

The generally accepted way to achieve effective 'anti-inflammatory' salicylate blood levels of 20 to 25 mg per cent is to titrate the dosage by starting with 2.6 to 3.9 g daily, according to the size, age and sex of the patient. If necessary, the dosage is then gradually adjusted by daily increments of 0.65 g until symptoms of salicylism e.g., auditory symptoms, occur. Then, the dosage is decreased by 0.65 g daily until these symptoms disappear and maintained at that level as long as necessary.

In adults the median dose at which tinnitus develops is 4.5 g per day, but the range extends from 2.6 to 6.0 g per day.

Intermittent administration is ineffective. Patients should be advised not to vary the dose from day to day depending on the level of pain because that often fluctuates independently of the intensity of the inflammation. A continuous regimen of 0.65 g four times daily is considered to be minimum therapy for adults. ENTROPHEN* should be administered four times daily. For nighttime and early morning benefits, the last dose should be given at bedtime.

Once maintenance dose is established, ENTROPHEN*-15 may be useful to encourage patient compliance.

Optimally, salicylate therapy should be monitored by periodic blood salicylate level determinations. If this is not practical, the appearance of auditory symptoms in the form of tinnitus or deafness are acceptable as an indication of the maximum tolerated salicylate dose.

There is an inverse relation between blood salicylate levels at which auditory symptoms appear and the age of the patient. In the young adult, this is usually in the range of 20 to 30 mg per cent. In children, however, the level may be much higher, or the effect apparently absent. Because salicylate toxicity may appear without such warning in children, the usual practice is to give ASA in a daily dose of 50 to 100 mg per kilogram of body weight and to follow blood levels aiming for a concentration of about 30 mg per cent.

Rheumatic Fever

A total daily dosage of 100 mg per kilogram of body weight administered in divided doses to allay the pain, swelling and fever.

Cerebral ischemic attacks (men)

The recommended dosage is 1,300 mg per day (650 mg twice a day or 325 mg four times a day).

AVAILABILITY

No. 472—ENTROPHEN*-15 tablets containing 975 mg of acetylsalicylic acid USP, coated with POLYMER 37*. Oval, pale yellow, film-coated tablets with the FROSST name engraved on one face and 472 on the other and supplied in bottles of 100 and 500.

No. 470—ENTROPHEN*-10 tablets containing 650 mg of acetylsalicylic acid USP, coated with POLYMER 37*. Oval, orange, film-coated tablets, with the FROSST name engraved on one face and 470 on the other and supplied in bottles of 100, 500 and 1,000.

No. 438—ENTROPHEN*-5 tablets containing 325 mg of acetylsalicylic acid USP, coated with POLYMER 37*. Round, brown, film-coated tablets, with the FROSST name engraved on one face and 438 on the other and supplied in bottles of 100, 500 and 1,000.

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Effect of Surface Roughness on Platelet Adhesion under Static and under Flow Conditions

W. ZINGG, MD, FRCS[C], A.W. NEUMANN, PH D, A.B. STRONG, PH D, O.S. HUM, M SC AND D.R. ABSOLOM, PH D

Normal blood clots when exposed to surfaces other than endothelial. Various unsuccessful attempts have been made to find a synthetic material that is compatible with blood. Both platelets and clotting factors are involved in thrombosis at foreign surfaces. The authors are concerned with platelet adhesion as a first step in thrombus formation. The determination of the number of platelets adhering per unit area, therefore, appears to be a useful criterion for the choice of appropriate biomaterials contacting blood. However, laboratory tests are often carried out with specially prepared, well-defined biomaterials with a smooth surface, whereas biomaterials in clinical use may have a variable degree of roughness.

In this paper the authors present data on platelet adherence to a hydrophilic (glass) and to a hydrophobic (silane) material, with smooth and rough surfaces. Additional data are presented that document the extent of platelet adhesion to a wide range of smooth polymer materials having a large variation in surface hydrophobic quality. There was no difference in platelet adherence between the smooth and rough surfaces when tested under static conditions. When the surfaces were tested in a laminar flow cell, the addition of roughness caused a decrease in platelet adhesion on the hydrophilic surface and an increase in platelet adhesion on the hydrophobic surface.

Le sang normal coagule au contact des surfaces qui ne sont pas endothéliales. Diverses tentatives infructueuses ont été faites dans le but de trouver un matériel synthétique qui serait compatible avec le sang. Les plaquettes aussi bien que les facteurs de coagulation sont impliqués dans le processus thrombotique sur les surfaces étrangères. Les auteurs s'intéressent à l'adhésion plaquettaire en tant que première étape dans la formation du thrombus. On présente des données additionelles qui établissent l'importance de l'adhésion plaquettaire pour une large gamme de polymères lisses possédant de grandes variations quant à la qualité hydrophobe de leur surface. La détermination du nombre de plaquettes adhérentes par unité de surface semble être un critère utile pour choisir les bio-matériaux appropriés devant venir en contact avec le sang. Toutefois, les épreuves de laboratoire sont souvent conduites avec des bio-matériaux bien définis, spécialement préparés pour offrir une surface lisse, alors que les bio-matériaux utilisés en clinique peuvent avoir divers degrés de rugosité.

Dans cet article, les auteurs décrivent les résultats d'adhésion plaquettaires sur des matériaux hydrophile (le verre) et hydrophobe (le silane), possédant des surfaces lisses et rugueuses. Dans des conditions statiques, aucune différence d'adhésion plaquettaire n'a été constatée entre les surfaces lisses et les surfaces rugueuses. Quand l'épreuve a été conduite dans une enceinte à flux laminaire, la rugosité a causé une diminution de l'adhésion plaquettaire sur la surface hydrophile et une augmentation de l'adhésion plaquettaire sur la surface hydrophobe.

Intact endothelium is the only known material whose surface does not induce clotting when blood is exposed to it. The reasons for this are not completely understood and it is unlikely that a man-made material will ever have all the properties of endothelium. The desirable properties of implant materials in general have been described under the heading of "biocompatibility", those of materials exposed to the blood stream as "nonthrombogenicity". Both terms are not entirely adequate because they describe a situation that probably never can be achieved: a synthetic material that is completely biocompatible and nonthrombogenic. However, this achievement does not appear to be absolutely necessary. The living body can tolerate a certain amount of irritation, chemical or physical, caused by an implant, and it reacts in a predictable way, as, for example, by the formation of a fibrous capsule around an implant. Similarly, complete nonthrombogenicity may not be necessary, as an intact fibrinolytic system can handle a limited amount of clot formation.

The important point, therefore, is to seek materials that induce predictable and limited adhesion of blood proteins and platelets as well as negli-

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gible activation of clotting factors — considered to be the first steps in the formation of a clot. Initially investigators tried to solve the problem with an empirical approach: identify a material with desirable properties, such as chemical composition, surface texture, surface charge or surface tension and then carry out in vitro clotting tests and animal studies by implanting the material into the blood stream. This approach has produced many of the materials in use today. In spite of this success, materials that are entirely satisfactory and predictable are not yet at hand. Indeed, in describing the current state of the art a recent symposium was entitled "Biomaterials Research — 20 Years of Frustration".[1]

Other investigators have attempted to apply the scientific method to the problems of blood clotting in the presence of foreign materials, breaking down the complex process into smaller steps, which individually allow scientific investigation. This procedure is much more time-consuming; there are no short cuts as there are in the empirical approach. As knowledge concerning individual steps gradually accumulates, correlations have to be sought between them, and finally a synthesis has to be attempted that eventually may explain the whole. With this approach, there is less frustration; in fact, considerable progress has been made, although correlations are few and a synthesis is still in the far future.

The viewpoint has been expressed that biomaterials research is not rewarding because clot formation is dependent on hemodynamic rather than surface factors. This opinion appears simplistic, but it is true that flow conditions influence clot formation and therefore have to be considered in the design of experiments.

There is confusion about the importance of surface texture — or the degree of roughness — in the initiation of a clot at the surface. Historically, smooth surfaces were preferred at first. In fact, the desirability of smoothness was accepted to the point that research on the effect of roughness was discouraged less than 20 years ago! Later, very rough, flocked surfaces were proposed to be less thrombogenic than smooth surfaces: blood components would enter the rough areas resulting in the formation of a smooth pseudointima. Porous surfaces have also been used with success. The addition of cultured cells to form a thin cellular lining over a polymer substrate appears to have merit.[2]

Our experimental program is designed to study the first two steps of clot formation at a foreign surface — the adsorption of plasma proteins and the adhesion of platelets — in order to identify the forces involved in the process. In this paper we report results on (a) platelet adhesion to smooth surfaces with a wide range of surface tensions under static conditions and (b) platelet adhesion to hydrophilic (glass) and hydrophobic (silane) surfaces, either smooth or with a known surface roughness, under static and under flow conditions. Thus, there are three variables: surface tension, surface texture and presence or absence of flow.

Materials and Methods

Platelet Preparation

Anticoagulated pig blood was obtained at the slaughterhouse and, following repeated centrifugation, the platelets were suspended in Tyrode-albumin solution[3] at a final concentration of 2×10^5 platelets/mm^3.

Preparation of Surfaces

The materials used are presented in Table I. Films were prepared and mounted on microscopic slides.[4] Rough surfaces were prepared by abrading with sandpaper. Silane surfaces were prepared by exposing smooth or roughened glass slides to dichlorodimethylsilane vapour. Contact angles were determined with a goniometer telescope using drops of normal saline on cleaned surfaces.

Static Platelet Adhesion Test[5]

Under controlled conditions a drop of platelet suspension was placed on the test surface for 4 minutes. The various test surfaces were rinsed under standard shear rates and then stained. The number of adhering platelets per unit area of test surface was determined microscopically.

Dynamic Platelet Adhesion Test

A newly designed flow cell was used[6] that assures laminar flow at the test surface together with minimal exposure of platelets to foreign surfaces before contact with the test surface. For the experiments with platelet suspensions a flow rate of 6 ml/min for 4 minutes was used, for blood 4 ml/min for 4 minutes; the flow cell was connected to the jugular vein of a dog and the flow rate was controlled by a withdrawal pump.

There were four experiments. In each experiment, the glass or silane-coated surface was investigated in triplicate; on each individual slide 10 microscopic fields were evaluated.

Table I—Substrates Used in the Platelet Adhesion Studies

Substrate	Source	Mode of preparation	Surface tension, ergs/cm^2
Gold	—	Vacuum deposition	—
Sulfonated polystyrene (SPS)	Central Research Laboratory, Dow Chemical Co., Midland, Mich.	Film	66.7
Polyethylene terephthalate	Celanese Canada Inc., Toronto, Ont.	Heat press	47.0
Acetal	Commercial Plastics & Supply Corp., Toronto, Ont.	Heat press	44.6
Nylon-6,6	Commercial Plastics & Supply Corp.	Solvent casting	41.1
Segmented polyurethane/glass	Ethicon Inc., Somerville, NJ	Polymerization	36.4
Segmented polyurethane/air			32.1
Segmented polyurethane/silane			20.6
Low-density polyethylene	Commercial Plastics & Supply Corp.	Heat press	32.5
Polystyrene	Central Research Lab., Dow Chemical Co.	Film	25.6
Silane/dichlorodimethylsilane	Eastman Kodak Co., Rochester, NY	Vapour deposition	17.6
Silastic rubber	Dow Corning Canada Inc., Streetsville, Ont.	Used as is	18.1
Teflon (FEP) (fluorinated ethylene-propylene copolymer)	Commercial Plastics & Supply Corp.	Heat press	16.4

Results

Static Platelet Adhesion Test

In Fig. 1 the relation between the contact angle measured at the smooth solid surface and the number of platelets adhering to the surface per unit area is shown using the static test. Platelet adhesion decreased with the increasing contact angle of the substrate. The contact angle measured on the surface of segmented polyurethane (SPU) depends on the surface to which the material is exposed during solidification: three such surfaces are included (glass, air and silane), and the results show the same relation between contact angle and platelet adhesion as other materials. Selected materials (glass and silane) were examined when smooth and when rough. The contact angle was slightly larger on the rough surface, and there was no difference in platelet adhesion to the same smooth or rough materials in the static test (Figs. 2 and 3). On smooth silane the platelets form long thin pseudopods. On both rough surfaces there appears to be the same preferential adherence in the vicinity of the crevices.

Dynamic Platelet Adhesion Test

The flow experiment provided differences with both platelet suspensions and fresh blood.[7] The total number of platelets adhering was smaller than in the static test. From the platelet suspension the adhesion to rough glass was diminished ($P < 0.01$, Student's *t*-test) and to rough silane it was increased ($P < 0.05$), compared with the adhesion to the smooth surfaces under the same flow conditions (Fig. 4). A similar situation was found with blood although the difference in platelet adhesion to smooth and rough silane was not significant.

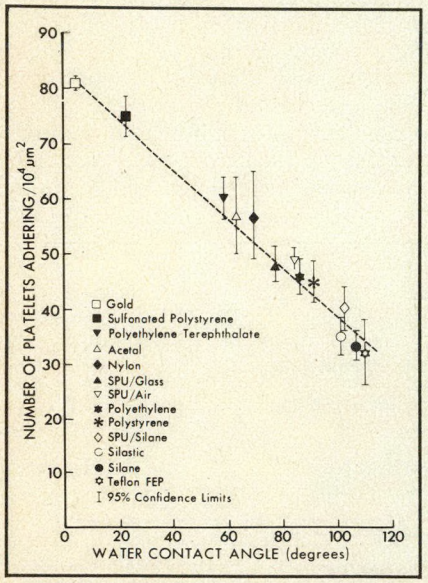

FIG. 1—Platelet adhesion to various smooth solid surfaces under static conditions. Platelet concentration = 200 000/mm³. Number of adhering platelets increases with decreasing contact angle of surface. SPU = segmented polyurethane, FEP = fluorinated ethylene-propylene.

Discussion

The purpose of the static experiments was to study the forces involved in the adhesion of platelets to surfaces. Platelets can be suspended in liquids with varying concentrations of electrolytes, plasma proteins and of the other blood cells. Thus, the different factors influencing platelet adhesion can be studied away from the dynamic forces of flowing blood. The results presented in Fig. 1 show the linear relation between the contact angle, which is an expression of the surface tension of the solid material, and the number of platelets adhering per unit area.

To differentiate between the physical surface characteristics and the effects of the chemical properties of the biomaterial on the blood–material interface, experiments have been carried out using the same material with different physical surface character-

Fig. 2a

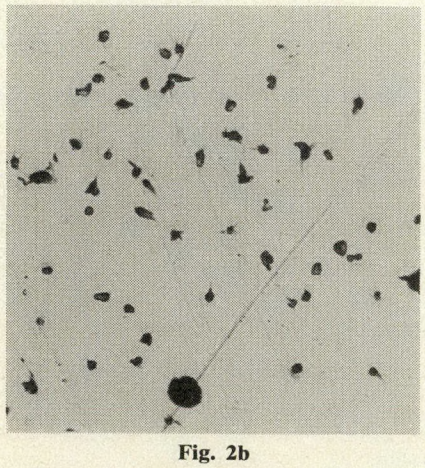

Fig. 2b

FIG. 2—Platelet adhesion to glass (static test): (a) smooth surface, (b) rough surface (reduced by 49% from ×1600).

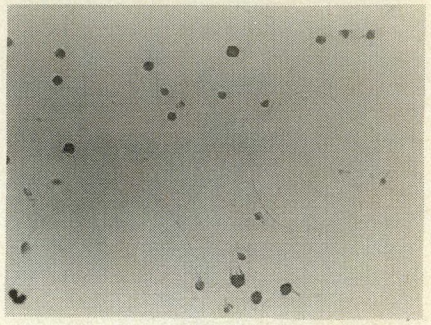

Fig. 3a

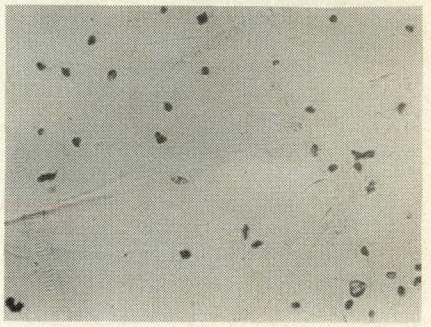

Fig. 3b

FIG. 3—Platelet adhesion to silane (static test): (a) smooth surface (note long pseudopods of platelets), (b) rough surface (reduced by 60% from ×1600).

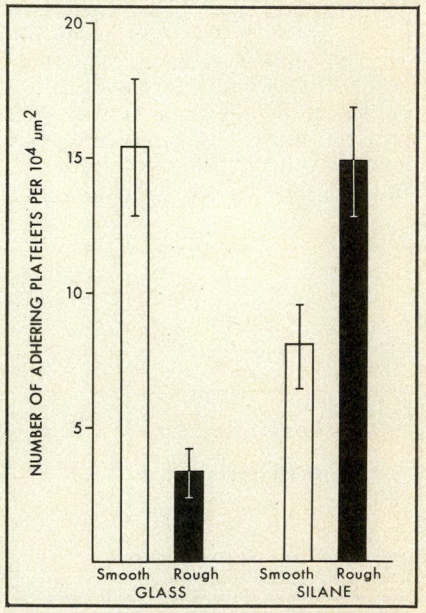

FIG. 4—Platelet suspension: adhesion to glass and to silane (smooth and rough) in flow cell (±SE). Platelet concentration = 200 000/mm³. Addition of roughness decreases platelet adhesion on glass surface and increases adhesion on silane surface.

istics. Wielogorski and colleagues[8] studied the influence of surface rugosity on hemolysis occurring in an extracorporeal circuit using three types of polyvinylchloride tubing. They found that during the initial period of pumping the rate of hemolysis in rough tubes was almost four times greater than in smooth tubes. They warned, however, that this finding may be caused not only by mechanical effects but also the large surface area, which increases the likelihood of plasticizer leaking into the blood. Again using polyvinylchloride tubing, Hecker and Edwards[9] found an association between roughness and thrombus formation experimentally when catheters with different surface roughness were inserted into the blood stream of animals. This may be due to the degree of adhesion of the thrombus rather than to differences in thrombogenicity. We have shown previously[10] that if surfaces with different tensions are produced with the same material, platelet adhesion under static conditions varies with the surface tension. This observation was confirmed with segmented polyurethane (Fig. 1). The three materials were prepared in an identical way, but during polymerization one batch was exposed to glass, one to air and one to silane. Clearly, platelet adhesion to the silane form was less than to the other two surfaces of the same material. Polymer chemists are familiar with the fact that the casting technique may influence the surface properties, such as surface tension. This should be remembered by investigators who produce devices for exposure to blood.

Under static conditions, a significant effect of roughness on platelet adhesion when compared with the same smooth material could not be demonstrated. Under flow conditions, the results were entirely different: fewer platelets adhere to rough than to smooth glass, and fewer platelets stick to smooth than to rough silane. In other words, the effect of roughness for a hydrophilic material (glass) is opposite to the effect for a hydrophobic material (silane). With a hydrophilic material water adheres to the surface and fills crevices of the rough material. Thus, the roughness may cause a layer of water to form at the surface so that blood moving along the surface is then in contact with this layer of water instead of the material surface. Although definite proof is still lacking, the available evidence (e.g., from hydrogels that have a high water content) suggests that the number of platelets adhering to such surfaces is greatly reduced.[11]

On a hydrophobic surface the degree of roughness is important. According to Merrill's definition[12] the surfaces were not "rough to cells"; the crevices were too small to retain blood cells. Ward and colleagues[13] have shown that on the rough surface of a hydrophobic material exposed to a fluid such as blood, gas pockets exist that are stable and are not dislodged by flowing blood. The platelets stick to the gas pockets in the crevices, rather than to the crevices themselves.[13] The addition of roughness to a hydrophobic surface therefore may be associated with stabilized gas pockets; this in turn explains the increase in platelet adsorption, followed by better and more prolonged adhesion, which may be the first step in the formation of a thrombus. The importance of the extended pseudopods that were found on smooth silane only is not known. The majority of the biomaterials to which blood is exposed are hydrophobic, such as silicone rubber, polyvinylchloride and polyethylene. The results of this investigation suggest that these surfaces should be very smooth, probably smoother than some of the commercially available biomaterials. If hydrophilic materials are used, such as hydrogels or metals, surface roughness may be less important; in fact, a certain degree of roughness may be beneficial.

In the experiments reported in this paper, only the surface tension and topography of the biomaterials was considered. In reality the situation is more complex. Nevertheless, it can be concluded that the static test — a valuable research tool — is limited in the practical evaluation of biomaterials exposed to blood, as the presence or absence of surface rugosity does not influence platelet adhesion. Under flow conditions, roughness of the surface is detrimental on a hydrophobic surface, whereas it may be beneficial on a hydrophilic surface. As commercially produced biomaterials usually exhibit a degree of surface roughness, these observations should be considered in the choice of materials in contact with blood for a given purpose.

Summary

The first step in the formation of a thrombus following the exposure of blood to a foreign surface is the adhesion of platelets to the surface. The determination of the number of platelets adhering per unit area therefore appears to be a useful criterion for the choice of appropriate biomaterials contacting blood. However, laboratory tests are carried out with specially prepared, well-defined biomaterials with a smooth surface, whereas a variable degree of roughness may be present on the biomaterials in clinical use.

In this paper we studied platelet adherence to a hydrophilic material (glass) and to a hydrophobic material (silane) with a smooth and with a rough surface. There was no difference in platelet adherence between the smooth and rough surfaces when tested under static conditions. When tested in a laminar flow cell, the addition of roughness caused a decrease in platelet adhesion on the hydrophilic surface and an increase in platelet adhesion on the hydrophobic surface.

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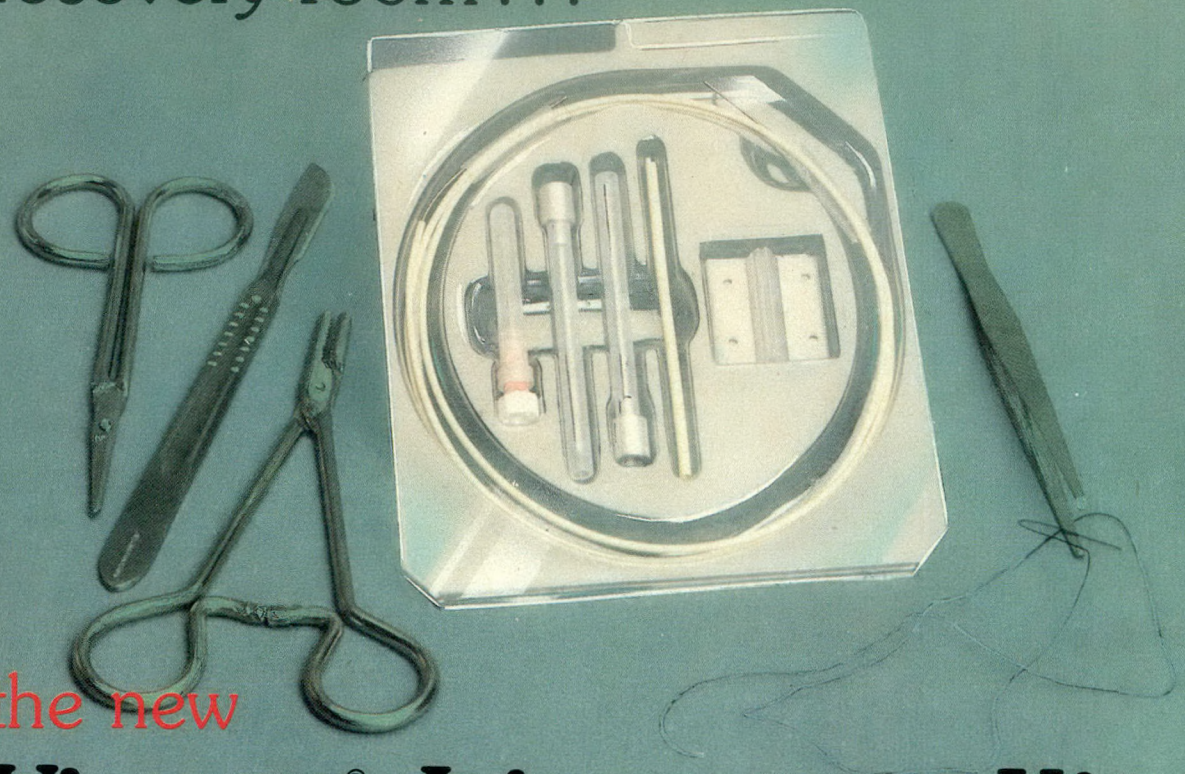

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Appendicovesical Fistula Caused by Ileocecal Actinomycosis

SAUL GONOR, MD, MICHAEL ALLARD, MD, FRCS[C] AND G. RENE BOILEAU, MD, FRCS, FRCS[C]*

An appendicovesical fistula, diagnosed at laparotomy in a 19-year-old man, was found to be due to actinomycosis. Both conditions are uncommon and this appears to be the first report of their coincident occurrence. Both present diagnostic problems because of nonspecific symptoms and biopsy findings, and a negative urine culture. A combined approach to therapy was required in this patient who was treated successfully by partial cystectomy and appendectomy with resection of the cecum. Penicillin G was given intravenously for 7 days then tetracycline was prescribed for 13 months.

Une fistule appendico-vésicale diagnostiquée à la laparotomie chez un homme de 19 ans, s'est avérée due à une actinomycose. Ces deux affections sont rares et ceci semble être le premier rapport de leur existence simultanée. Les deux présentent des difficultés diagnostiques à cause de la non spécificité des symptômes et des observations de biopsie, ainsi que d'une culture d'urine négative. Une approche thérapeutique combinée a été nécessaire chez ce patient qui fut traité avec succès par cystectomie partielle et par appendicectomie avec resection of the cecum. Penicillin G G fut administrée pendant 7 jours suivie d'une prescription de tétracycline pendant 13 mois.

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Actinomycosis is an indolent, suppurative infection characterized by the formation of multiple abscesses and draining sinuses, and by granulation and dense fibrous tissue. It is caused by gram-positive anaerobic actinomycetes, most often *Actinomyces israelii*. The infection is abdominal, predominantly in the ileocecal region, in about 20% of reported cases;[1] genitourinary involvement is uncommon and bladder involvement is rare.

Appendicovesical fistula constitutes less than 5% of all vesicointestinal communications;[2] we could find no report of such a fistula due to actinomycosis as described in this report. Our patient presented with features of both conditions making diagnosis difficult and necessitating a combined approach to therapy. The nonspecific symptoms and biopsy findings, and the negative urine culture, underline the difficulty in diagnosing both of these entities.

Case Report

A 19-year-old Caucasian man was admitted on Oct. 26, 1980. He had suffered from lower abdominal discomfort and severe dysuria for 5 months and had had one episode of gross total hematuria. A course of co-trimoxazole, instituted because urinalysis had demonstrated moderate pyuria, relieved the symptoms only temporarily. There were no gastrointestinal symptoms and the history was otherwise noncontributory.

The patient was rather thin, but physical findings were normal apart from lower abdominal tenderness on deep palpation and rectal examination. Results of routine laboratory investigations were normal except for eosinophilia (5%) in the peripheral blood and the finding of innumerable leukocytes and two to five red cells per high-power field in the urine. Culture of the urine yielded no growth.

An intravenous pyelogram appeared normal. A cystogram was reported as normal, but on retrospective review showed a filling defect on the right side of the dome of the bladder and an irregularity superiorly in the post-voiding film (Fig. 1). Cystoscopy revealed a mass lesion in the dome of the bladder; this resembled a bowel polyp and initially was thought to be a urachal tumour or urachal cyst-abscess, but a transurethral biopsy specimen showed only nonspecific cystitis with patchy chronic inflammation.

At laparotomy through a lower midline abdominal incision an inflammatory mass was seen involving the appendix, cecum and urinary bladder. Partial cystectomy and appendectomy were performed, the cecum was resected and the mass removed *en bloc*. Gross examination of the specimen confirmed an appendicovesical fistula (Fig. 2). Microscopic examination demonstrated "sulfur granules" characteristic of actinomycosis. The actinomycotic lesions were surrounded by exuberant fibrosis and chronic inflammation (Fig. 3).

The patient's postoperative course was uncomplicated. He was given penicillin G intravenously (2 million units *q4h* for 7 days), followed by tetracycline orally (500 mg *qid* for 1 month, then 250 mg *qid* for 1 year). At last report (February 1981) he was well and had had no recurrence of symptoms.

Discusssion

Actinomyces israelii is a normal constituent of the anaerobic flora of the oral cavity in humans. It is an opportunistic pathogen, invading and proliferating only under anaerobic conditions, such as those produced by

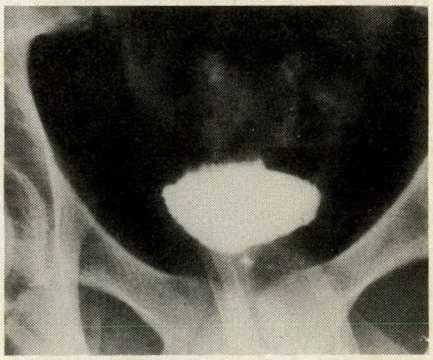

FIG. 1—Post-voiding cystogram showing irregular margin of bladder dome.

the local trauma of dental extraction.[3] Once in the tissues, the bacterium gives rise to a subacute chronic inflammatory reaction with surrounding fibrosis, sinus tracts and fistulas. At the centre of the inflammatory reaction is the actinomycotic abscess, characterized by the presence of sulfur granules (masses of filamentous organisms) radiating outward, thus the misnomer "actinomyces" from the Greek for ray fungus.

The mechanism by which *A. israelii* gains access to the abdominal organs is a subject of controversy. The most widely held theory is that the organism is swallowed and that it escapes from the intestinal lumen when this is damaged by trauma or disease.[4] Thus, an inflamed appendix provides a likely portal of entry, in which case the infection produces a tender periappendiceal mass, usually with multiple draining sinuses that contain the pathognomonic sulfur granules. Clinical features other than abdominal pain include insidious onset, variable low-grade fever, loss of weight, lethargy, microcytic anemia and leukocytosis. Lymphadenitis may occur, due to secondary infection with *Staphylococcus aureus* or *Escherichia coli*. Definitive diagnosis depends on histologic demonstration of the characteristic granules or culture of the organism on an enriched medium under anaerobic conditions. Therapy consists of a prolonged course of penicillin or tetracycline, to which the organism is uniformly sensitive. It is generally agreed that surgical drainage and excision of the lesion facilitate recovery.

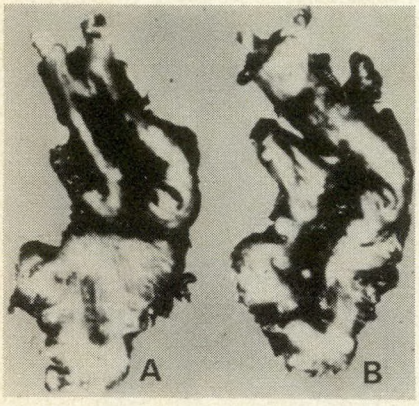

FIG. 2—Cut surfaces of gross specimen showing (A) fistula extending from vesical mucosa inferiorly and (B) appendiceal lumen and greatly thickened appendiceal wall superiorly.

Vesicointestinal fistula is most commonly associated with colonic carcinoma or diverticular disease and thus is found most frequently in the age group 50 to 60 years.[5] In younger patients the condition is usually secondary to Crohn's disease. It occurs predominantly in males, because the uterus acts as a barrier to fistula formation.[6]

In 1969, Gross and Peng[2] were able to find only 82 reported cases of appendicovesical fistula, but spontaneous healing of the fistula in some cases led Holmlund[5] to surmise that the condition probably is less rare than reports indicate. Holmlund stressed the need for awareness of this condition by all who treat patients, particularly young men, for repeated urinary infection — the majority of the patients are males, between the ages of 10 and 40 years. The commonest cause of appendicovesical fistula is perforation of a pelvic appendix, resulting in the formation of an abscess and fistula. The clinical picture is variable, and either appendiceal or vesical symptoms may predominate; chronic lower abdominal pain, dysuria, pyuria and hematuria are common.

In contrast to other forms of vesicointestinal fistula, communication between the bladder and appendix rarely gives rise to fecaluria and pneumaturia. Cystoscopy reveals localized or generalized cystitis, bullous edema or a depressed necrotic area, and in a few cases the aperture of the fistula is seen. Prolapse of appendiceal mucosa into the bladder may simulate a neoplasm.[7] A cystogram or roentgenogram after barium enema with delayed exposures may aid in diagnosis. Treatment consists of appendectomy, excision of the fistula and a surrounding cuff of bladder, drainage of the abscess cavity and administration of appropriate antibiotics.

Renal involvement in the actinomycotic process is commonest when the genitourinary system is affected;[8] about 50 cases have been reported, mostly evolving from subclinical infection elsewhere.[9] An association with intrauterine contraceptive devices is said to be common in cases of pelvic involvement, and one such case of isolated actinomycosis of the bladder has been described.[10] Five other cases of vesical actinomycosis not involving the appendix have been reported.[11]

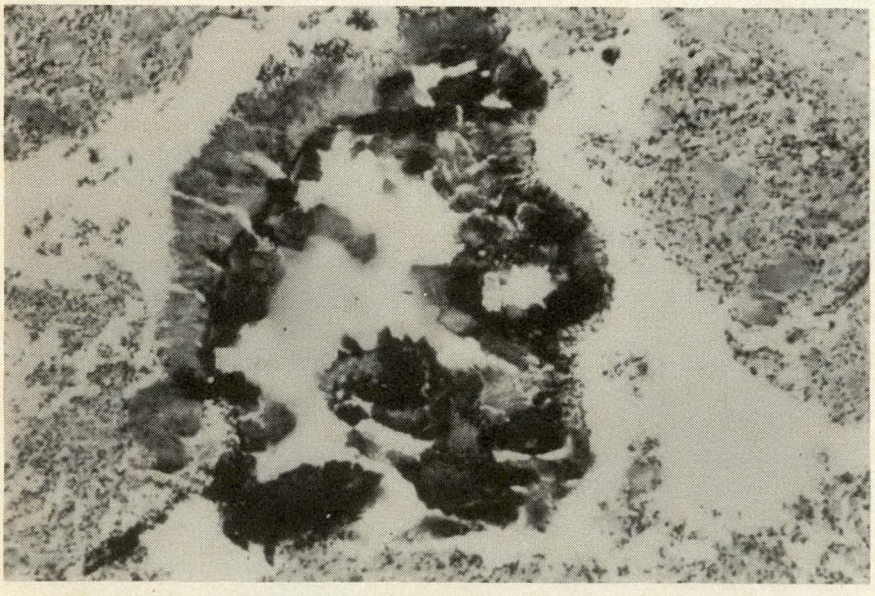

FIG. 3—Photomicrograph showing "sulfur granule" of actinomycosis within lumen of fistula, lining of granulation tissue, and wall of acute and chronic inflammation (hematoxylin and eosin, enlarged 1.7× from ×100).

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Blunt Renal Trauma: the Value of a Conservative Approach to Major Injuries in Clinically Stable Patients

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A 10-year retrospective study of 393 cases of blunt renal trauma was carried out to evaluate the use of a conservative approach to therapy in clinically stable patients with major renal injuries. Injuries were minor in 357 patients who were successfully treated conservatively. Major injuries occurred in 36 patients; 28 were treated conservatively. Of the 28, 17 had no complications. Seven required total or partial nephrectomy to control bleeding and four had drainage, one with marsupialization of a large renal cyst, 1 year after injury. The authors advocate conservative treatment of major blunt renal injuries in clinically stable patients.

On a mené une étude rétrospective portant sur une période de 10 ans, de 393 cas de traumatisme rénal fermé afin d'évaluer l'emploi des méthodes conservatrices chez les malades souffrant de lésions rénales majeures dont l'état clinique est stable. Les contusions étaient mineures chez 357 patients qui furent traités de façon conservatrice avec succès. Des lésions majeures sont survenues chez 36 malades; 28 ont été traités de façon conservatrice. Des 28, 17 n'ont subi aucune complication. Sept ont nécessité une néphrectomie totale ou partielle afin de juguler l'hémorragie, quatre ont subi un drainage, un avec une marsupialisation d'un gros kyste rénal 1 an après le traumatisme. Les auteurs préconisent le traitement conservateur des traumatismes rénaux fermés majeurs chez les patients dont l'état clinique est stable.

The great controversy in blunt renal trauma is the management of major renal injury in the patient who is clinically stable. Most (80%) blunt renal injuries are minor and do well with conservative management alone, and there is little argument that clinically unstable patients with major injuries require immediate operation. But in the relatively small group of clinically stable patients with major renal injuries there is considerable disagreement about management. In most centres, if this group of patients is managed surgically, there is a 50% likelihood that nephrectomy will be carried out.[1] On the other hand, if the same group is managed conservatively, nephrectomy will usually be performed in only 5% to 20% of patients.[2,3] To evaluate the effectiveness of the conservative approach, which we use, we reviewed 393 cases of blunt renal trauma seen over a 10-year period.

Patients and Methods

Between 1968 and 1978, 393 patients with blunt renal injury were admitted to one of five McGill University hospitals, two of which were major referral centres, two community hospitals and one a major pediatric hospital.

All patients initially underwent intravenous pyelography. When this study proved inadequate and the patient was clinically stable, nephrotomography, with either a double dose of contrast material or an infusion of 200 ml of Renografin-76, was done. Renal scanning was often used after intravenous pyelography, especially in children, to evaluate deficits in function of the renal parenchyma. It was also used as a follow-up study to assess the progress of healing. Arteriography was used selectively in cases of suspected pedicle injury or when operative intervention was contemplated.

All cases were classified as minor, major or pedicle injuries as advocated by Hodges and associates.[4] Parenchymal lacerations not involving the vasculature or collecting system to an appreciable degree (extravasation beyond the capsule) were classed as minor injuries. Most major injuries in our series were associated with functional failure of at least one third of the renal parenchyma.

Results

Of all blunt renal injuries, 88% occurred in patients under the age of 40 years (Table I). Motor vehicle accidents (in 45%) accounted for most of the multiple injuries; 55% of the cases were due to other causes and were most often isolated events (Table II).

Most (357) injuries were minor and responded well to conservative management. There were 36 major injuries including 2 pedicle injuries. In both these patients immediate nephrectomy was necessary because the patient was clinically unstable. Of the other 34 patients, 6 required immediate operation for continued acute uncontrollable bleeding and 28 were treated conservatively. Many patients in the latter group manifested an initial period of clinical instability, but were easily stabilized in the emergency department or in the initial period after admission.

The temperature, hematocrit and renal function (serial intravenous pyelograms) were monitored closely in this group of 28 patients. Seventeen of them had no clinical problems. At the time of discharge half had better renal function (as demonstrated on the intravenous pyelogram) than they had at the time of admission. None showed deterioration of function. The other 11 patients with major blunt renal injuries managed conservatively had complications (Table III). Seven required either a nephrectomy or a partial nephrectomy for the control of

Table I—Age Distribution (N = 393)

Age, yr	No. (%)
0–10	69 (18)
11–20	171 (43)
21–40	105 (27)
41–60	40 (10)
>60	8 (2)

Table II—Etiology (N = 393)

Cause	No. (%)
Motor vehicle accident	177 (45)
Fall	97 (25)
Sport	88 (22)
Blow	31 (8)

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secondary bleeding. One patient in this group was stabilized easily with blood transfusion before operation. Four secondary drainage procedures were necessary. One patient returned 1 year later with a large renal cyst and complaining of persistent pain (Table III). One 17-year-old boy had hypertension (diastolic blood pressure of 90 mm Hg); the pressure returned to normal within 2 years.

Of the 28 patients who had major injuries managed conservatively, 5.5 kidneys were subsequently removed, a nephrectomy rate of 19.6%.

Discussion

Preservation of functioning renal parenchyma was the goal in managing blunt renal injuries especially in view of the young age of our patients: 60% of the major injuries occurred in patients under the age of 20 years.

In the clinically stable patient we found the conservative approach satisfactory. Our 19% nephrectomy rate is reasonable and in four patients with complications a simple drainage procedure was all that was needed. The patients who were managed conservatively and who had no complications showed no deterioration in renal function; 50% had better function, as shown by pyelography, than on admission.

Intravenous pyelography was adequate in 85% of cases to diagnose the extent of the renal injury. When greater renal definition was required, nephrotomography proved to be a simple, cost-effective addition and, when coupled with double- or high-dose infusion of contrast medium, will demonstrate 90% of the findings achieved by angiography.[5] Renal scanning is easy to carry out and is unaffected by the presence of stool, gas or contrast material from previous examinations. We found it most useful for following major injuries in clinically stable patients, especially children, as the radiation dose is lower than that of intravenous pyelography. Angiography is best reserved for patients suspected of having a pedicle injury and for those with a major injury who are in a clinically unstable state. In the latter, angiography will not only display the extent of the renal injury, but will also demonstrate associated splenic and hepatic bleeding.

Table III—Complications and Treatment (n = 11)

Complication	No.	Treatment	No.
Uncontrolled hemorrhage	7	Nephrectomy	4
		Partial nephrectomy	3
Abscess	1	Drainage	1
Urinoma	2	Drainage	2
Unremitting hematuria	1	Marsupialization of renal cyst	1

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Vesicopsoas Hitch: a Versatile Procedure

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The vesicopsoas hitch is an ideal operation for the management of lower ureteral injury and disease requiring replacement of varying lengths of ureter. It is safe and easy to perform, complications are minimal and the success rate is high. In combination with the Boari flap and downward mobilization of the kidney, up to 70% of the ureter may be replaced by this technique.

The authors describe their experience between 1970 and 1980 with 52 patients treated by the vesicopsoas hitch, with and without the Boari flap.

La cystopexie au muscle psoas est l'opération idéale pour le traitement des lésions urétérales basses et celui des maladies nécessitant le remplacement de diverses longueurs d'uretère. Elle est sûre et simple à réaliser, les complications sont minimes et le taux de réussite est élevé. En association avec le lambeau de Boari et une mobilisation du rein vers le bas, on peut remplacer par cette technique jusqu'à 70% de l'uretère.

Les auteurs décrivent leur expérience chez 52 patients qui, entre 1970 et 1980, ont été traités par cystopexie au muscle psoas, avec ou sans le lambeau de Boari.

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The vesicopsoas hitch is easily and quickly performed and is a reliable method of replacing the lower ureter in cases of ureteral injury or disease of the lower ureter. It was originally described by Whitsall in 1896[1] and was repopularized by Warwick and Worth,[1] and Gross and associates.[2] Ehrlich and associates[3] and Kishev[4] emphasized the fact that this procedure fixed a portion of the bladder wall extending the functional trigone and allowing better "backing" of ureteral implants with increased length of the tunnels to prevent reflux. They also pointed out that the fixation of the bladder base prevents angulation and kinking of the ureter with bladder filling and emptying. The combination of the psoas hitch and the Boari flap with downward mobilization of the kidney allows for replacement of up to 70% of the lower ureter. The procedure has the advantage of simplicity over transureteral ureterostomy. The other ureter is not involved in this operation thus avoiding possible compromise of the contralateral renal unit.

Between 1970 and 1980 we man-

aged 52 patients in this manner with excellent results in 55 ureters. In 44 patients the problem was unilateral and in 8 it was bilateral. This has become our procedure of choice for patients with lower ureteral disease requiring excision and replacement of varying lengths of ureter (Table I).

Table I—Indications

Indication		No. of ureters
Iatrogenic injuries		22
Gynecologic	18	
Colorectal	3	
Urologic (basket)	1	
Failed reimplantation		13
Radiation fibrosis		7
Congenital distal obstruction		7
Gross reflux		4
Endometriosis		2
Malacoplakia		2
Carcinoma of the distal ureter (solitary kidneys)		2
Tuberculosis		1

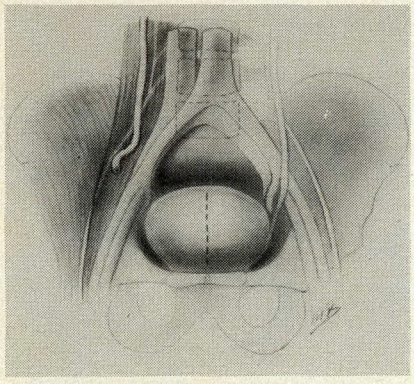

FIG. 1—Midline bladder incision.

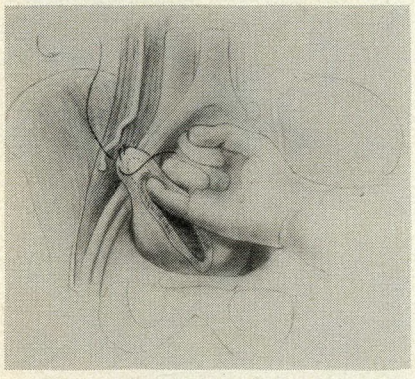

FIG. 2—Fixation of bladder to psoas with 3-0 silk sutures.

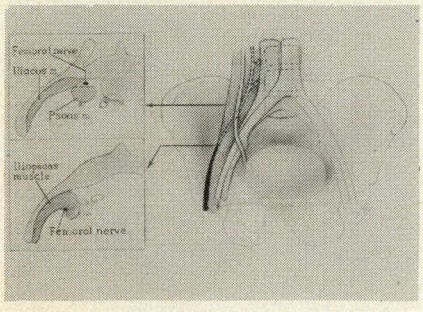

FIG. 3—Relation of femoral nerve to psoas muscle.

Technique

A Pfannenstiel incision is usually used. In cases requiring extensive replacement of the lower half of the ureter, with or without downward mobilization of the kidney, a midline incision is preferred. The bladder and ureter are approached through an extraperitoneal route. The extent of ureteral disease is assessed by mobilizing the ureter from above in the usual manner. The injured or diseased portion of the ureter is then excised (Fig. 1). A midline incision is made in the bladder and the peritoneum is dissected from the bladder dome to allow free mobility of the dome over to the psoas area. We do *not* divide the contralateral superior vesical artery and obliterated umbilical artery, as other authors have done, unless there is a need to relieve tension. The bladder floor is visualized and the opposite ureteral orifice identified. The site of the new tunnel is selected. An attempt is made to bring the ureter as close to the trigone as possible, just medial to the ipsilateral orifice. A tunnel may then be constructed after the fashion of Leadbetter–Politano or may be constructed following the fixation of the bladder. By evaginating the posterolateral angle of the bladder over the little finger (Fig. 2), the site of fixation can be selected. We use 3-0 silk sutures placed into the psoas fascia above the external iliac vessels, through the muscle of the bladder without penetrating the mucosa. It is important to bear in mind that the femoral nerve passes deep in the psoas muscle. The sutures should therefore not be placed too deeply (Fig. 3). The ureter is then placed through a submucosal tunnel in the usual manner. The submucosal tunnel and the bladder hiatus must be wide enough to prevent stenosis of the ureter (Fig. 4a). The ureter should lie in a straight tunnel from the entrance of the bladder to its exit as close to the trigone as possible. Sutures of 4-0 chromic catgut are used to anchor the distal ureter (Fig. 4b). A Silastic ureteral stent, cystostomy catheter and perivesical Penrose drains are left in situ. Firm backing for the reimplanted ureter is obtained by the use of the vesicopsoas hitch maneuver.

This procedure can be used in bilateral ureteral injuries, full mobilization of the superior vesical and obliterated umbilical arteries being mandatory. Tension at the lower end of the bladder incision may prevent adequate closure but this may be overcome by a rotation flap as illustrated in Figs. 5 and 6.

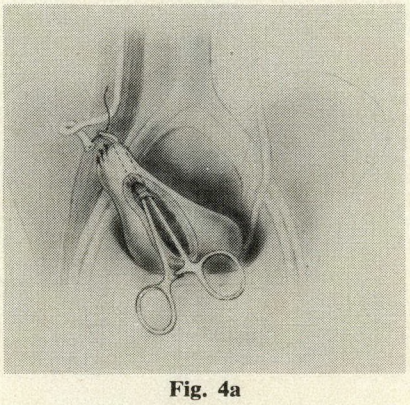

Fig. 4a

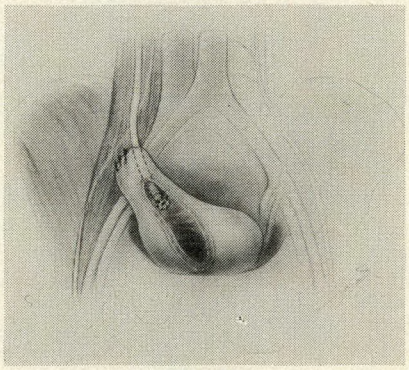

Fig. 4b

FIG. 4—Reimplantation of ureter by submucosal tunnel.

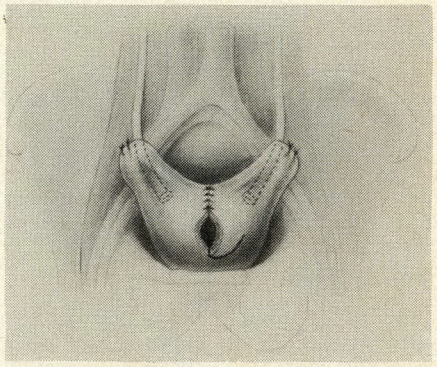

FIG. 5—Bilateral psoas hitch with relaxing incision.

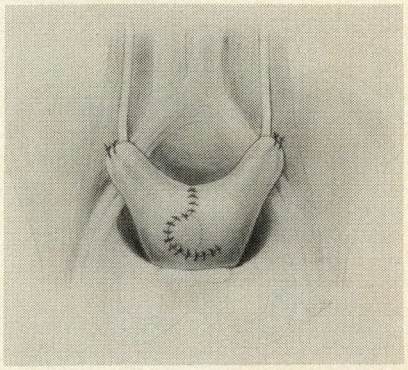

FIG. 6—Closure of bladder using relaxing incision and rotation of bladder flap.

Large dilated ureters may require trimming of varying lengths of the distal ureter. The elongation of the trigone produced by the psoas hitch procedure allows placement of the entire ureteral suture line in an intravesical position, greatly reducing the possibility of ureteral fistulas.

In patients with extensive injury or disease of the ureter, the defect may be bridged by a combination of psoas hitch and Boari flap (Fig. 7). This, combined with downward mobilization of the kidney, has allowed us to replace up to 70% of the ureter in two patients. Although it was not necessary in our cases, further downward displacement of the right kidney can be achieved with translocation of the renal vein as described by Gil-Vernet.[5] Penrose drains are placed extravesically. The bladder is closed in two layers.

Case Reports

Case 1

A 53-year-old woman, who had undergone vaginal hysterectomy for menorrhagia, presented with pain in the left flank. An intravenous pyelogram demonstrated a nonfunctioning left kidney. Retrograde pyelography revealed partial ligation of the distal left ureter (Fig. 8). Examination under anesthesia revealed a large edematous pelvic mass. The patient was managed with a ureteral catheter for 14 days and was readmitted in 4 weeks with persistent hydronephrosis. At exploration dense periureteral scar was found below the pelvic vessels. The left ureter was reimplanted using the vesicopsoas hitch procedure. Follow-up cystography and pyelography (Fig. 9) showed satisfactory drainage with no evidence of ureteral reflux as shown in a voiding cystourethrogram. The urine was sterile when the patient was discharged from hospital.

Case 2

After undergoing a difficult abdominal hysterectomy, this 57-year-old woman was noted to be anuric in the recovery room. Intravenous pyelography demonstrated bilateral delay in function, and gross hydroureteronephrosis was evident on delayed films. Immediate retrograde pyelography revealed bilateral obstruction of the lower ureters. The patient was returned to the operating room about 8 hours after her original operation. There was extensive injury to both ureters. Bilateral ureteroneocystostomies were carried out using the vesicopsoas hitch procedure. There was tension on closure of the bladder, which was relieved by use of a rotation flap. The patient had an uncomplicated postoperative course. Within 3 months the findings of intravenous pyelography and voiding cystourethrography were normal.

Case 3

A 52-year-old woman, who had renal failure due to bilateral renal obstruction secondary to malacoplakia, was managed by bilateral nephrostomy and administration of urecholine[6] for 18 months. At the time of operation her urinary creatinine value was 4.1 mg/kg daily and her creatinine clearance was 16 ml/min (Fig. 10).

She underwent a right to left transureteroureterostomy and a left vesicopsoas hitch with combined Boari flap and left ureteral reimplantation.

Internal stents were left in situ for 4 months (Fig. 11). Following removal of the stents her creatinine value increased to 8 mg/kg daily and a left nephrostomy was performed. Renal function did not improve so she was placed on maintenance hemodialysis.

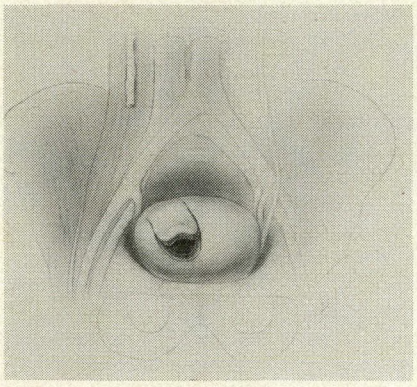

Fig. 7a

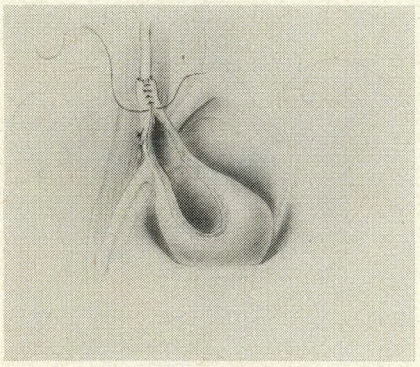

Fig. 7b

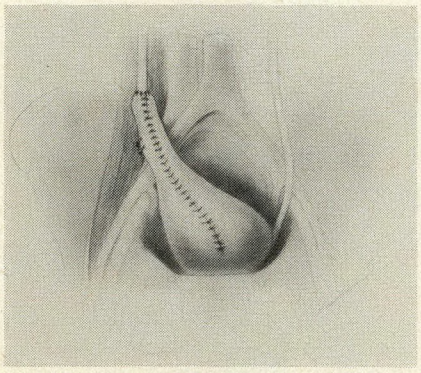

Fig. 7c

FIG. 7—Use of psoas hitch plus Boari flap technique.

Case 4

This 61-year-old man presented with right renal tuberculosis and was treated with triple-drug therapy for 2 years.

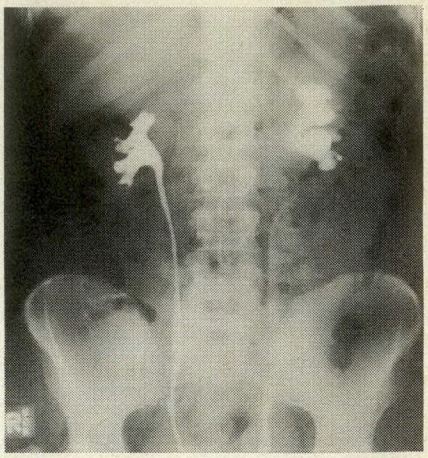

FIG. 8—Case 1. Retrograde pyelogram showing partial ligation of distal left ureter.

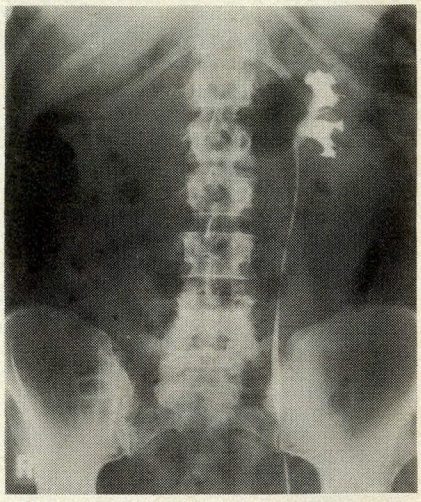

FIG. 9—Case 1. Follow-up pyelogram shows good drainage of left ureter.

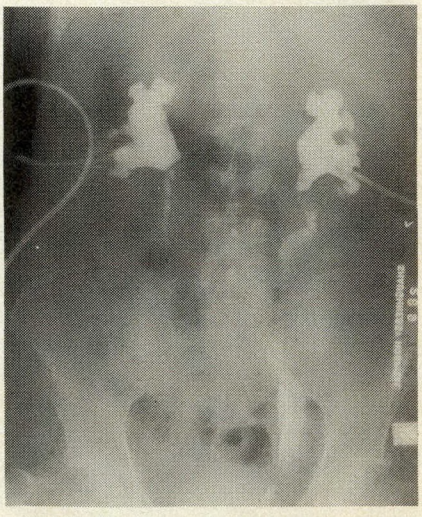

FIG. 10—Case 3. Pyelogram shows renal obstruction bilaterally due to malacoplakia.

His urine became sterile, but progressive stricture of a 4-cm segment of the lower right ureter developed with progressive hydroureteronephrosis. He underwent a right vesicopsoas hitch and reimplantation of the ureter. Three months later the ureteral calibre had returned to normal. There was no reflux on the voiding cystourethrogram. The patient continues to do well.

Case 5

Ten years after treatment for carcinoma of the cervix with radiation and radium implants, a 41-year-old woman was admitted complaining of pain in the right flank. She had progressive hydroureteronephrosis. Her ureter was reimplanted with a psoas hitch procedure. Ten days later a fistula developed. After 4 weeks of drainage right nephrectomy was necessary. At operation the lower end of the ureter was found to be necrotic. Three years later she had an ileal loop diversion for progressive hydronephrosis of the left unit and a contracted bladder due to radiation fibrosis.

Case 6

A vesicopsoas hitch was used to correct a stenotic right ureter, reimplanted because of gross reflux in a 45-year-old woman. Two days after operation she was noted to have an incomplete femoral nerve palsy. This did not respond to conservative therapy. Another operation was performed 7 days after the psoas hitch procedure and the sutures in the psoas area were removed. (It was noted at the time that she did not have a well-developed psoas tendon and consequently the sutures were placed somewhat deeper than usual into the psoas muscle.) She recovered completely over a 3-month period. Her intravenous pyelogram and voiding cystourethrogram remain normal.

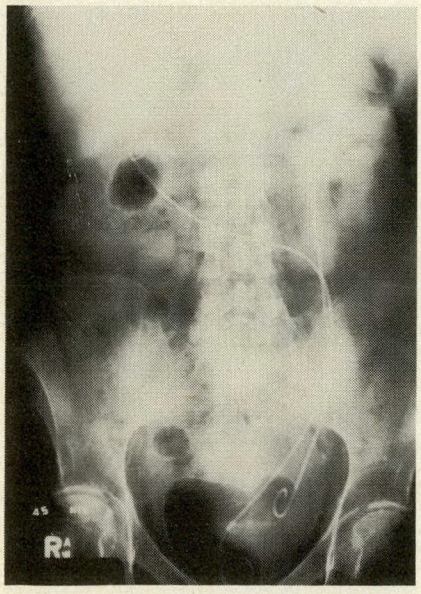

FIG. 11—Case 3. Internal stents in position after right to left transureteroureterostomy and left vesicopsoas hitch with Boari flap.

Indications

The indications for vesicopsoas hitch are noted in Table I. Iatrogenic injury was the most common indication (in 22 patients) with injury of the ureter during gynecologic procedures being the most frequent. Over the 10-year period of the study there were 14 ligated ureters and 8 ureterovaginal fistulas. These cases were referred to our hospital. Failed reimplantation was the next most common indication (13 patients).

On the basis of persistent reflux or stenosis 4 ureters (two patients) demonstrating gross ureteral reflux and 13 reimplanted ureters that had failed were reoperated on using this technique. In 16 of the 17 ureters the procedure was successful; 1 ureter exhibited minimal nonobstructing reflux.

Seven patients had combined radium implant and external irradiation to the pelvis for carcinoma of the cervix up to 14 years before the psoas hitch procedure was performed. These patients were carefully selected for the procedure on the basis of progressive hydroureteronephrosis without evidence of residual disease and minimal evidence of radiation changes in the dome of the bladder. Successful reconstruction was achieved in six of the seven patients. One (case 5) had a fistula that led to sacrifice of the right kidney. Three years later progressive radiation changes in the bladder and opposite ureter necessitated diversion to an ileal loop.

The vesicopsoas hitch was also used for seven cases of congenital distal obstruction (megaureter), two cases of endometriosis, two cases of malacoplakia, two cases of distal carcinoma of the ureter in solitary kidneys and one case with distal ureteral tuberculosis with progressive hydronephrosis.

Results

The results were generally good. The stenosis and reflux were corrected in 56 of the 60 ureters. One patient continued to have mild nonobstructive reflux. Another patient had a ureterocutaneous fistula that healed satisfactorily after placement of a ureteral stent for 3 weeks. One of the seven patients treated for the effects of radiation on the ureter lost her kidney as noted earlier. Another patient with extensive malacoplakia had renal failure despite aggressive surgery, placement of a stent and nephrostomy (the ureteral anastomoses appeared to be intact but the ureters became virtually adynamic due to progressive malacoplakia); she had to be placed on maintenance hemodialysis. One patient had a transient femoral nerve palsy caused by sutures too deeply placed in the psoas muscle, which did not have a well-developed tendon. We now avoid going deeply into the muscle and find that even without a well-developed psoas tendon, adequate attachment to muscle can be obtained with superficial stitches no deeper than 3 mm.

Discussion

The vesicopsoas hitch is useful when replacing the lower ureter in patients with a variety of lower ureteral problems. By combining it with a Boari flap and downward mobilization of the kidney, 70% of the ureter may be replaced. On the right side, by mobilizing the kidney and repositioning the renal vein caudad on the vena cava, most of the ureter may be replaced. Larger ureters requiring trimming may be brought entirely into the bladder following a psoas hitch because of elongation of the trigone; this virtually prevents the formation of ureteral fistulas.

A highly selected group of women with ureteral stricture following irradiation for carcinoma of the cervix (radium implants and external radiation) were successfully treated, using a psoas hitch, by reimplantation into tissue from the dome of the bladder, avoiding the heavily irradiated tissues at the base. Six out of seven patients treated in this manner achieved good results; one patient had a nephrectomy because of stenosis of the ureter. The vesicopsoas hitch has become our procedure of choice for dealing with lower ureteral injury or disease requiring lower ureteral resection. The procedures of transureteral ureterostomy, ureteral replacement with ileum and autotransplantation are rarely needed.

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Intravesical Therapy with Adriamycin in Urothelial Dysplasia and Early Carcinoma in Situ

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The authors studied the effect of instilling Adriamycin intravesically in 21 patients with urothelial dysplasia and early carcinoma in situ. The effectiveness of the treatment was assessed by repeated urine cytology, cystoscopy and repeated biopsy of the bladder mucosa. No serious side effects were noted.

Adriamycin causes the death of malignant cells, general improvement in the appearance of the bladder mucosa at cystoscopy and histologic evidence of endothelial damage to the bladder mucosa. The cytologic changes continue for many months after treatment.

Les auteurs ont étudié les effets de l'instillation intravésicale d'Adriamycine chez 21 patients atteints de dysplasie urothéliale et d'un cancer pré-invasif précoce. L'efficacité du traitement a été mesurée par cytologies urinaires répétées, cystoscopie et biopsies répétées de la muqueuse vésicale. Aucun effet secondaire sérieux n'a été observé.

L'Adriamycine a entraîné la mort des cellules malignes, une amélioration générale de l'apparence de la muqueuse vésicale à la cystoscopie et des signes histologiques de dommages à l'endothélium de la muqueuse vésicale. Ces changements cytologiques persistent plusieurs mois après le traitement.

Over the past 20 years much attention has been focused on the extent and behaviour of precancerous intraepithelial lesions such as carcinoma in situ of the bladder. This lesion consists of a flat area of epithelium with cells that have anaplastic features and a disordered pattern of growth.[1-8] Acceptance of this condition as a precancerous state has become more widespread and there now seems little doubt that this is an early phase in the evolution of bladder cancer.

For 12 years we have worked in a region where bladder cancer is common, because many people working in the chemical industry were exposed in the past to carcinogens during the manufacture of α- and β-naphthylamine, magenta, auramine and benzidine. Because there may be a 20- to 30-year latent period before bladder cancer develops, a widespread cytologic screening program has been instituted, resulting in the early detection of atypical cells in the urine. The term "urothelial dysplasia" refers to the dysplastic changes seen in a biopsy specimen of the bladder mucosa in the presence of an apparently normal bladder, or one showing only minimal reddening or slight swelling of the mucosa at cystoscopy but with abnormal urine cytology, suggesting a premalignant or malignant change. Primary carcinoma in situ is comparatively uncommon and cystoscopic examination of patients with bladder tumours often reveals other areas of slightly abnormal mucosa that show signs of carcinoma in situ in biopsy specimens; this has been termed secondary carcinoma in situ.

Patients and Methods

At the Royal Infirmary in Huddersfield, between February 1980 and May 1981, 34 patients with precancerous lesions of the bladder were given Adriamycin intravesically; but only 21, followed up for 9 months or more, are presented here. All 21 patients were men. They were classified into three groups (Table I).

Because of exposure of the study population to industrial carcinogens, specific enquiry was made into each patient's occupational background (Table II). In all patients a complete blood count was done and serum electrolyte levels were measured. Intravenous pyelography, urine culture and cytologic examination of the urine were carried out. Cystoscopy was then performed under general anesthesia and multiple biopsies of the bladder mucosa were done. Only patients with histologic evidence of urothelial dysplasia or carcinoma in situ and malignant cells in the urine were entered into the study. All urine specimens were graded cytologically using the Papanicolaou technique.

Informed consent was obtained from all patients. They were treated on an out-patient basis. The bladder was emptied by a small urethral catheter and 50 mg of Adriamycin dissolved in 50 ml of sterile saline was introduced into the bladder and the catheter withdrawn. The patient was placed in a different position (e.g., left lateral, head down, prone) every 20 minutes and after 2 hours was allowed to empty the bladder. The patients were not

Table II—Occupation of the 21 Patients

Occupation	No. of patients
Chemical workers*	9
Furnace workers*	3
Woodworkers	2
Rubber processor*	1
Dyehouse foreman	1
Asphalt worker*	1
Electrician	1
Hairdresser	1
Coal miner	1
Textile worker*	1

*Probable exposure to industrial carcinogens.

Table I—Patient Groups

Group	Description	No. of patients
	Primary tumour	
1	Dysplasia/carcinoma in situ	6
	Secondary tumour	
2	Previous T_1 tumour + carcinoma in situ	7
3	Papillary T_1 tumour + carcinoma in situ	8
Total		21

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dehydrated but were asked not to drink excessively for several hours before treatment. The procedure was repeated at weekly intervals for 6 weeks, so that a total of 300 mg of Adriamycin was given to each patient. The first 12 patients had the bladder filled with normal saline to assess the size of the bladder and to note any changes in the cytologic findings caused by the introduction of saline; none were found.

Assessment of Adriamycin Therapy

The effectiveness of Adriamycin therapy was assessed in three ways: (a) Early morning urine specimens were examined cytologically before treatment, after three and after six instillations of Adriamycin, after 1, 2 and 3 months, and thereafter at 3-month intervals. (b) Cystoscopic examinations were made every 3 months. (c) Serial biopsy specimens of the bladder mucosa were examined.

Cytologic Assessment

There is ample evidence that intravesically administered Adriamycin damages and kills malignant cells. Cytologic examination of the urine shows many grossly enlarged cells with disruption of the nuclear membrane and fragmentation of the nucleus. The cytoplasm becomes ragged and vacuolated; phagocytosis is often seen and large pink inclusions are a consistent finding; eventually the cells become anucleate. After two instillations of Adriamycin and for many months after treatment has ended large numbers of degenerated cells can be seen in the urine, suggesting that the changes caused by Adriamycin therapy are progressive.

Attempts were made to quantify the number of cells being exfoliated but this number is variable and the procedure was not practical. In the first few weeks, large degenerate malignant cells were predominant in the urine but eventually the cells became smaller and it became apparent that these were basal cells from the deeper layers of the mucosa.

Results

Cytologic Response

The initial assessment of the course of treatment was made 1 month after the last Adriamycin treatment (Table III). In 17 of 21 patients the tumour had regressed at 1 month, and in 12 of them the cells became benign; in the other 4, although damaged malignant cells were found, the cytologic grading did not appreciably alter and these patients were classified as showing no change. At 3 months, 15 continued to improve but in 2 patients the lesion became more malignant and carcinoma in situ was shown to have progressed to invasive carcinoma. In retrospect, on reviewing the original biopsy, one of these patients should not have been included in the trial, since the lamina propia had already been invaded by malignant cells before he received any treatment. In three other men, at 6 months, the cytologic pattern, which had initially improved in two and was unchanged in one, showed signs of deterioration and, in each case, this was associated with the development of a papillary tumour.

The overall cytologic response was that of marked damage to malignant cells in 20 of 21 patients. In 12 the cells reverted to a benign form; in the other 8, marked cellular damage was shown, which, in some cases, continued for many months. In these patients the Adriamycin therapy should have been continued because the dose of Adriamycin was probably not large enough to kill all the malignant cells. Further treatment has been instituted in these patients.

Table III—Cytologic Assessment

Cytologic findings	Group, no. of patients 1 (n = 6)	2 (n = 7)	3 (n = 8)	Total
At 1 mo				
Regression	4	6	7	17
No change	2	1	1	4
Progression	0	0	0	0
At 3 mo				
Regression	4	4	7	15
No change	1	3	0	4
Progression	1	0	1	2
At 6 mo				
Regression	5	5	6	16
No change	0	2	0	2
Progression	1	0	2	3

Cystoscopic Response

In three patients, bladders that appeared normal before treatment continued to have a normal appearance. The bladders of 17 others were greatly improved as shown by the marked reduction in the reddened areas of mucosa noted before treatment. In only one man did the carcinoma in situ become worse cystoscopically; this was the patient who probably had an invasive carcinoma before he received any treatment. New tumours developed in six patients; five tumours were small, superficial transitional cell carcinomas, which gave the bladder an unhealthy friable appearance, and one was a squamous cell carcinoma.

Histologic Changes

Repeated mucosal biopsy specimens showed marked surface damage to the bladder epithelium following the instillation of Adriamycin. The degree of this damage is probably related to the total dose of drug used.

Adriamycin causes localized necrosis and mucosal ulceration of the superficial layers of the bladder mucosa and this is associated with obvious cystoscopic improvement and marked alteration in the exfoliative cytology. We have noticed that some patients who had histologic changes of carcinoma in situ in the Brunn's nests and crypts of the bladder mucosa required a longer course of Adriamycin before any cytologic changes were observed.

Side-Effects

Repeated complete blood counts and serum electrolyte determinations confirmed the earlier observations of Edsmyr and colleagues,[9] that intravesical instillation of Adriamycin does not cause any important systemic upsets. In 136 catheterizations for the instillation of Adriamycin, only three urinary infections were noted; in two, the patient had a long history of urinary infection. One patient had dysuria without evidence of infection and three had minimal hematuria which cleared up within 24 hours. Only 1 patient had the signs and symptoms of irritative cystitis, but in 12 other patients not reported in this series, 3 had evidence of quite severe spasm brought on by the introduction of Adriamycin into the bladder; in 2 of these the treatment had to be stopped after four instillations.

Discussion and Conclusions

Repeated cystoscopic examination in the follow-up of patients with bladder cancer may reveal no evidence of

active tumour but may reveal mucosal abnormalities that, histologically, are precancerous. In such cases it is reasonable to assume that these abnormal areas are new tumours in the early stages of development. The importance of these findings has been emphasized by Weinstein and associates[10] and by Farrow and associates,[11] who stated that in patients with extensive carcinoma in situ but with no previous history of a bladder tumour, the probability of finding a focus of microinvasive carcinoma at cystectomy is approximately 20%. According to Daly,[12] in a patient with a previously resected bladder carcinoma and the finding of a carcinoma in situ, the likelihood of an invasive tumour developing is 42% and when the in-situ changes are in close proximity to a low-grade carcinoma the likelihood is 83%.[13] The clinical progression of bladder carcinoma from its premalignant state is variable and it is difficult to know how best to treat this condition. We have found that the response to radiotherapy varies. In the opinion of De Voogt[14] the prognosis of carcinoma in situ is so poor that patients with this condition should be treated by total cystectomy. This is a radical form of therapy for a disease that may take years to develop; therefore, it is reasonable to treat carcinoma in situ, particularly if an early diagnosis is made, by intravesical chemotherapy.

As a result of treating 21 patients, who had either malignant urothelial dysplasia or carcinoma in situ, with Adriamycin instilled intravesically we found that (a) Adriamycin caused the death of malignant cells, (b) reddened areas of bladder mucosa disappeared in 17 of 18 bladders, (c) histologic evidence of endothelial change was shown, (d) cytologic changes occurred after two treaments but may occur after many months, (e) new tumours developed in 6 patients and (f) there were minimal side-effects.

There seems little doubt that Adriamycin given intravesically is effective in treating carcinoma in situ. In patients treated early in this series the improvement has been maintained for up to 1 year. This agrees with the observations of Edsmyr and colleagues[9] and Eposti and colleagues,[15] although Jakse and Hofstadter[16] found a good response in only three of six patients. It is reasonable to continue this form of treatment and to obtain a much longer follow-up before reaching any final conclusions. Previous experience with other agents administered intravesically, such as thiotepa, cyclophosphamide, Epipodophyllotoxin VM 26 and Epodyl, leads us to believe that Adriamycin is superior to other drugs in treating carcinoma in situ. Some patients may require treatment for a longer period than we used. This could be explained by the histologic changes that occurred in the Brunn's nests and crypts of the bladder mucosa. Nevertheless the preliminary results of this trial suggest that many patients show substantial regression of the premalignant condition at cystoscopy and as judged by serial urine cytologic examinations and may be improved even more by treatment for a longer period.

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Vasoepididymostomy: the Role of the Microscope

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Reconstructive surgery of the epididymis has been facilitated by the use of the microscope. The author describes his technique for end-to-end and end-to-side anastomoses and reports the results of reconstruction in 23 patients over a 10-year period. The pregnancy rate following reconstructive surgery was 39% overall: 40% after vasoepididymostomy (performed in 10 patients) and 35% after repair of primary epididymal obstruction (performed in 13 patients). With the aid of the microscope end-to-side and end-to-end anastomoses between the vas deferens and epididymis can be performed with greater precision because the anatomy can be defined precisely and reconstruction planned better.

La chirurgie reconstructive de l'épididyme a été facilitée par l'emploi du microscope. L'auteur décrit la technique qu'il utilise pour les anastomoses termino-terminales et termino-latérales et il rapporte ses résultats de reconstruction chez 33 patients au cours d'une période de 10 ans. Globalement, le taux de grossesse consécutif à la chirurgie reconstructive a été de 39%: 40% consécutif à la vasoépididymostomie (chez 10 sujets) et 35% consécutif à la réparation de l'obstruction primaire de l'épididyme (chez 13 sujets). A l'aide du microscope, les anastomoses termino-terminales et termino-latérales entre le vas deferens et l'épididyme peuvent être pratiquées avec une plus grande précision car l'anatomie peut être définie avec précision et la reconstruction mieux planifiée.

Since Martin first described vasoepididymostomy in 1902,[1] the surgical technique has continued to improve and, recently, with the introduction of microsurgical techniques, has become more sophisticated. Reports by Hagner in 1936,[2] Humphreys and Hotchkiss in 1939,[3] Phadke in 1956[4] and Dubin and Amelar in 1977[5] have popularized the use of the macroscopic technique. We report our experience with the microscopic technique.

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Patients, Method and Results

Between 1977 and 1979, 100 vasectomy reversal operations were performed at the University of British Columbia. Ten of the patients required vasoepididymostomy for reconstruction. During this time 13 patients had primary epididymal blockage. All patients underwent vasoepididymostomy with microscopic control.

In the 10 patients who required vasoepididymostomy, 8 had a primary end-to-end anastomosis and 2 had an end-to-side anastomosis. Four pregnancies (40%) resulted in this group. Of the 13 patients who had primary epididymal obstruction, 11 had end-to-end anastomosis and 2 had end-to-side anastomosis. Five pregnancies (35%) resulted.

Development of Technique

The surgical treatment is divided into two categories, the end-to-side and the end-to-end techniques. Both utilize the microscope since it facilitates direct mucosal approximation and anatomical reconstruction of the tubule. Exploration of the scrotum is similar in both techniques, which differ only in the type of anastomosis used.

Under general anesthesia, we explore the scrotum to define the abnormality and decide on the reconstructive technique to be used. The incision is generous enough that the testes may be delivered into the wound to define the epididymal abnormality. The vas deferens is identified and traced to its junction with the epididymis. A tense and turgid epididymis with tortuous tubules visible under the epididymal serosa is suggestive of obstruction to epididymal outflow. Blue zones or white sclerotic tissue found in the epididymis indicates severe, long-standing obstruction, which is often seen in primary epididymal obstruction; in this type, inspissated material is often found in the tubules. The inspissated material does not allow teasing out of the tubules and therefore end-to-side anastomosis is preferable. Identification and preservation of the vessels to the vas deferens and epididymis are important as injury will result in a scarred and compromised anastomosis. The vas deferens is then mobilized to provide a tension-free vasoepididymal anastomosis. A 1-cm longitudinal incision is made as distal as possible in the epididymis but proximal to any obvious site of obstruction (Fig. 1). The epididymal ducts are then squeezed and opened to look for milky fluid that may extrude from the lumen. If the material is inspissated or if sclerotic areas are seen, an end-to-side anastomosis is performed. If the fluid from the tubules is liquid and the tubules can be separated, then a primary end-to-end anastomosis is carried out. The material from the cut end of the epididymis is placed on a glass slide and examined for live motile sperm. If none are found, a more proximal incision is made in the epididymis to search for live sperm. We make the initial incision in the epididymis as distal as possible because this will allow a longer transit time for the sperm and thus may provide better sperm maturation and fertility. A suitable site in the

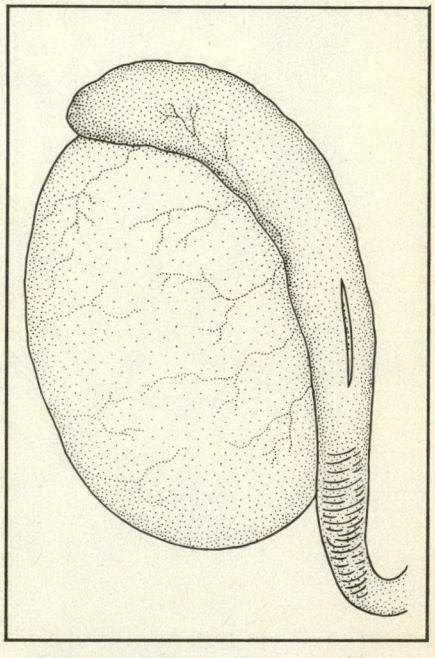

FIG. 1—Incision into epididymis proximal to obstruction in tail.

vas is then selected and the patency checked by injecting saline proximally. We then join either an end of the vas deferens to the side of the epididymis or make an end-to-end anastomosis. Up to this point, the preparation of the epididymis and vas has been performed macroscopically. The microscope is used for the anastomosis.

In the end-to-side anastomosis, the distal end of the vas deferens is spatulated and anastomosed to an elliptical incision in the epididymis using 6× to 10× magnification (Fig. 2). The anastomosis is carried out with 8-0 Dexon. We use a modified suction apparatus consisting of a tuberculin syringe attached to a no. 20 blunt needle and copious irrigation. After placement of the two corner sutures, the individual sutures are placed full thickness. With rotation of the epididymis, we can then suture the posterior wall.

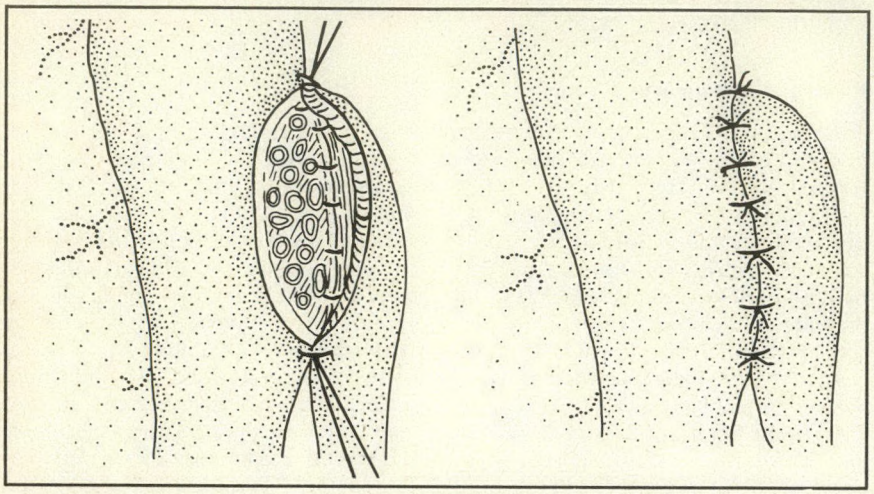

FIG. 2—End-to-side anastomosis performed in area where viable sperm are found in fluid from epididymis.

Usually, when we reverse a previous vasectomy that requires epididymal reconstruction, end-to-end anastomosis is superior. After making the incision in the epididymis and checking the fluid for sperm, we use the microscope to identify the epididymal ductule that leads proximally. With 16× to 25× magnification, we can tease out the cut ends of the epididymis and finally the epididymal ductule and dilate the lumen with no. 5 jewellers' forceps. The lumen of the vas deferens is also dilated. We can then place four sutures between the dilated ductule and the mucosa above the vas deferens (Fig. 3), using 8-0 Dexon or 9-0 monofilament nylon. These sutures are mucosa to mucosa, but in the vas deferens they incorporate some submucosa. After completion of the mucosal sutures, a second row of serosal sutures of 8-0 Dexon is placed approximating the muscular wall of the vas deferens to the serosal wall of the epididymis.

After these anastomoses have been completed the testis is placed back in the scrotum and the dartos muscle is closed with 2-0 chromic catgut. The skin is closed with 4-0 Dexon and a pressure dressing is applied for 24 hours.

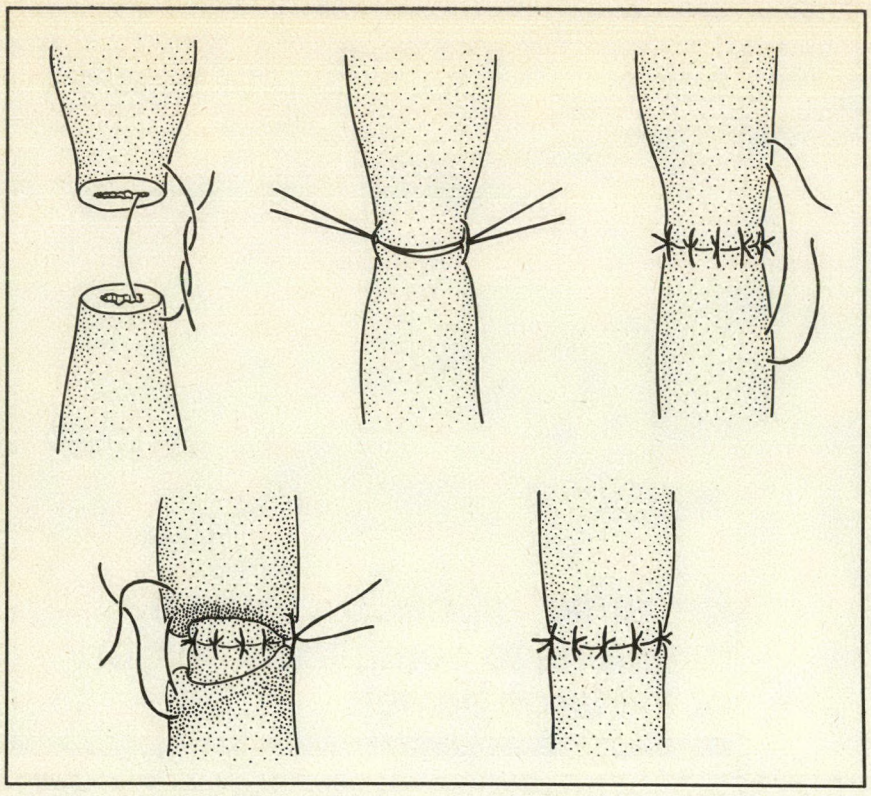

FIG. 3—End-to-end anastomosis between dilated end of epididymal duct and lumen of vas deferens.

Discussion

Patients with epididymal obstruction may benefit from vasoepididymostomy. In patients presenting with primary epididymal obstruction, Hanley and Hodges[6] found a 50% incidence of obstructive congenital anomalies in the epididymis on microdissection. Many patients had multiple obstructions. The most common anomaly seen was macroscopic — the normal head of the epididymis faded into a poorly developed body or tail. With the microscope we can define the anatomy and therefore plan reconstructive surgery with more precision.

Epididymal obstruction secondary to vasectomy is usually not recognized until exploration has been carried out for reversal of the vasectomy. We now perform vasoepididymostomy if, on exploration, the cut end of the testicular side of the vas does not show any dilatation of the lumen, if no sperm are found in this lumen and if the vasectomy has involved the junction of the epididymis and the vas deferens, resulting in the possible removal of a segment of the epididymis. These patients undergo epididymal exploration to find a region in the epididymis, most preferably in the tail, where the lumen is adequate and there are viable motile sperm in the fluid. This condition often lends itself best to an end-to-end anastomosis. The microscope is invaluable to the surgeon who must perform reconstructive surgery of the epididymis. It facilitates accurate suture placement and allows the surgeon to perform the end-to-end or the end-to-side anastomosis with good mucosa to mucosa apposition. This will decrease the likelihood of anastomotic leaks and scar formation and stenosis.

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NOTICES

Pan-Pacific International Symposium on Biomaterials

The Japanese and Canadian societies for biomaterials invite participation in a joint conference session to be held at the University of British Columbia, Vancouver, July 28-30, 1982. Invited are papers on orthopedic, cardiovascular and dental materials and tissue mechanics. All papers must be received by Apr. 2, 1982. Commercial exhibitors and sponsors are welcome to take a complimentary role in the conference; exhibit space is available. Further information can be obtained from: Dr. R.H. Roydhouse, Conference chairman, Secretariat Biomaterials '82, #1704, 1200 Alberni St., Vancouver, BC V6E 1A6.

Clinical Application of Hyperbaric Oxygen

The 7th Annual Conference on the Clinical Application of Hyperbaric Oxygen is scheduled for June 9 to 11, 1982 at the Disneyland Hotel in Anaheim, California. Included in the conference will be plenary sessions on the use of hyperbaric oxygen in neurologic disorders and anaerobic infections. Original papers will be presented and there will be workshops and exhibits. For more information, write: Baromedical department, Memorial Hospital Medical Center, 2801 Atlantic Ave., Long Beach, CA 90801-1428, or call (213) 595-3613.

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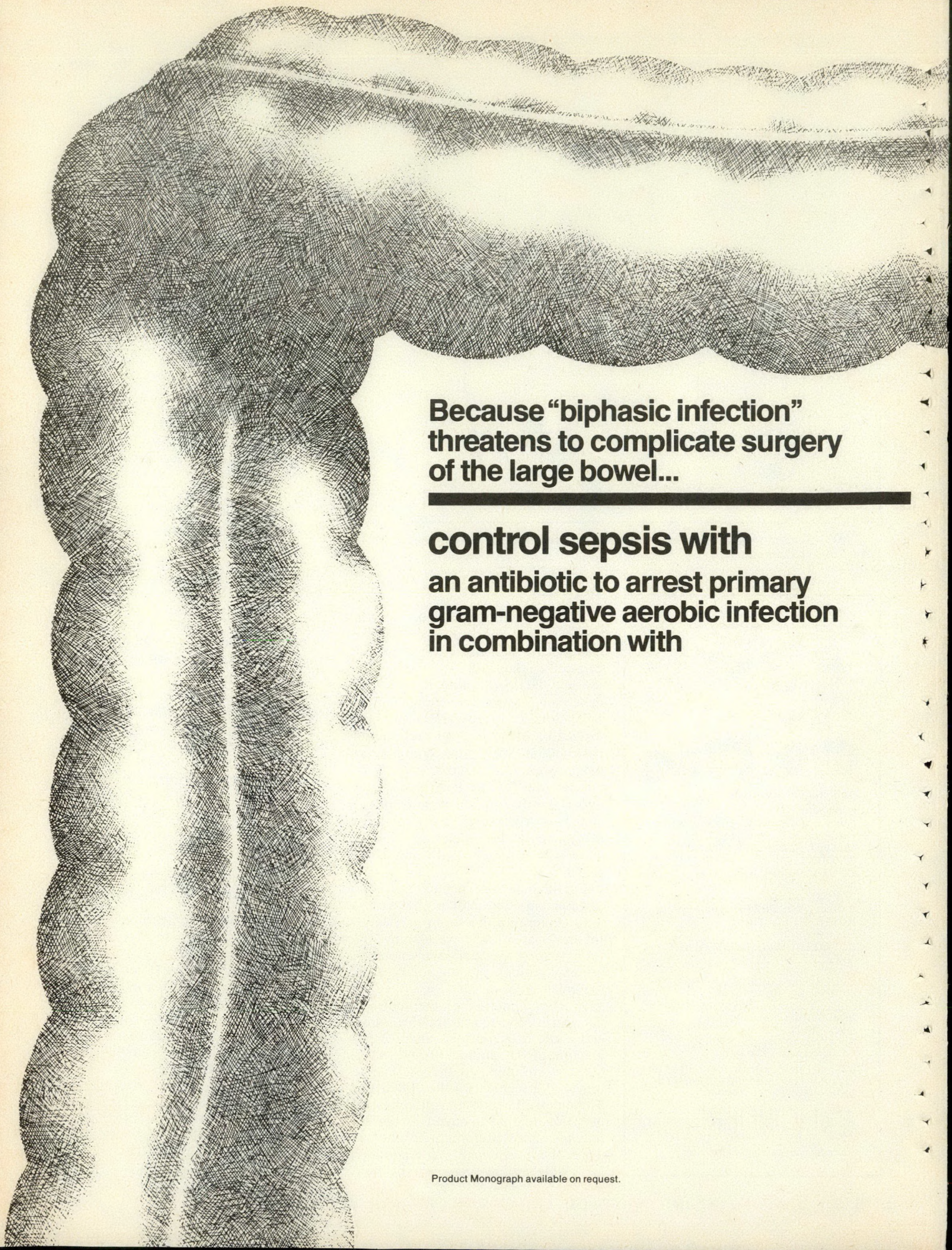

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Intermittent Percutaneous Infusion into the Hepatic Artery of Cytotoxic Drugs for Hepatic Tumours

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R. BUGALA, C. GOLLISH, RN AND P. KALMAN, MD

Between June 1, 1976 and Apr. 30, 1981, 157 patients were treated for inoperable cancer of the liver by intermittent percutaneous infusion of chemotherapeutic agents into the hepatic artery. The majority of these patients had metastatic colorectal cancer. The regimen of chemotherapeutic infusion evolved during the study and is described. The survival of the total group of patients is analysed according to type of cancer, extent of disease, dosage and combination of drugs. This therapeutic modality appears to benefit patients with metastases from colorectal cancer confined to the liver. The complication rate for this procedure is relatively low. The results from this study suggest that intermittent percutaneous infusion of cytotoxic agents into the hepatic artery is worthwhile for selected patients and should be studied further in combination with other forms of therapy.

Entre le 1er juin 1976 et le 30 avril 1981, 157 malades ont été traités pour un cancer inopérable du foie par perfusion percutanée intermittente d'agents chimiothérapeutiques dans l'artère hépatique. La majorité de ces patients souffraient de cancer métastatique du côlon ou du rectum. Le régime chimiothérapeutique qui a évolué durant l'étude est décrit. On a analysé la survie du groupe de malades selon le type de cancer, l'étendue de la maladie, la dose et l'association de médicaments. Ce régime thérapeutique semble profiter aux patients atteints de métastases confinées au foie d'un cancer du côlon ou du rectum. Le taux de complications rattaché à cette procédure est relativement bas. Les résultats de cette étude indiquent que la perfusion percutanée intermittente d'agents cytotoxiques dans l'artère hépatique est utile pour les cas choisis et que l'étude de ce régime thérapeutique mérite d'être poursuivie en association avec d'autres formes de traitement.

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The prognosis of neoplastic disease of the liver, primary or metastatic, remains poor.[1] Current methods of treatment are unsatisfactory. The use of standard systemic chemotherapy with 5-fluorouracil (5-FU) has resulted in a response in 10% to 20% of patients, with a median duration of 3 to 5 months, but improvement in survival has been minimal.[2,3]

The rationale for infusing cytotoxic drugs via the hepatic artery is that it will give a much higher concentration of drug in the tumour, compared with the surrounding normal hepatic tissue, for a longer time.[4,5] This route of administration will allow concentrations of drug to be administered that would be lethal if given systemically.[6] The techniques for regionalized chemotherapy to the liver include infusion via the hepatic artery alone,[7,8] in combination with hepatic artery occlusion[9] or in combination with radiotherapy.[10]

Although the success of this therapeutic approach has varied over the last 15 years, a number of encouraging studies have reported response rates of 30% to 60%, with slightly longer survival and improved quality of life.[7-9,11]

Patients

From June 1, 1976 to Apr. 30, 1981, 157 patients with primary or secondary hepatic tumours received chemotherapy by intermittent percutaneous infusion into the hepatic artery. Nine patients died within the first month of therapy (Table I) and were excluded from further analysis. All patients had unresectable tumours. There were 94 men and 54 women

Table I—Cause of Death in First Month

Cause	No. of patients
Sepsis	
Catheter-related	2
Other	1
Liver failure	1
Disseminated tumour	5

ranging in age from 20 to 77 years. The majority had carcinoma metastatic to the liver; the site of the primary tumour was colorectal in 98 (66%), gastric in 7 (5%), breast in 6 (4%), pancreatic in 6 (4%) and at other sites in 10 (7%). The primary hepatic tumours were hepatocellular carcinoma in 14 (9%) and cholangiocarcinoma in 7 (5%).

Methods

After initial assessment a percutaneous transfemoral catheter was placed in the common hepatic artery, except in those patients in whom the bulk of the tumour in the right hepatic lobe was supplied by a right hepatic artery arising from the superior mesenteric artery. In these patients the catheter was placed in the aberrant right hepatic artery.

Cytotoxic drugs were infused at a constant rate with an IMED pump (IMED Canada, Streetsville, Ont.). Patients were kept on strict bed rest for the duration of the infusion and for 12 hours following removal of the catheter; then they were discharged.

The choice of cytotoxic drugs and regimen used for the patients with liver metastases from gastrointestinal malignant tumours (colorectal, gastric and pancreatic carcinoma) and breast cancer evolved during the study. Initially, 5-FU was infused at 1 to 2 g/d for 3 to 7 days. In the last 3 years, 7.5 to 12 g were infused over 3 to 5 days. At the conclusion of the latter regimen, one group of patients received mitomycin C (5 to 10 mg) as an intra-arterial bolus over a 10-minute period.

The cytotoxic drugs given to the patients with hepatoma were 5-FU and Adriamycin; patients with melanoma received dacarbazine (DTIC) and melphalan, and those with sarcoma received Adriamycin and actinomycin D. Six of the 148 patients received cytotoxic drugs other than 5-FU.

Each patient was readmitted at 4- to 8-week intervals for reinfusion if the leukocyte and platelet counts allowed. Patients with extrahepatic neoplastic disease were treated with drugs systemically in addition to hepatic artery infusion. All patients remained on the intermittent infusion regimen which was discontinued if the hepatic artery became occluded, if the tumour enlarged rapidly despite the infusion, if the blood counts became too low or if the patient could not tolerate the 3 to 5 days of bed rest.

Results

The 157 patients in the group were infused 338 times. Most received 3 to 6 infusions (range from 1 to 18). The nine patients who died within the first month either were severely cachectic or had widespread metastatic disease before hepatic artery infusion was begun. In most, death was not directly attributable to the infusion.

The life-survival curves are shown in Fig. 1. The median survival time was 11.5 months and the 1- and 2-year survival rates were 44% and 12% respectively.

Of the 157 patients, 148 had metastatic tumour; 110 had hepatic metastases only and the other 38 also had major systemic metastases. The 1- and 2-year survival rates of the patients with hepatic metastases only were 50% and 19% respectively compared with 31% and 7% for those with systemic metastases also (Fig. 2). The 98 patients with colorectal carcinoma were similarly analysed. The 1- and 2-year survival rates of those with metastases to the liver only were 60% and 17% respectively compared with 32% and 5% for patients with metastases to other sites in addition to the liver (Fig. 3).

The results in the 98 patients with colorectal carcinoma were analysed to determine if mitomycin C therapy had any additional effect (Fig. 4). The 1- and 2-year survival rates for the 52 patients receiving 5-FU only were 52% and 15% respectively compared with 52% and 8% for the 46 patients receiving 5-FU and mitomycin C.

Thirty-nine patients received low-dose 5-FU (7.5 g total per infusion); the 1- and 2-year survival rates were 38% and 18% respectively. This compares with 49% and 11% for 103 patients receiving more than 7.5 g of 5-FU per infusion (Fig. 5).

Complications

There were 23 complications during the 338 catheter placements and infusions (Table II). Two patients died of clostridial infection that developed during the infusion. Currently, our protocol includes intravenous admin-

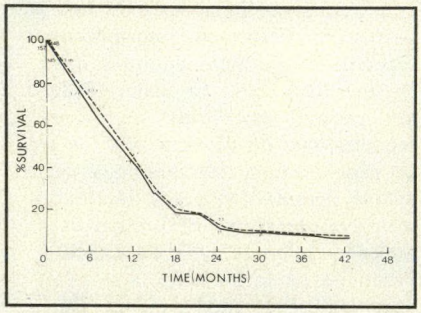

FIG. 1—Life-survival curves for total patient population (157) (dotted line) and for those who survived first month of infusion (148) (solid line), calculated from date of first infusion.

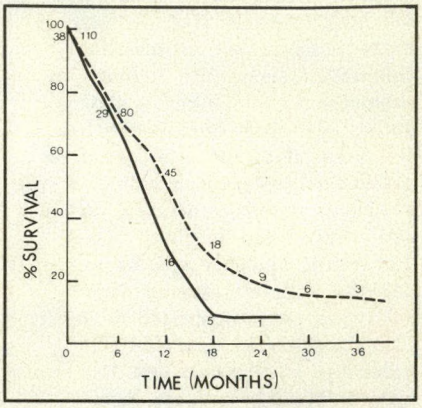

FIG. 2—Life-survival curves for patients with metastases confined to liver (dotted line) and for those with additional systemic metastases (solid line).

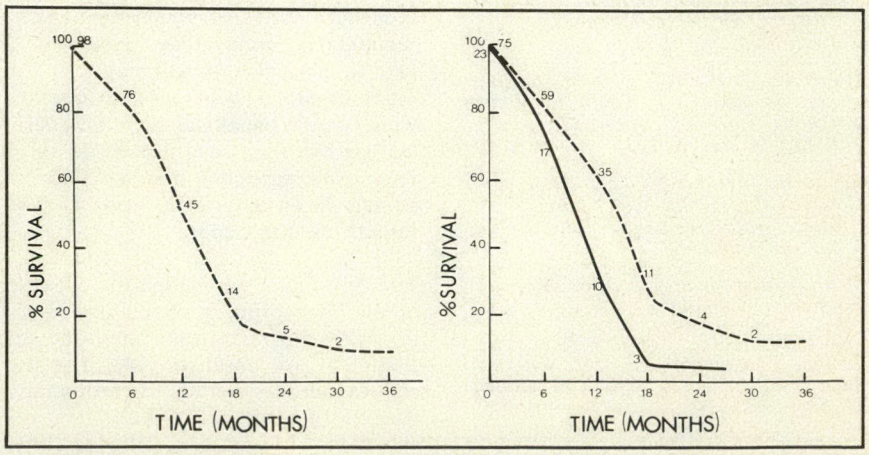

FIG. 3—Left: life-survival curve for all patients with colorectal carcinoma. Right: curves for patients with colorectal carcinoma with metastases confined to liver (dotted line) and for those with additional systemic metastases (solid line).

istration of antibiotics whenever the temperature rises above 38°C, after blood samples have been cultured, and this has avoided repetition of that complication.

Injury to the hepatic artery occurred in 13 patients. Occlusion was demonstrated subsequently in two patients by arteriography; recannulation in both cases allowed resumption of the infusion. The development of a hepatic artery aneurysm in one patient forced us to stop the infusion.

Dislodgement of the catheter was suspected whenever a patient had acute nausea, vomiting or upper abdominal pain. When these symptoms occurred, the infusion was temporarily stopped and the catheter position checked by angiography and corrected when necessary.

Discussion

Current therapy and survival figures for primary and metastatic neoplasms involving the liver are unsatisfactory. The mean survival time quoted in the literature for systemic therapy or treatment by infusion of cytotoxic drugs continues to be 6 to 9 months depending on the series of patients studied.[7,8,11,12] Moreover, there is a substantial number of complications for the various methods of infusional treatment and for systemic drugs when used alone. The long-term survival is limited.

The present series is noteworthy for several reasons. First, the complication rate related to intermittent catheter placement is low. In contrast to a previously reported series,[13] thrombosis of the hepatic artery occurred in only 10 patients. These patients did not survive longer than the others in this group, as has been previously reported;[9] however, the number of patients in this series who had thrombosis of the hepatic artery may be too small to draw such conclusions. Second, our median survival rate for the entire group of patients is slightly beter than what is reported in the literature. Third, the quality of life in the survivors was better because the therapy, which is always toxic to a variable extent, is administered intermittently for short periods. Fourth, it is apparent that when this form of therapy is used, patients whose disease is limited to the liver have an improved survival rate. The survival rate is the same or slightly better when a larger dose of drug is administered over a shorter period. Since this is not associated with any notable increase in side-effects, giving a larger dose of 5-FU shortens hospital stay and the period of bed rest. This period is further shortened bv giving a bolus infusion of mitomycin C at the end of the 5-FU infusion. Thus, patients can be treated at 4- to 8-weekly intervals for 72 hours with no intervening therapy if their disease is limited to the liver.

Patients with advanced, widespread tumour and those with severe liver dysfunction from tumour invasion are not candidates for hepatic artery infusion as shown by the nine deaths that occurred in the first month.

Patients with colorectal disease metastatic to the liver alone, survived longer than 1 year. It is these patients who are of greatest interest relative to the present therapeutic regimen. It is suggested that because this subgroup of patients appears to be surviving substantially longer and because the method is safe, this approach be continued and perhaps combined with regional hyperthermia,[14] limiting the therapy to those patients who have hepatic involvement only. This does not exclude its use occasionally for patients with systemic metastases. The extrahepatic metastases may respond to appropriate systemic cytotoxic therapy while those in the liver fail to regress. In such a situation the use of infusional therapy for the hepatic disease can be worthwhile. We have noted this in a number of patients with metastases from carcinoma of the breast, but the experience is limited to these patients. In this small group an 80% remission rate has been observed. But systemic therapy adequate to prevent progression of the disease in the majority of these patients has not yet evolved.

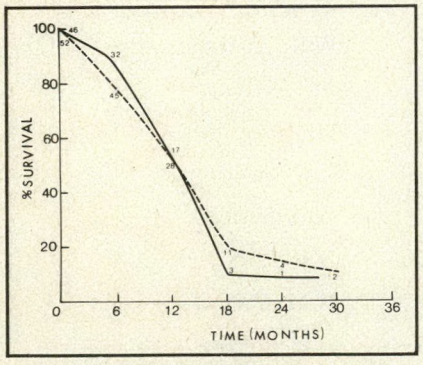

FIG. 4—Life-survival curves for patients with colorectal carcinoma who received hepatic infusion with 5-fluorouracil (5-FU) alone (dotted line) and for patients who received hepatic infusion with 5-FU and mitomycin C (solid line).

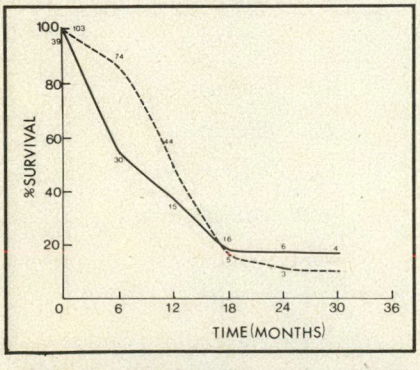

FIG. 5—Life-survival curves comparing low-dose (less than 7.5 g, solid line) and high-dose (more than 7.5 g, dotted line) 5-FU hepatic artery infusion for 142 patients.

Table II—Complications in 338 Catheter Placements for Hepatic Artery Infusion

Complication	No.
Sepsis	
Clostridium sp.	2*
Septic emboli	1
Infection at site	2
Catheter-related	
Hepatic artery occlusion	10
Occlusion and recannulation	2
Hepatic artery aneurysm	1
Femoral artery injury	4
Other	
Myelosuppression	1

*Resulting in death.

Summary

Hepatic metastases due to gastrointestinal or breast cancer can be treated with intermittent high-dose infusions of drugs through a percutaneously placed catheter, with relatively low morbidity and mortality. A dose of 5-FU up to 4 g/d can be administered safely without substantial side-effects. The quality of life that is produced by such intermittent therapy is superior to that of patients on weekly regimens. The results of this study require further evaluation in conjunction with other regional therapeutic modalities and more experience is required with breast cancer metastatic to the liver to evaluate whether this treatment is worthwhile in providing remission in patients whose disease involves a critical organ.

The authors wish to thank Lana Bryant for the preparation of the manuscript.

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Structure and Function of Small Bowel Allografts in the Dog: Immunosuppression with Cyclosporin A

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Pairs of mongrel dogs received orthotopic total small bowel allografts. Half were treated with the immunosuppressive agent cyclosporin A and the other half were not.

Ten untreated dogs survived a mean of 12.5 days (range from 7 to 25 days). They lost up to 30% of their initial body weight and rejection with hemorrhagic necrosis was usually the cause of graft failure. The mean survival of 11 dogs treated with cyclosporin A was 90.6 days (range 9 to 287 days) with early deaths being due to pneumonia or volvulus. Intestinal mucosa appeared normal, but there was some smooth muscle hypertrophy. Reconnection of lymph vessels was complete in all dogs examined more than 21 days after allografting. Two dogs survived for 203 and 221 days, respectively, and one dog remains alive and well 287 days after operation. The long-term survivors remained healthy, with steady body weights, formed stools, normal plasma protein values and xylose absorption curves that did not differ from those of autografted dogs. Roentgenography after a barium meal and follow-through study showed normal mucosa. The transit time was around 60 minutes (normal 150 minutes). Late, acute episodes of rejection occurred in two dogs, when blood levels of cyclosporin A were low (less than 400 ng/ml). Bowel mucosa showed ulceration and villous atrophy, with lymphoid infiltration, leading to malabsorption as a terminal event.

Cyclosporin A is effective in increasing the duration of survival in dogs with small bowel allografts while maintaining essentially normal bowel structure and good function.

Des paires de chiens bâtards ont reçu des allogreffes orthotopiques totales d'intestin grêle. La moitié a reçu un traitement à la cyclosporine A, l'autre moitié restant intraitée.

Dix chiens non traités ont survécu durant 12.5 jours en moyenne (écart de 7 à 25 jours). Ils perdirent jusqu'à 30% de leur poids initial et le rejet accompagné de nécrose hémorragique furent habituellement la cause de la défaillance du greffon. La survie moyenne des 11 chiens traités à la cyclosporine A fut de 90.6 jours (entre 9 et 287 jours), les décès précoces étant dûs à la pneumonie ou à un volvulus. La muqueuse intestinale paraissait normale bien qu'il y ait eu un peu d'hypertrophie de la musculature lisse. La revascularisation lymphatique était complète chez tous les chiens qui ont été examinés plus de 21 jours après la greffe. Deux chiens ont survécu pendant 203 et 221 jours respectivement, et un chien est toujours vivant et en bon état, 287 jours après l'opération. Les chiens qui ont eu une survie prolongée sont demeurés en santé, conservant un poids corporel constant, des selles normalement moulées des protéines plasmatiques normales et des courbes d'absorption du xylose qui ne différaient pas de celles des chiens qui reçoivent une autogreffe. Le temps du transit intestinal était d'environ 60 minutes (la normale est de 150 minutes). Des crises tardives de rejet sont survenus chez deux chiens alors que leurs taux sanguins de cyclosporine A étaient bas (moins de 400 ng/ml). La muqueuse intestinale montrait de l'ulcération et de l'atrophie villositaire avec infiltration lymphoïde, entraînant une malabsorption comme événement terminal.

La cyclosporine A est efficace pour prolonger la survie chez le chien qui a reçu une allogreffe d'intestin grêle tout en maintenant une structure intestinale essentiellement normale et une bonne fonction.

Allotransplantation of the small bowel has been reported in seven patients.[1,2] The longest survival was 76 days, but no useful intestinal function was obtained from this or any of the other small bowel transplants. Many attempts at small bowel allografting have been made in animals, mainly in dogs, but results have been discouraging. Lillehei and colleagues[3] showed that short segments of small bowel are rejected following allotransplantation; dogs survived an average of 9 days. Animals not treated with immunosuppressive agents who had long segments of bowel transplanted all died within 10 days, of what was thought to be graft-versus-host disease.[4] The addition of azathioprine,

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prednisone and antilymphocyte globulin to the therapeutic regimen increased average survival to 20 days. Cohen and colleagues[5] confirmed Lillehei's findings in the case of untreated total small bowel orthotopic allotransplants and showed that graft survival could be increased to a mean of 28 days by pretreating the donor bowel with 50 rad of x-radiation. One such animal lived for 58 days after transplantation — the longest survivor yet reported.

A new immunosuppressive agent cyclosporin A has been shown to be the most effective single agent in preventing rejection of kidney, liver, pancreas and heart transplanted in laboratory animals and man.[6] It is also effective in preventing and treating graft-versus-host disease in patients with bone-marrow transplants.[7] Cyclosporin A is a unique immunosuppressant in that it almost specifically inhibits the early stages of T-cell transformation,[8] without having a marked effect on other lymphocytes or polymorphs. Thus, it was considered ideal for use with small bowel transplantation where the three main obstacles to success have been rejection, graft-versus-host disease and sepsis. This experiment was undertaken to test the efficacy of cyclosporin A in prolonging survival of animals after total small bowel transplantation.

Material and Methods

Pairs of adult mongrel dogs of approximately equal size and weight were randomized into either control or treated groups. Preoperatively all dogs had bowel preparation, which included orally administered neomycin (500 mg) and a fluid diet. They also received 1 g cephalothin intramuscularly. Dogs assigned to the treatment group received 25 mg/kg of cyclosporin A dissolved in mygliol, intramuscularly, the day before the operation.

The animals were anesthetized with thiopentone and anesthesia was maintained with nitrous oxide, oxygen and halothane. A long, midline, abdominal incision was made. The complete small bowel was removed from both donor and recipient. The donor bowel, from the duodenojejunal flexure to the ileocecal valve, was mobilized in the manner described by Lillehei and colleagues.[9] This was harvested along with its mesentery and vascular pedicle, consisting of superior mesenteric artery and vein just distal to the duodenal and middle colic vessels. The intestine to be transplanted was perfused through the superior mesenteric artery with 1 litre of cold Ringer's lactate solution containing 2000 units of heparin (Fig. 1). This allowed at least 2 hours of safe ischemic time.[10] The average time required to re-establish circulation was 45 minutes. In the recipient, the vascular anastomoses were performed between the superior mesenteric artery and vein and the abdominal aorta and inferior vena cava respectively, as described by Monchik and Russell[11] (Fig. 2). To reduce the chance of twisting the anastomotic pedicle, the vein was placed just below the origin of the renal veins and the artery about 4 cm distal to that point. Intestinal anastomoses were performed end-to-end using a two-layer technique so that the transplanted intestine was orthotopic. The intestine was placed in an appropriate position in the abdomen and totally covered with recipient omentum.

Postoperatively all dogs were maintained on intravenous fluid infusions until they were able to drink normally, about 48 hours. Three doses of cephalothin were administered intravenously (1 g *q8h*)

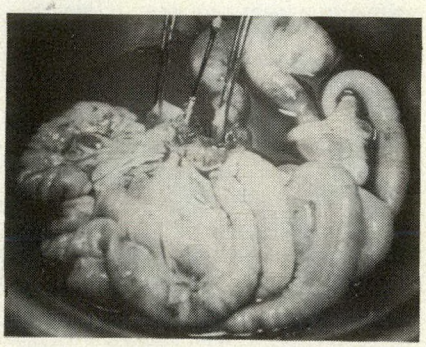

FIG. 1—Donor bowel being perfused with cold heparinized Ringer's lactate through superior mesenteric artery.

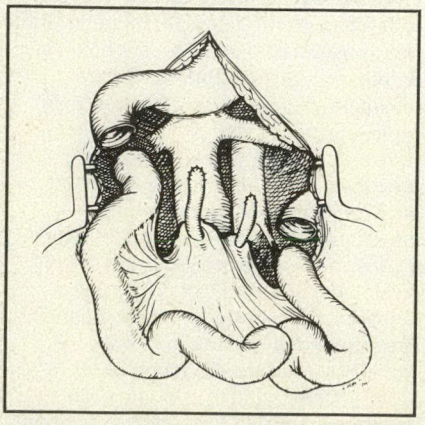

FIG. 2—Superior mesenteric artery and vein are anastomosed to abdominal aorta and inferior vena cava respectively.

The first 30 animals were fed a standard diet of beef chow (Romar Pet Supplies Co., Toronto, Ont.). Then the diet was changed to intestinal diet (Hill's Ltd., Topeka, Kan.), a rapidly absorbed high protein, high calorie mixture of eggs, rice and cheese, designed for dogs with chronic diarrhea.

Animals in the treatment group received cyclosporin A (25 mg/kg daily) intramuscularly, dissolved in mygliol, for 30 days, and thereafter orally, dissolved in olive oil. Surviving dogs were weighed regularly and the hemoglobin level, leukocyte count and serum electrolyte levels were measured. During the latter part of the experiment, when the technique of radioimmunoassay for cyclosporin A became available, blood levels of the drug were measured in several animals. All animals that died underwent complete autopsy. In four of the long-term survivors, immediately after death, a lymphatic channel of the transplanted intestinal mesentery was cannulated and methylene blue injected to ascertain if lymphatic reconnection had occurred.

Xylose tolerance tests were performed on healthy (nontransplanted) dogs, dogs receiving autografts but not cyclosporin A and two of the long-term survivors from the treated group.

Results

All animals that died within 6 days of operation were excluded from the study and were considered technical failures (Table I). Thirty dogs were thereby excluded; most deaths were due to vascular problems, mainly thrombosis of either artery or vein. Of the dogs receiving small bowel allografts 21 survived beyond 6 days, 10 in the control group (not given cyclosporin A) and 11 receiving cyclosporin A as their only form of immunosuppression.

Survival

The 10 control animals survived a mean of 12.5 days (range from 7 to 25 days) (Table II). During this time the animals initially appeared well and

Table I—Technical Failures

Reason	No. of dogs
Venous infarction	12
Arterial thrombosis	7
Hemorrhage	4
Intestinal perforation	3
Sepsis	2
Unknown	2

Table II—Survival after Transplantation

Controls (n = 10)		Cyclosporin A (n = 11)	
Survival, d	Cause of death	Survival, d	Cause of death
25	Rejection	54	Pneumonia
23	Rejection	60	Pneumonia
13	Rejection	221	Rejection
9	Rejection	10	Peritonitis
12	Rejection	9	Dehydration
8	Rejection	37	Pneumonia
7	Rejection	203	Rejection
12	Rejection	40	Pneumonia
8	Rejection	36	Internal hernia
8	Rejection	40	Pneumonia
		287*	

*Still alive.

tolerated their diet but soon became anorectic, had severe diarrhea and lost up to 30% of their initial weight.

Eleven treated animals survived a mean of 90.6 days (range from 9 to 287 days). Their clinical course was different from the untreated animals. Many of the deaths were unrelated to primary intestinal problems. They maintained a good appetite and despite an initial weight loss often regained all the lost weight. Of the 11 treated dogs, 1 was sacrificed at 9 days because it would not eat or drink. A second dog died at 10 days of peritonitis. Another died at 36 days of herniation of small bowel through the defect in the transplanted mesentery. Five others died at 37, 40, 40, 54 and 60 days respectively, all of pneumonia. Two animals survived 203 and 221 days respectively. Both were clinically well until 3 weeks before death when they became anorectic, had diarrhea and died quickly. Both had blood levels of cyclosporin A during the last 3 weeks of life below 400 ng/ml (therapeutic range greater than 400 ng/ml) suggesting they were absorbing suboptimal doses of the drug (Fig. 3). One animal remains alive and well at 287 days.

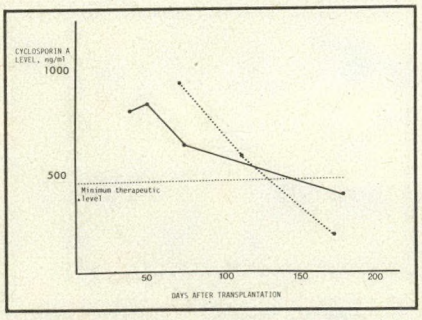

FIG. 3—Blood levels of cyclosporin A in two long-term survivors.

Autopsy Findings

Control animals.—Dogs that received total small bowel allografts and no immunosuppression all died of intestine-related complications. In some the degree of postmortem autolysis of the transplanted small bowel was such that a specific pathologic diagnosis was precluded. However, major changes were present in the transplanted bowel in all these dogs. The most common finding was a patchy hemorrhagic necrosis of the small bowel, often with perforations through the necrotic segments. The resultant sepsis was probably the immediate cause of death. Grossly, the large blood vessels in these transplanted bowels appeared normal as did all other organs studied.

The histologic findings in the transplanted bowel were nonspecific and showed a gross loss of epithelium with polymorphonuclear infiltration of the whole thickness of the bowel wall. The adjacent host small bowel was histologically normal (Fig. 4).

The mesenteric lymph nodes were frequently enlarged and occasionally contained obvious gas bubbles. Histologically, these nodes showed reactive changes and occasional bacteria. Sections of the transplanted blood vessels and host kidney, liver, spleen and lymph nodes were all normal. No convincing evidence of graft-versus-host disease was found and the final diagnosis in all control animals was acute rejection of the transplanted bowel.

Treated animals.—The findings on gross and microscopic examinations of the intestines of the animals that died 9 days after operation were entirely normal. The animal that died at 10 days had gross peritonitis and a presumed intestinal perforation. Histologic examination of the transplanted bowel was normal. The animal that died at 36 days with an internal hernia demonstrated normal intestinal architecture. Five dogs died between 37 and 60 days after operation. They had pneumonia with or without empyema. In each case the transplanted intestine appeared normal except for a thickened bowel wall. This thickening was due to hypertrophy of the smooth muscle layer (Fig. 5). In all these cases the mucosal architecture was normal. Spleen and lymph nodes (both donor and host) were noted to be smaller than normal and there was a central depletion of lymphoid elements (Fig. 6).

Two animals survived 203 and 221 days respectively. The findings were similar. The transplanted bowel showed smooth muscle hypertrophy as the only gross abnormality. Microscopically, however, abnormalities were seen in the entire transplanted segment. These changes were most severe at the caudal end of the graft and least extensive cephalad. Near the cephalic intestinal anastomosis the

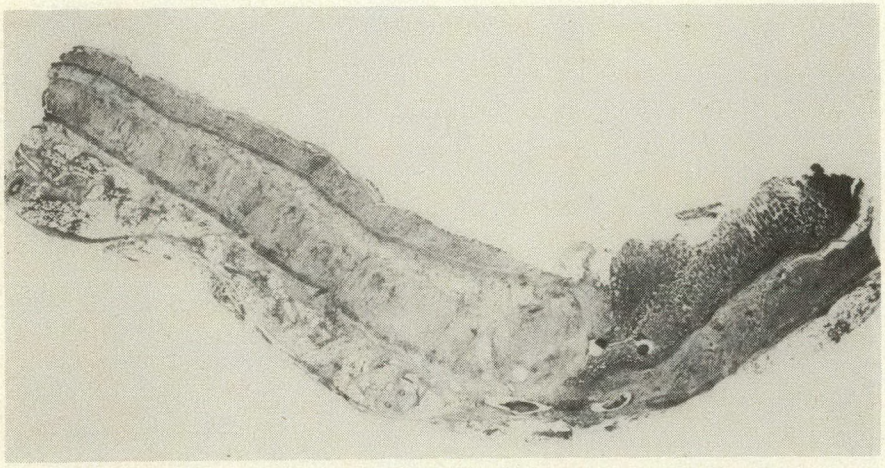

FIG. 4—Whole mount of bowel anastomotic region in control animal. Host bowel (right) shows preservation of mucosal architecture. Transplanted bowel (left) shows diffuse hemorrhagic necrosis (hematoxylin and eosin, original magnification ×5).

mucosal architecture was almost normal. There was evidence of epithelial regeneration as manifest by hyperchromasia and an increased number of mitoses. There was round cell infiltration in the lamina propria and patches of round cell infiltration in the muscle. At the other end the mucosal damage was extensive. There was complete circumferential ulceration. There were transmural round cell and polymorphonuclear cell infiltrations, which were limited to the mucosal surface. The middle zones of the transplanted segment showed changes intermediate between the other two with rapidly regenerating areas in ulcerated portions. These changes were compatible with rejection as the cause of death in these two animals (Fig. 7). The spleen and lymph nodes were small and showed central depletion of lymphoid elements.

Side-Effects

The long-term survivors all showed gingival hypertrophy, a recognized effect of cyclosporin A.[12] This hypertrophy receded about 1 month before death in both dogs surviving over 200 days. One animal had an injection site ulcer that healed spontaneously. No important abnormalities were found in the leukocyte count and levels of blood urea nitrogen, serum electrolytes, creatine, bilirubin, alkaline phosphatase and glutamic oxaloacetic transaminase.

Lymphatic Reconnection

Four animals were studied at 36, 40, 40 and 203 days respectively after transplantation to determine whether lymphatic reconnection had occurred. In all animals the injection of methylene blue into transplant lymphatics was followed by rapid spread of the dye to host lymphatics and nodes, confirming lymphatic recannulation.

Xylose Tolerance Test

Carbohydrate absorption was measured in two long-term survivors treated with cyclosporin A and compared to that of two healthy nontransplanted dogs and two animals receiving autografts but no cyclosporin A. Absorption in the transplanted intestine was less than that seen in healthy nontransplanted dogs but equalled that seen in dogs receiving autografts (Fig. 8).

Discussion

Increasing numbers of patients with a variety of crippling intestinal conditions are surviving at present because of total parenteral nutrition programs administered at home.[13] Although this treatment has achieved unparalleled success with those patients who have a short segment of functioning small bowel or malfunctioning small intestine, there have been several problems in its application. There are patients who are not capable of handling the rather sophisticated home equipment, and another group of patients, who, after long-term total parenteral nutrition at home, have had catheter-related problems and difficulties with venous access sites. Because these patients survive longer and live productive lives, renewed interest in the potential of small bowel transplantation seems justified.

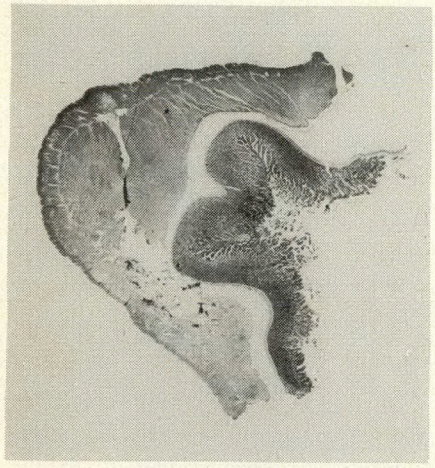

FIG. 5—Whole mount of transplanted intestine showing marked smooth muscle hypertrophy (hematoxylin and eosin, original magnification ×5).

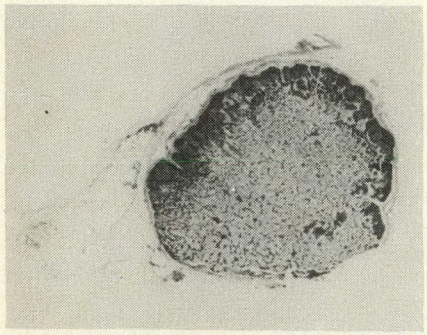

FIG. 6—Whole mount of host lymph node showing central depletion of lymphoid elements (hematoxylin and eosin, original magnification ×5).

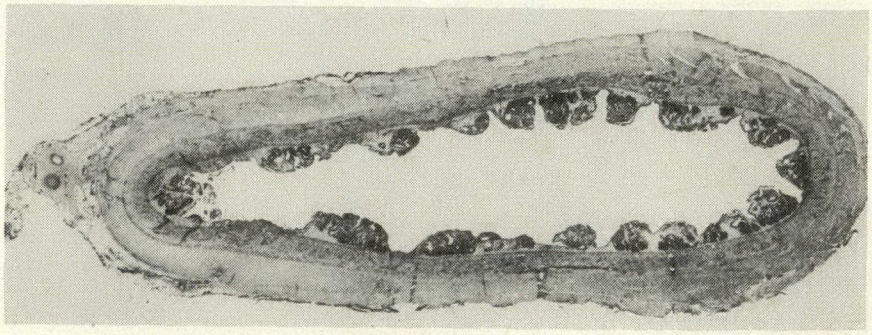

FIG. 7—Whole mount of transplanted intestine of long-term survivor treated with cyclosporin A. There is extensive mucosal ulceration, loss of villi and chronic inflammatory infiltrate (hematoxylin and eosin, original magnification ×5).

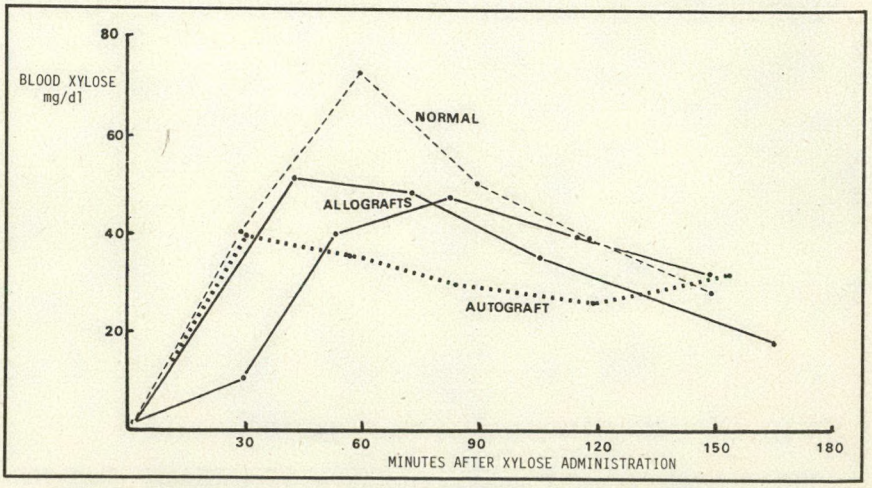

FIG. 8—Xylose tolerance test. Absorption in two allografted dogs treated with cyclosporin A (solid line) compared with two autografted dogs (dotted line) and two nontransplanted dogs (broken line).

To date no human small bowel allograft has been successful and the longest survival of an animal in laboratory experiments has been 58 days. Excluding technical failures, the most important causes of death in experimental small bowel transplantation have been rejection and graft-versus-host disease. The major difference between these two entities is the status of the transplanted intestine. In cases of rejection this shows extensive mucosal ulceration and round cell infiltration. In graft-versus-host disease, the transplanted intestine is normal. Moreover, the diagnosis can only be made if there is histologic evidence of an immunocyte infiltration of host tissue. This is most reliably seen in host intestine and skin.[14]

In this experiment dogs receiving total small bowel orthotopic allografts and no immunosuppressive therapy all died of intestine-related complications due to rejection. Several previous studies have shown what was thought to be graft-versus-host disease, but evidence for this is circumstantial. Like others[1,15,16] we found no evidence of such disease in our control animals. Several variations in technique may account for these pathologic differences. In other studies[17] the venous drainage of the intestine was into the portal system whereas in our experiment the superior mesenteric vein drained into the inferior vena cava. Bypass of the liver alters the immunologic responses to allografting in some systems studied[16] and may have altered the balance towards rejection in these animals. Transfusion of donor blood may delay the rejection reaction. A third factor is that of splenectomy, which Cohen and associates[18] performed in all their experiments with small bowel transplantation. In our experiments the spleens were not removed and this might also promote rejection rather than development of graft-versus-host disease.

The mean survival of animals treated with cyclosporin A shows clearly that this drug is effective in prolonging graft and animal survival. Moreover, we have seen useful bowel function in 9 of 11 treated dogs as manifest by weight gain, near-normal xylose tolerance tests and normal-appearing, formed stools. Only two animals died of gut-related causes and these survived over 200 days. Both had changes in the transplanted small bowel segment compatible with acute rejection. The cyclosporin A absorption curves in these animals clearly showed that they were achieving suboptimal levels of the drug during the month before they died. This is further corroborated by the recession of gingival hypertrophy in both animals during the same period.

The reason for falling levels of the drug despite a constant maintenance regimen may be malabsorption. This may be secondary to smooth muscle hypertrophy or chronic rejection resulting in a cycle leading to malabsorption and decreased levels of cyclosporin A and further rejection. What may have initiated this cycle is uncertain; we suspect our treatment regimen was suboptimal. We have recently obtained cyclosporin A absorption curves in small bowel transplanted dogs and have found that the peak level after an oral dose of the drug occurs 2 hours after administration. This may mean that the animal remains unprotected for long periods during each day when a single daily dose is given.

There was a gradation of changes in the transplanted intestine of long-term surviving dogs that died of rejection. The cephalic portion of the transplanted bowel was minimally affected whereas the changes in the caudal portion were severe. The reason for this remains uncertain; however, it leads to speculation that cyclosporin A has a local protective effect in the more cephalic areas of the bowel.

The large numbers of cyclosporin A-treated dogs that died of pneumonia suggests that these dogs were more subject to infection although there was no important change in peripheral total blood or differential counts. Immunologic studies were not done.

Conclusions

Increased survival has been achieved with cyclosporin A given to dogs that underwent total small intestinal allotransplantation. In the model described, the control animals died of rejection rather than graft-versus-host disease.

We believe that these promising results justify interest in animal and human small bowel transplantation. Small bowel allografts may in future become an alternative in the management of patients whose only hope for survival at present rests with long-term total parenteral nutrition.

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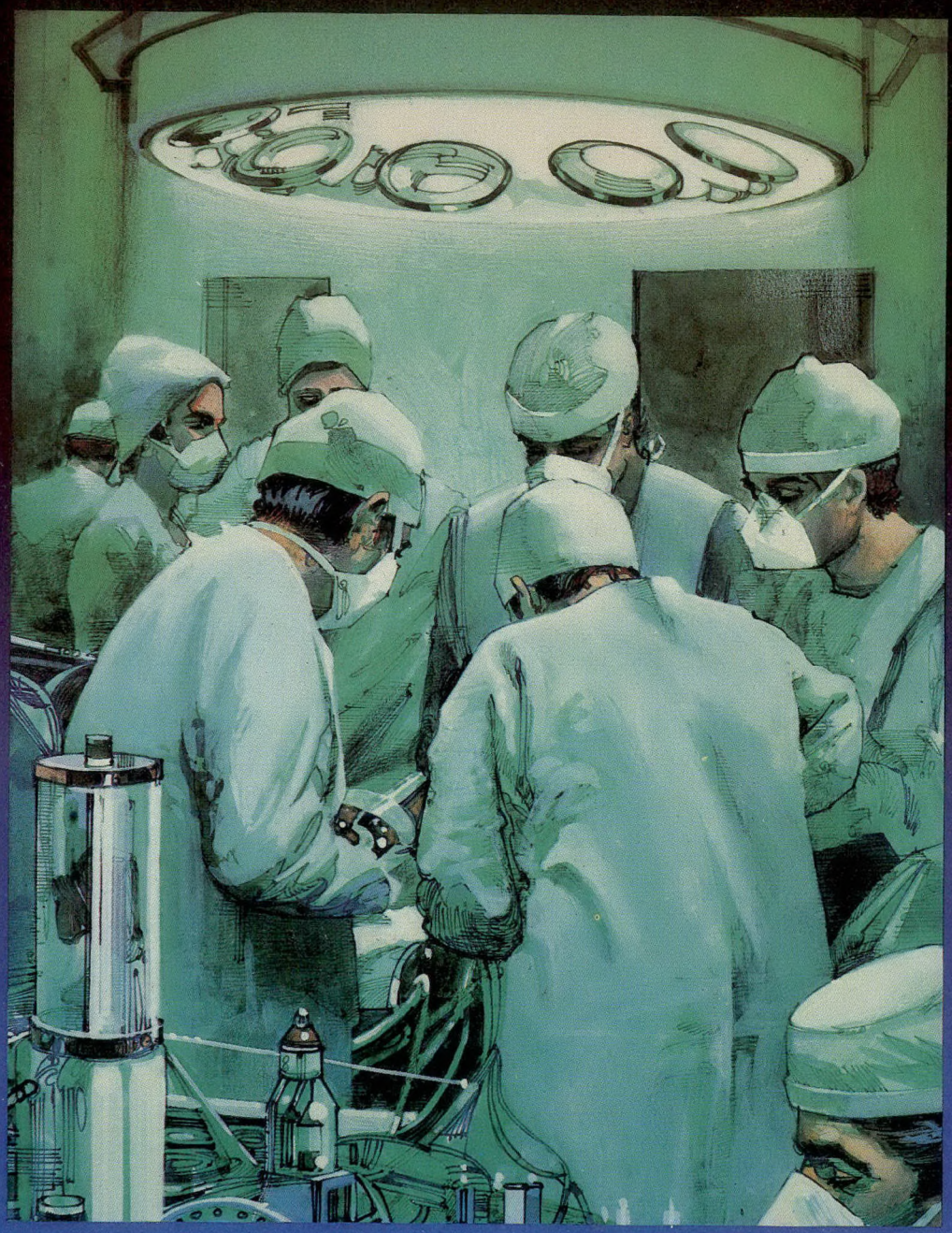
To Treat Many Mixed Infections Without Multiple Antibiotics



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Usual Adult Dosage

Type of Infection	Daily Dosage	Frequency and Route
Uncomplicated forms* of infections such as pneumonia, urinary tract infection, soft tissue infection	3-4 grams	1 gram every 6-8 hours IV or IM
Moderately severe or severe infections	6-8 grams	1 gram every 4 hours or 2 grams every 6-8 hours IV
Infections commonly needing antibiotics in higher dosage (e.g. gas gangrene)	12 grams	2 grams every 4 hours or 3 grams every 6 hours IV

*Including patients in whom bacteremia is absent or unlikely.

Therapy may be started while awaiting the results of susceptibility testing.

Antibiotic therapy for group A beta-hemolytic streptococcal infections should be maintained for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. In staphylococcal and other infections involving a collection of pus, surgical drainage should be carried out where indicated.

Dosage in Adult Patients with Impaired Renal Function

MEFOXIN* may be used in patients with reduced renal function but a reduced dosage should be employed and it is advisable to monitor serum levels in patients with severe impairment.

In adults with renal insufficiency, an initial loading dose of 1 g to 2 g should be given. After a loading dose, the following recommendations for maintenance dosage may be used as a guide:

RENAL FUNCTION	CREATININE CLEARANCE mL/min	DOSE	FREQUENCY
Mild impairment	50-30	1-2 g	every 8-12 hrs
Moderate impairment	29-10	1-2 g	every 12-24 hrs
Severe impairment	9-5	0.5-1 g	every 12-24 hrs
Essentially no function	<5	0.5-1 g	every 24-48 hrs

In the patient undergoing hemodialysis, the loading dose of 1-2 g should be given after each hemodialysis, and the maintenance dose should be given as indicated in the table above.

Infants and Children

The recommended dosage in children three months of age and older is 80 to 160 mg/kg of body weight per day divided into four to six equal doses. The higher dosages should be used for more severe or serious infections. The total daily dosage should not exceed 12 g.

At this time no recommendation is made for children from birth to three months of age (see PRECAUTIONS).

At present there is insufficient data to recommend a specific dosage for children with impaired renal function. However, if the administration of MEFOXIN* is deemed to be essential the dosage should be modified consistent with the recommendations for adults (see Table above).

PROPHYLACTIC USE

For prophylactic use, a three-dose regimen of MEFOXIN* is recommended as follows:

Vaginal hysterectomy and abdominal surgery

2 g administered intramuscularly or intravenously just prior to surgery (approximately one-half to one hour before initial incision).

The second and third 2 g doses should be administered at 2-6 hour intervals after the initial dose.

Cesarean Section

The first dose of 2 g should be administered intravenously as soon as the umbilical cord has been clamped. The second and third 2 g doses should be given intravenously or intramuscularly four hours and eight hours after the first dose.

DOSAGE FORMS

Sterile MEFOXIN* is a dry white to off-white powder supplied in vials containing cefoxitin sodium as follows:

No. 3356—1 g cefoxitin equivalent in boxes of 10 vials
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BOOKS RECEIVED

This list is an acknowledgement of books received. It does not preclude review at a later date.

Infection in Surgery. Basic and Clinical Aspects. Edited by J. McK. Watts, P.J. McDonald, P.E. O'Brien, V.R. Marshall and J.J. Finlay-Jones. 405 pp. Illust. Churchill Livingstone, Inc., New York, 1981. $81.25. ISBN 0-443-02246-1.

Manual of Medical Care of the Surgical Patient. 2nd ed. Edited by Solomon Papper and G. Rainey Williams. 256 pp. Illust. Little, Brown and Company, Boston, 1981. $17.50, paperbound. ISBN 0-316-69048-1.

Medical Examination Review. Vol. 5. Surgery. 1000 Multiple Choice Questions with Referenced Explanatory Answers. 7th ed. M.D. Ram. 304 pp. Medical Examination Publishing Co., Inc., New York, 1981. $9.75, paperbound. ISBN 0-87488-105-6.

Medical Examination Review. Vol. 18. Thoracic Surgery. 1062 Multiple Choice Questions and Referenced Explanatory Answers. 3rd ed. Hooshang Bolooki. 237 pp. Illust. Medical Examination Publishing Co. Inc., New York, 1981. $20, paperbound. ISBN 0-87488-118-8.

Organ Preservation for Transplantation. 2nd ed. Revised and expanded. Edited by Armand M. Karow, Jr. and David E. Pegg. 705 pp. Illust. Marcel Dekker, Inc., New York, 1981. $69.25. ISBN 0-8247-1083-5.

The Patient and the Plastic Surgeon. Robert M. Goldwyn. 255 pp. Little, Brown and Company, Boston, 1981. Price not stated. ISBN 0-316-31974-0.

Précis d'anesthésie. G. François, M. Cara, J. Du Cailar, F. D'Athis, F. Gouin et M. Poisvert. 583 pp. Illust. Masson, Paris, 1981. Prix non mentionné. ISBN 2-225-67430-2.

Progress in Clinical and Biological Research. Vol. 48. Cloning of Human Tumor Stem Cells. Edited by Sydney E. Salmon. 367 pp. Illust. Alan R. Liss, Inc., New York, 1981. $44. ISBN 0-8451-0048-3.

Recent Advances in Plastic Surgery. 2. Edited by Ian T. Jackson. 266 pp. Illust. Churchill Livingstone, Inc., New York, 1981. $73.75. ISBN 0-443-01943-6.

Repair and Reconstruction in the Orbital Region. A Practical Guide. 2nd ed. J.C. Mustardé. 400 pp. Illust. Churchill Livingstone, New York, 1980. Price not stated. ISBN 0-443-01698-4.

Trauma and After. Ciba Foundation Volume. Edited by Ruth Porter, Janet Price and Robert Read. 122 pp. Pitman Books Limited, London, 1981. Price not stated, paperbound. ISBN 0-272-79623-9.

Les troubles de la sensibilité cutanée. Rééducation fonctionnelle. J.M. André, D. Lustig et J. Xenard. 91 pp. Illust. Masson, Paris, 1981. Prix non mentionné, broché. ISBN 2-225-69124-X.

Rotator Cuff Tears: the Role of Surgery

PETER EARNSHAW, MB, BS, LRCP, MRCS,* DENIS DESJARDINS, MD, FRCS[C],†
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The indications for operative intervention in patients with rotator cuff tears and the reasonable expectations of such surgery are not well defined. This retrospective study of 37 such patients treated operatively at Ottawa General Hospital showed good results in 65% of cases. However, efforts to re-establish continuity of the cuff did not always result in a permanent cuff reconstruction. The persisting defect did not impede functional recovery as long as the edges of the tear were debrided along with division of the coracoacromial ligament, acromioplasty, or excision of osteophytes at the greater tuberosity. Impingement plays a major role in the disability associated with this condition.

Les indications d'une intervention chirurgicale chez les patients souffrant d'une rupture de la coiffe des rotateurs et les espérances raisonnables qu'on peut attendre d'une telle opération ne sont pas bien définies. Cette étude rétrospective portant sur 37 patients qui ont été opérés à l'Hôpital Général d'Ottawa montre de bons résultats dans 65% des cas. Toutefois, les tentatives pour rétablir la continuité de la coiffe n'ont pas toujours résulté en une reconstruction permanente de la coiffe. Le défaut résiduel n'a pas empêché la récupération fonctionnelle, en autant que les bords de la déchirure aient été débridés avec une division du ligament acromio-coracoïdien ou une acromioplastie. Un empiètement contribue de façon importante à l'invalidité associée à cette affection.

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The diagnosis and treatment of rotator cuff tears may present manifold problems. The findings of a painful shoulder with weak abduction of the arm, atrophy of supraspinatus and infraspinatus muscles and a palpable defect of the cuff with crepitus on movement are all highly suggestive but not diagnostic of a tear. The accuracy of clinical diagnosis is enhanced by roentgenography, a decrease in the acromiohumeral gap and sclerosis of the undersurface of the acromion due to superior subluxation of the humerus being indicators of a cuff tear.[1-4]

According to De Palma,[5] 90% of patients with rotator cuff tears will respond to conservative measures including rest, the administration of analgesics and anti-inflammatory agents, and physiotherapy. Who, then, should be considered for operative intervention and what are reasonable expectations of such surgery?

Since Codman[6] introduced surgical repair for rotator cuff tears, others have recommended many refinements in operative technique to re-establish continuity between the tendon and its humeral insertion, because they postulated that functional recovery depends upon successful anatomical reconstruction. Several authors[7-10] have reported a successful outcome in about 70% of patients operated on.

The purpose of this retrospective study of surgical treatment for rotator cuff tears, carried out at the Ottawa General Hospital, was to determine whether reconstruction of the cuff was maintained and to correlate these findings with the clinical outcome. Furthermore, we re-examined histologically the ruptured edges of the tendon to determine if there were specific morphologic factors that could have influenced postoperative recovery.

Patients

From 1970 to 1979, 37 patients (28 men, 9 women) underwent operation for tears of the rotator cuff at the Ottawa General Hospital. Their ages ranged from 31 to 68 years (mean 55 years). Twenty (54%) patients were manual workers while among the other 17 (46%) there were office workers and housewives, and 2 were physicians. The onset was acute in 15 (40%) patients. All reported a traumatic incident, such as falling on an outstretched arm, heavy lifting or pulling before the sudden appearance of symptoms. The other 22 (60%) had an insidious onset generally extending over several months. Operation was performed when conservative management for more than 3 months failed to ameliorate the symptoms.

For this study, 27 of the 37 patients were available for re-examination. Four of the 27 patients had bilateral tears, hence 31 shoulders were clinically evaluated.

Methods

Operation

An anterior approach was used in 29 shoulders and the posterior approach described by Debeyre and colleagues[11] was used for the other 2. All the tears were complete or of full thickness. The tear was massive (more than 2 cm long) in 10 and localized (less than 2 cm) in 19. There was a peripheral or rim tear in two. A simple repair was performed on 18 shoulders (58%). In nine (29%), a trough was cut in the greater tuber-

osity and the tendon reattached by drill holes made in the bone. In only one patient was the biceps tendon used to close the defect. Simple débridement was performed on three shoulders in which repair was not possible because of the large size of the tear and retraction of the fibres.

Other conditions associated with the rotator cuff tear included biceps tendinitis in two patients, biceps rupture in two, biceps subluxation in one, humeral osteophytes in two and calcium deposits in one patient. The operative procedures are summarized in Table I.

Postoperatively, immobilization was achieved in two ways with an almost equal number of patients in each group: (a) by a spica cast or splint in abduction for an average of 5 to 6 weeks or (b) by a sling or Velpeau bandage for an average of 3 to 4 weeks. There was only one postoperative complication, a superficial wound infection that resolved within 2 weeks.

Table I—Operative Procedures

Procedure	No. of shoulders
Débridement and repair	28
Simple débridement and repair	7
Trough cut in greater tuberosity	9
Coracoacromial ligament divided	5
Biceps excised or transplanted	3
Partial acromionectomy	2
Distal clavicle resected	1
Calcium deposits curetted	1
Débridement only	3
Biceps excised or transplanted	2
Synovectomy	1

Table II—Scoring Method

Factor	Score
Pain	
Absent	5
Mild with vigorous activity	4
Moderate, restricting some activity	3
Moderate, restricting most activity	2
Severe, constant, disabling	1
Strength	
Able to lift 4 kg for 2 min	2
Able to lift 2.5 kg for 2 min	1
Able to overcome gravity only	0
Abduction against resistance	
> 500 mm Hg	1
< 500 mm Hg	0
Range of movement, % of normal	
>75	2
75 to 50	1
<50	0
Maximum score possible	10

Assessment

At follow-up examination of 31 shoulders, performed 3 months to 10 years after operation, we assessed the degree of pain, strength and range of movement. Points were given for each (Table II). We considered pain to be by far the most important factor and therefore allocated half the points available (5 points). Pain was graded according to its severity and effect on the patient's daily life. Strength was graded according to the ability to carry out sustained weight lifting; it was further quantitated by using a sphygmomanometer, the cuff of which was rolled on itself and inflated to 20 mm Hg. It acted as a pressure transducer to measure the power of abduction when held by the examiner against the patient's arm at the midpoint between olecranon and acromion. This was done with the arm in three positions: at 30°, 60° and 90° of abduction. The readings obtained were added. When the total was greater than 500 mm Hg, one point was given. Totals in normal subjects averaged 800 mm Hg. The active range of movement was measured in all six directions (flexion, extension, abduction, adduction and internal and external rotation). The result was then expressed as a percentage of the range of movement in a normal shoulder and rated accordingly.

The maximum score possible was 10. A score of 10 or 9 was rated excellent, 8 or 7 good, 6 or 5 fair and 4 or less poor. The patients were also asked for their own opinion about the outcome of the operation. Their assessment correlated well with our scoring.

Roentgenograms of both shoulders were taken in several positions. Anteroposterior views with the arm at the side and abducted to 40°, however, proved to be the most useful for this study.

Results

By our scoring method, the results in 16 of 23 shoulders in men were excellent or good, while 4 of 8 in women were in this category (Table III). Patients in the fourth and fifth decades of life generally did well except for one 42-year-old man whose rupture was complicated by villonodular synovitis. Repair was not possible and after synovectomy he had a stiff, painful shoulder and weak arm.

Table III—Clinical Results

Category	No. of patients (N = 31)	Rating, no. (%) Excellent/good (n = 20)	Fair/poor (n = 11)
Sex			
Male	23	16 (70)	7 (30)
Female	8	4 (50)	4 (50)
Age, yr			
<40	2	2 (100)	0
41–50	2	2 (100)	0
51–60	17	10 (59)	7 (41)
>60	10	6 (60)	4 (40)
Occupation			
Manual	17	12 (70)	5 (30)
Other	14	8 (57)	6 (43)
Onset			
Sudden	13	9 (70)	4 (30)
Insidious	18	11 (61)	7 (39)
Previous operation	3	1 (33)	2 (66)
Previous steroids			
Yes	19	11 (58)	8 (42)
No	12	9 (75)	3 (25)
Operative findings			
Massive tear	10	6 (60)	4 (40)
Local tear	19	12 (60)	7 (40)
Rim tear	2	2 (100)	0
Bilateral tear	4	1 (25)	3 (75)
Repair			
Possible	28	18 (64)	10 (36)
Impossible	3	2 (66)	1 (33)
Secondary procedure on acromion or acromioclavicular ligament	7	6 (86)	1 (14)
Postop immobilization, wk			
<4	15	10 (67)	5 (33)
>4	16	11 (69)	5 (31)

In contrast, only 60% of patients in the sixth and seventh decades had good results. Of patients in manual occupations and those with a sudden onset of symptoms, 70% had an excellent or good result, compared with about 60% of patients in other occupations or with insidious onset.

Of the 28 shoulders that were repaired, excellent or good results were obtained in 18. The same outcome was seen in two out of three shoulders in which repair was not possible. The result of repair of rim tears was uniformly good. The success rate decreased to 60% for massive and localized tears and to 25% for bilateral tears. Secondary procedures involving the acromion or coracoacromial ligament, performed on seven shoulders, gave excellent or good results in six. Whether a spica cast was applied for more than 4 weeks or a sling for less than 4 weeks, the results were similar.

Radiologic Appearance

The radiologic findings were divided into four groups: group 1—nonspecific changes around the affected shoulder, such as acromioclavicular joint disease, humeral cysts, humeral sclerosis and glenoid changes; group 2—changes more specific for a rotator cuff tear, namely, superior subluxation of the humerus and sclerosis of the undersurface of the acromion; group 3—calcific deposits in the tendon; group 4—no changes.

Preoperative roentgenograms of 15 of the 31 shoulders showed group 1 changes in 6 shoulders, group 2 changes in 4 and group 3 changes in 1. Four shoulders showed no changes. At follow-up examinations, roentgenograms of 28 of the 31 shoulders showed group 1 changes in 24, group 2 changes in 10 and group 3 changes in 4. Three shoulders showed no changes (Fig. 1 and Table IV).

Histologic Appearance

The histologic examination revealed that in the majority of instances the ruptured edges of the tendon were close to the bone insertion. Sharpey's fibres were in disarray. Marked fragmentation of tendon fascicles in the area of rupture was frequently accompanied by irregular projections of mesenchymal tissue with villous configurations. Vascular channels of variable number were present in these villous structures. In some the vessels were abundant while in others the tissue was completely hyalinized. Microscopic calcification, which did not appear on the roentgenograms, was found in three specimens (Fig. 2).

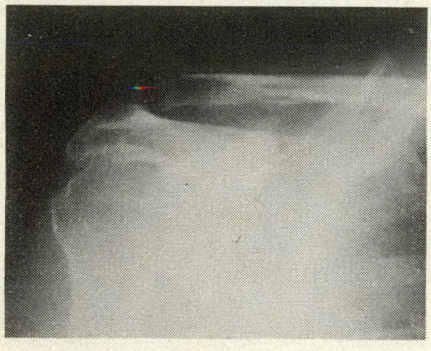

Fig. 1a

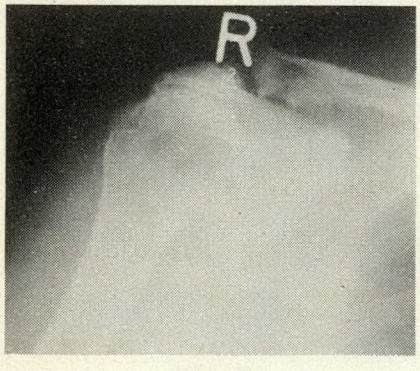

Fig. 1b

FIG. 1—(a) Preoperative view of rotator cuff tear in 61-year-old man who fell from ladder onto his outstretched arm. There is subluxation of humerus, sclerosis of undersurface of acromion and degenerative changes in acromioclavicular joint. (b) Follow-up view 5 years after reconstruction shows marked progression and acromiohumeral articulation.

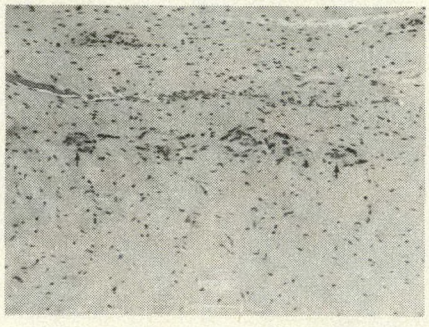

FIG. 2—Calcification in tendon (arrows) (hematoxylin and eosin).

Discussion

Although conservative treatment of rotator cuff tears is usually adequate, a patient with severe persistent symptoms may require operative intervention.

According to Adams,[12] the results of surgery in older patients are so poor that repair should not be performed in patients over 40 years of age. Wolfgang[9] stated that good results were less likely with advancing age. All our patients under 50 years of age did well and 60% of patients over 50 had good results. We believe, therefore, that, although the chance of success is not as good in the older patient, surgery should not be refused on the grounds of age alone.

Neither the mode of onset of the tear nor the timing of repair have a bearing on the outcome. In fact, a cuff with a sudden traumatic tear repaired early does not function any better than a tear of insidious onset repaired many months or years later. Also the size of the tear has surprisingly little influence on the outcome. The repair of a massive tear will give a result comparable to that of a small tear. Contrary to Nixon and DiStephano's[13] observations, both our patients with a tear of the rim did well. Patients with bilateral tears did not do well. Three of four patients had

Table IV—Radiologic Appearances Preoperatively (15 Shoulders) and Postoperatively (28 Shoulders)

Group	Radiologic features	Before operation, no. (%)	At follow-up: No. of shoulders (%)	At follow-up: Score: Excellent/good (n = 19)	At follow-up: Score: Fair/poor (n = 9)
1	Degenerative changes Humeral cysts, sclerosis, glenoid changes and acromioclavicular joint disease	6 (40)	24 (86)	15	9
2	Definitive signs of a cuff tear Superior subluxation of the humerus and sclerosis of the undersurface of the acromion	4 (27)	10 (36)	5	5
3	Calcific deposits	1 (7)	4 (14)	3	1
4	No change	4 (27)	3 (10)	3	0

problems in one or both shoulders sufficiently disabling to prevent their return to work.

The importance of calcium deposits, macroscopic or microscopic, is not well understood. Wolfgang[9] found that 23% of such deposits were visible on preoperative roentgenograms. On the other hand, McLaughlin and Asherman[14] found calcium deposits only twice in several hundred cases of rotator cuff tear. We believe that localization of the calcium deposit is important. Radiologically visible deposits in the body of the tendon away from its insertion into bone must be distinguished from the microscopically visible deposits at the site of Sharpey's fibres where the tendon is anchored to the bone. The former deposits, indicating calcifying tendinitis and resulting from a primary metaplasia of tendon, did not prevent a good outcome, but microscopic calcium deposits found in three patients were all associated with a poor result. Here, calcification seems to occur in response to previous trauma, inflammation, degeneration and the reparative process. In addition to the microscopic presence of calcium at the tendon insertion, villonodular synovitis was associated with a poor outcome. Whether villonodular synovitis is the cause of the tear, as Neviaser[15] has postulated, or is the result of a tear, as Cotton and Rideout[1] believe, is still open to discussion.

The kind of postoperative immobilization used seems to be of little importance. We advocate McLaughlin's method of support in a sling. This is simple and permits earlier mobilization. Prolonged splinting in abduction offers no advantage.

Most shoulders showed progression of the radiologic features of the disease despite surgical repair (Fig. 1). Particularly common were the acromioclavicular joint changes and superior subluxation of the humeral head. A prime function of the rotator cuff is to hold the humeral head against the glenoid when the arm abducts. When the cuff is not intact, subluxation occurs and leads to articulation with the acromion and sclerosis of its undersurface.

The success of surgery has always been associated with an intact reconstruction. Thus, it is not surprising that many reconstructive techniques have been described using fascia lata,[16] biceps tendon[17] and freeze-dried rotator cuff;[18] all of them have been claimed to give good results. The question is whether a good functional result is synonymous with a successful repair. Can one expect normal healing of a degenerated and torn cuff by approximating the fibres? Our follow-up study shows an increase in the radiologic signs of cuff tear such as a positive arthrogram and superior subluxation of the humeral head with sclerosis of the undersurface of the acromion. If one adds to this the two cases in which, despite the impossibility of a repair, a good result was obtained one wonders if the joint débridement carried out at operation is not as important as repair of the cuff.

Conclusions

Our study suggests that the majority of patients treated surgically for rotator cuff tear have pain-free, functioning shoulders even though most cuffs do not remain intact postoperatively and radiologic evidence of osteoarthritis tends to develop. We believe, therefore, that functional improvement depends less on a meticulous cuff repair than on careful débridement of the ruptured edges and removal of the sources of impingement. The impingement can best be treated either by dividing the coracoacromial ligament, resecting osteophytes around the greater tuberosity or by a limited anterior acromioplasty as described by Neer.[19] Radical acromionectomy is undesirable because persistent pain and instability of the joint may result.[20]

Operation should not be withheld from older persons on the grounds that the capacity to repair decreases with age. Relief of pain with restoration of function, rather than the anatomical reconstitution of the rotator cuff, should be the prime objective of operation.

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NOTICES

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American Association for Hand Surgery

The American Association for Hand Surgery will sponsor the second Rocky Mountain Hand Symposium in Vail, Colorado, Feb. 13–20, 1982. For further information please contact: Dr. Ronald Tegtmeier, 9950 West 80th Ave., Arvada, Colorado 80005. Telephone: (303) 424-1174.

Medical and Biological Engineering Conference

The 9th Canadian Medical and Biological Engineering Conference and Exposition will be held at the University of New Brunswick, Fredericton, NB, Aug. 15 to 18, 1982. Invited are papers on biomedical engineering topics, particularly: clinical engineering with emphasis on cost containment, bioethics as related to technology in health care, biological signal processing and control, and extracorporeal circulation.

Manuscripts must be submitted by Mar. 1, 1982. Further information and kits for authors can be obtained from: The conference secretariat, Bio-Engineering Institute, University of New Brunswick, PO Box 4400, Fredericton, NB E3B 5A3.

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Gastrointestinal Complications after Radiotherapy for Carcinoma of the Uterine Cervix

H.R. SHIBATA, MD, M SC, FACS, FRCS[C], C.R. FREEMAN, MB, BS, FRCP[C] AND T.N. ROMAN, MD, FRCS[C]

Radiotherapy for invasive carcinoma of the uterine cervix caused gastrointestinal complications in 52 of 441 patients. External beam and intracavitary radiation together caused greater bowel damage than either method alone. Twenty-eight of the 52 patients required surgical intervention. Ileal stenosis in nine patients required primary resection with anastomosis in seven while the stenosis was bypassed in the other two. Acute perforation with peritonitis would require a diverting ileostomy and creation of a mucous fistula. A defunctioning colostomy was indicated for relief of pain, bleeding and stenosis of the rectum in 11 of 15 patients; 2 patients were treated by primary resection, 1 underwent abdominoperineal resection and another a pelvic exenteration. Of four patients with ileal and rectal involvement, one underwent right hemicolectomy and transverse colostomy, two had ileal resection and sigmoid colostomy and the other had hemicolectomy and rectal resection. All patients were well at follow-up from 3 to 120 months after operation. A Hartmann's procedure is indicated when it appears that primary closure may not succeed. Individualized management is essential.

La radiothérapie d'un cancer invasif du col utérin a été la cause de complications gastro-intestinales chez 52 patientes sur 441. Un faisceau externe et une irradiation intra-cavitaire ont causé ensemble plus de dommages intestinaux que chacune des méthodes utilisée seule. Vingt-huit des 52 malades ont nécessité une intervention chirurgicale. De neuf patientes, une sténose iléale a commandé une résection primaire suivie d'une anastomose chez sept, alors qu'un pontage de la sténose était pratiqué chez les deux autres. Une perforation aiguë avec péritonite nécessiterait une iléostomie de dérivation et la création d'une fistule muqueuse. Une colostomie de mise au repos a été indiquée pour soulager la douleur, le saignement et la sténose du rectum chez 11 des 15 patientes; 2 malades ont été traitées par résection primaire, 1 ayant subi une résection abdomino-périnéale et l'autre une exentération pelvienne. Des quatre patientes qui ont souffert d'une atteinte iléale et rectale, une a subi une hémicolectomie et une colostomie transverse, deux ont eu une résection iléale avec colostomie sigmoïdienne et l'autre a eu une hémicolectomie avec résection du rectum. Toutes les patientes sont en bonne santé de 3 à 120 mois après l'opération. Une opération de Hartmann est indiquée quand il paraît que la fermeture primaire ne réussira pas. Une traitement adapté à chaque patiente est essentiel.

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Accepted for publication Oct. 7, 1981

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Radiotherapy is the treatment of choice for the majority of patients with invasive carcinoma of the uterine cervix. The overall 5-year survival rate, which was about 35% in the 1940s, is now about 65%,[1,2] and much of this improvement can be attributed to refinements in radiotherapy equipment and techniques. The most common complication of such treatment is damage to the rectum and rectosigmoid colon and, to a lesser extent, the terminal ileum. Injury to the genitourinary tract is considerably less frequent.

At the Royal Victoria Hospital in Montreal, a large number of patients with invasive carcinoma of the uterine cervix are seen each year. The overall 5-year survival rate in our patients treated with radiotherapy is 64%.[3] This paper reviews the gastrointestinal complications of such treatment and their management.

Patients and Methods

From Jan. 1, 1968 to Dec. 31, 1978, 441 patients with invasive carcinoma of the uterine cervix were selected for radiotherapy. Of these, 347 (78.7%) were treated with combined external beam and intracavitary radiation; 51 (11.6%) were treated by external beam radiation alone and 43 (9.8%) by one or more intracavitary applications of radioactive material alone.

Fifty-two patients (11.8%) presented, from 6 to 24 months (mean 12 months) following radiotherapy, with symptoms indicating gastrointestinal complications. Abdominal pain was the primary complaint in 71% of the patients, diarrhea was present in 51%, rectal bleeding in 22% and constipation in 15%. Severe anemia requiring blood transfusion occurred in 5%.

Seventeen of the 52 patients had undergone some form of abdominal surgery before radiotherapy. Five patients had had total abdominal hysterectomy and bilateral salpingo-oophorectomy, six had undergone subtotal hysterectomy, three laparotomy only, two appendectomy and one had had bilateral salpingo-oophorectomy alone.

Management and Results

Twenty-four (46.2%) of the 52 patients had a mild form of radiation enterocolitis that was managed successfully by conservative means. However, 28 patients (53.8%) required surgical intervention. The site of gastrointestinal involvement by radiation changes in this group of patients is shown in Table I.

Of the nine patients with involvement of the ileum, five were managed by segmental ileal resection with primary anastomosis, two by right hemi-

Table I—Site of Complications Requiring Surgical Intervention

Site	No. of patients
Ileum alone	9
Rectosigmoid alone	15
Ileum and rectosigmoid	4
Total	28

colectomy and two underwent bypass procedures only.

Nine of the 15 patients who had severe proctosigmoid changes underwent sigmoid colostomy only, 2 had transverse colostomies, 2 underwent anterior resection with primary anastomosis, 1 was treated by abdominoperineal resection and 1 patient underwent pelvic exenteration.

Four patients had both ileal and proctosigmoid involvement requiring extensive surgical intervention. One underwent right hemicolectomy for the ileal involvement and transverse colostomy for the sigmoid lesion. The colostomy was closed later without resection of the involved site. Two underwent ileal resection and permanent sigmoid colostomy. One patient was treated by a right hemicolectomy and anterior resection of the rectum. All of the patients who underwent operation remained well. The follow-up period ranged from 3 to 120 months.

Discussion

In the management of invasive carcinoma of the cervix with radiotherapy, the proximity of the rectum, rectosigmoid and colon and, to a lesser extent, the terminal ileum, predisposes to radiation colitis or enteritis that may require surgical intervention. Of factors such as age, obesity, individual susceptibility, the presence of diabetes mellitus, diverticulosis, diverticulitis and pelvic inflammatory disease, and previously performed surgical procedures, the two last appear to be the most important because of tethering of the normally mobile small bowel in the pelvis.[4] Seventeen (32.7%) of our patients with complications of radiotherapy had previously undergone abdominal surgery.

The dose and technique of radiotherapy are important. A risk of injury ranging from 1% to 5% is incurred when 4500 rad is given to the small intestine and 5500 rad to the colon and rectum. However, at doses of 6500 rad to the small intestine and 8000 rad to the colon and rectum, the risk of injury escalates to 25% to 50%.[5] The dose of radiation given for cure to patients with carcinoma of the cervix will, therefore, result in a risk of gastrointestinal morbidity that increases with the dose delivered. This in turn usually increases with the stage of the disease.[6,7] In spite of our treatment policy, which involves the use of higher doses of radiation to the parametrium in the more advanced stages of disease, there was surprisingly little variation in total dose and an increased risk of complications in the more advanced stages was not demonstrated.[3] However, the combined use of external beam and intracavitary radiation did lead to a higher complication rate than the use of either modality alone (Table II).

Radiation injury to the gastrointestinal tract can be temporally classified into two types. An acute or immediate phase is the result of damage to the radiosensitive mucosal cells and the characteristic symptoms are crampy lower abdominal pain and diarrhea. Such symptoms will be present in the majority of patients with carcinoma of the cervix who receive radiotherapy. They occur during treatment, will usually subside with conservative measures and almost always do so after a few days without treatment. Rarely, symptoms are more severe and include tenesmus and rectal bleeding. Even then they can usually be controlled with low residue diet, analgesics and antispasmodics, stool softeners, steroid enemas and rest. Such transient effects on the gastrointestinal tract do not correlate with later injuries[6] and are not the object of this communication.

A chronic delayed phase may occur at any time, but most often, as with our patients, occurs between 6 and 24 months after treatment. The pathological changes observed include vascular obliteration, mucosal atrophy and fibrosis of the intestinal wall.[5] Symptoms arising in the chronic phase can be managed initially in the same manner as those of the acute phase, but intractability to medical management with severe rectal bleeding, persistent pain and tenesmus, formation of a fistula, progressive constipation with bouts of diarrhea gradually leading to obstruction, and deterioration in general health, both physical and mental, are indications for surgical intervention. Such symptoms can easily be confused with recurrent carcinoma of the cervix. Pelvic examination under anesthesia is mandatory and thorough investigation, including rectosigmoidoscopy with biopsy, intravenous pyelography and cystoscopy are necessary to rule out this possibility.

There is still controversy as to the best operative procedure for treating complications of radiation in this area. The main point of contention is whether the involved segment of ileum, rectosigmoid colon or rectum should be bypassed or resected. The proponents of bypass only[8,9] in radiation enterocolitis think that the extensive dissection required to free multiple adhesions between loops of bowel further jeopardizes an already tenuous blood supply to some of these loops, leading to further necrosis of other segments of the intestine. On the other hand, those who advocate resection[10,11] believe that the injury due to radiation is progressive and when bypass procedures alone are done, further complications will almost certainly arise from the involved segment, especially if it is in the small intestine. Others caution that each situation must be individualized.[12]

In our series, the procedures were individualized. In the few patients with ileal involvement alone, the primary intent was resection (ileal resection with anastomosis in five patients, right hemicolectomy in two patients) and ileal bypass was performed in only two patients. Similarly, in the four patients with both ileal and rectal involvement, ileal resection was performed in all four. Eleven of the 15 patients with involvement of the rectum initially underwent diverting colostomy alone. Resection of the involved portion followed by closure of the colostomy was performed in three of these patients later. One patient underwent an abdominoperineal resection for a low-lying stenosis and rectosigmoid fistula. One patient underwent pelvic exenteration for a "frozen" pelvis, with a rectovaginal and vesicovaginal fistula. In neither was there evidence of recurrent tumour in the resected specimen.

The two broad categories of injury may be best managed in different ways. For radiation enteritis, where

Table II—Complications and Method of Radiotherapy

Method	No. of patients	No. of patients with complications (%)
External beam alone	51	2 (3.9)
Intracavitary alone	43	4 (9.3)
External beam and intracavitary	347	46 (13.3)
	441	52 (11.8)

stenosis is the main problem, the involved segment should be resected with primary anastomosis whenever possible. If a fistula is the main problem, the involved segment of intestine, including the fistula and its opening into the adjacent viscera, should be resected. If the intestine has perforated and there is peritonitis, the safest procedure is to resect the involved segment and create a diverting ileostomy and a mucous fistula. These two exteriorized ends can then be anastomosed later.

For radiation colitis or proctitis the procedures should also be individualized but when ulceration leading to bleeding occurs and there is pain and spasm with mild or no stenosis, a diverting colostomy of the transverse or descending colon, followed by closure of the colostomy 6 to 8 months later, may be the operative procedure of choice. For a fistula or stenosis, however, resection with primary closure is preferable, if possible. If not, Hartmann's procedure with secondary closure should be performed. In the event of perforation, Hartmann's procedure is again the treatment of choice. If it is difficult or impossible to resect the perforated segment, diverting colostomy and drainage should be performed. Abdominoperineal resection or pelvic exenteration may be required in certain situations, especially if the low rectosigmoid is involved or if recurrent carcinoma is suspected. In such instances a gracilis myocutaneous flap, as recommended by Palmer and Bush,[13] may help in closing the perineal portion and in decreasing functional disability.

Conclusions

Enterocolitis is the main complication of radiotherapy for carcinoma of the cervix; it occurred in 52 of 441 patients treated over an 11-year period at our institution. Resection, whenever possible, is the operation of choice. However, when resection is not technically possible, bypass may provide satisfactory relief of symptoms and may be followed later by more definitive surgery.

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Mediastinal Lymph-Node Biopsy is a Definitive Staging Procedure for Bronchogenic Carcinoma

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Mediastinal lymph-node biopsy has been performed as a staging procedure in most cases of bronchogenic carcinoma since 1965. This study was carried out to assess the results of staging by this method in 75 patients. Biopsy sites were marked with hemoclips. Three zones were defined: zone 3 (inoperable), beyond the midline and above the lower border of the aortic arch; zone 1 (operable), more than 3 cm from the carina, ipsilateral to the tumour; and zone 2, between zones 1 and 3.

Forty of 75 patients had biopsy specimens showing carcinoma. The proportion was highest in small cell anaplastic carcinoma and lowest in squamous cell tumours. Of the 40 positive biopsies 35 were from zone 3. All the positive biopsy specimens showing small cell anaplastic carcinoma were from zone 3. Positive specimens correlated strongly with other evidence of inoperability. Mediastinal lymph-node biopsy is a definitive staging procedure.

La biopsie des ganglions lymphatiques médiastinaux a été pratiquée comme procédure de classification du stade clinique dans la plupart des cas de cancers broncho-pulmonaires depuis 1965. Cette étude a été réalisée pour évaluer les résultats de classification par cette méthode chez 75 malades. Les localisations de biopsie ont été marquées avec des pinces hémostatiques. Trois zones ont été définies: la zone 3 (inopérable) située au-delà de la ligne médiane et au-dessus de la bordure inférieure des arcs aortiques; la zone 1 (opérable) située à plus de 3 cm de l'éperon,

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ipsilatérale à la tumeur; la zone 2, intermédiaire entre les zones 1 et 3.

Quarante des 75 patients ont eu une biopsie démontrant la présence d'un cancer. La proportion était la plus élevée pour les cancers anaplasiques à petites cellules, et la plus faible pour les épithéliomas. Des 40 biopsies positives, 35 étaient de la zone 3. Toutes les biopsies positives de cancers anaplasiques à petites cellules étaient dans la zone 3. Les échantillons positifs ont montré une forte corrélation avec les autres preuves que la tumeur était inopérable. La biopsie des ganglions lymphatiques médiastinaux est une procédure décisive dans la classification du stade clinique des carcinomes broncho-pulmonaires.

Since 1965 mediastinal lymph-node biopsy has been carried out in most cases of bronchogenic carcinoma as a staging procedure to assess operability and chance of cure. Techniques have been devised by Daniels[1] (scalene node biopsy), Harken and colleagues[2] (cervicomediastinal exploration), Radner[3] (suprasternal biopsy), Carlens[4] (mediastinoscopy through a suprasternal incision), McNeill and Chamberlain[5] (left parasternal mediastinotomy with resection of second and third costal cartilages) and Jolly and associates[6] (left anterior mediastinotomy without cartilage resection). Each procedure has produced better prediction of resectability in patients with lung cancer. This study was performed to correlate the site of positive biopsy with pathological findings, treatment and results.

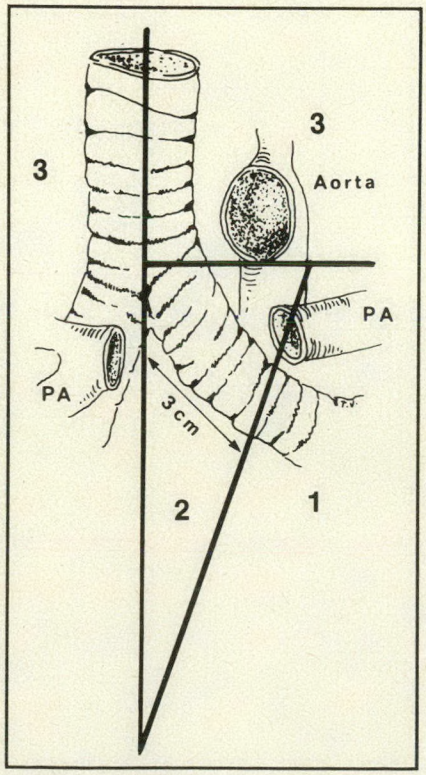


FIG. 1—Three zones defining resectability of tumour.

Method

The Carlens' technique[4] was used for mediastinoscopy in 75 patients with bronchogenic carcinoma for whom resection of the lung was considered. The mediastinal biopsy sites were marked with hemoclips and postoperative chest roentgenograms were obtained.

The sites of the clips were correlated with the cell type of carcinoma and with evidence of operability.

To establish some relation between the site of biopsy and operability of tumours confirmed by biopsy, we defined three zones by which to locate the positive biopsy (Fig. 1). Zone 1, indicating a lesion that was resectable, was more than 3 cm from the carina, along the main bronchus on the side of the tumour. Zone 3, including contralateral and high mediastinal metastases that indicated an inoperable tumour, was beyond the midline or cephalad to the lower edge of the aortic arch. Zone 2 was intermediate between zones 1 and 3.

Results

Biopsy specimens showed malignant cells in 40 of the 75 patients (Table I). Ten of 12 patients with small cell anaplastic carcinoma had positive nodes, but only 18 of 48 patients with squamous cell carcinoma had biopsy specimens that were positive for malignant cells.

The distribution of the positive biopsy specimens by zone is shown in Table II. All the small cell anaplastic carcinomas were in zone 3, indicating that the tumour was inoperable. In the 18 patients with squamous cell carcinoma, 14 of the positive specimens were from zone 3 and 11 of these patients had other evidence of inoperability. In the three less common types of carcinoma, 11 of the 12 metastases were in zone 3.

Eighty-six percent of all patients with positive biopsy specimens had cancer in zone 3, clearly beyond the limits that make surgical cure likely.

A further comparison was carried out between patients having positive mediastinal lymph-node biopsies and other evidence of inoperability, such as a widened mediastinum on chest roentgenogram, superior vena caval obstruction, paralysis of the vocal cords or diaphragm, pleural effusion and evidence of distant metastases. Other evidence of inoperability was present in 22 of the 35 patients with zone 3 biopsy specimens containing malignant cells. In 8 of 10 patients with small cell anaplastic cancer the tumour had metastasized. It is of particular interest that four of the five

Table I—Results of Mediastinal Lymph-Node Biopsy in 75 Cases of Bronchogenic Carcinoma

Type of carcinoma	Positive biopsy	Negative biopsy	Total
Small cell anaplastic	10	2	12
Squamous cell	18	30	48
Adenocarcinoma	6	1	7
Mixed cell	3	1	4
Large cell anaplastic	3	1	4
Total	40	35	75

Table II—Location of Biopsies Showing Evidence of Malignant Tumour according to Cell Type

	Zone			
Type of carcinoma	1	2	3	Total
Small cell anaplastic	0	0	10	10
Squamous cell	0	4	14	18
Adenocarcinoma	0	0	6	6
Mixed cell	0	0	3	3
Large cell	0	1	2	3
Total	0	5	35	40

As the treatment of the patient in shock has progressed in recent years, various organ systems have, in turn, been the "weak link" limiting recovery. The deterioration often becomes apparent first in the kidney where disruption of cellular metabolism causes acute tubular swelling with resulting oliguria.

Soon, the pulmonary vasculature begins to exhibit a pattern of interstitial oedema, pooling of blood in the stagnant microcirculation and aggregation of the formed elements of the blood. Diffusion of oxygen from the alveoli is greatly decreased, commonly resulting in arteriovenous shunting – a phenomenon in which blood passes through the lung without oxygenation.

If the shock state continues, lysosomal enzymes in the anoxic pancreas trigger the release of myocardial depressant factor (MDF), a vasoactive peptide which can cause further deterioration of the microcirculation.

Although cerebral blood flow is maintained early in shock at the expense of the other organs, this state of adequate perfusion does not persist for long. Relatively soon, available oxygen becomes critically low, and the brain, too, turns to anaerobic metabolism. Lactate acid levels rise and fluids leak into the intestitial spaces. Continued oxygen deprivation threatens both the cellular integrity of the brain and the central nervous system function.

Once shock has progressed beyond its early stage, fluid administration alone is usu-

severe shock threatens each link in the body's chain of organ systems

Solu-Medrol exerts a protective effect on the cell to preserve tissue function and increase survival rates

ally not sufficient to reverse the haemodynamic and cellular disruptions.

Solu-Medrol, administered in pharmacologic doses as part of a comprehensive treatment regimen, can reduce vasoconstriction and increase tissue perfusion. The multiphasic activity of Solu-Medrol helps restore haemodynamic balance, preserve lysosome and cell membranes, and protect cellular and intracellular structures and function.

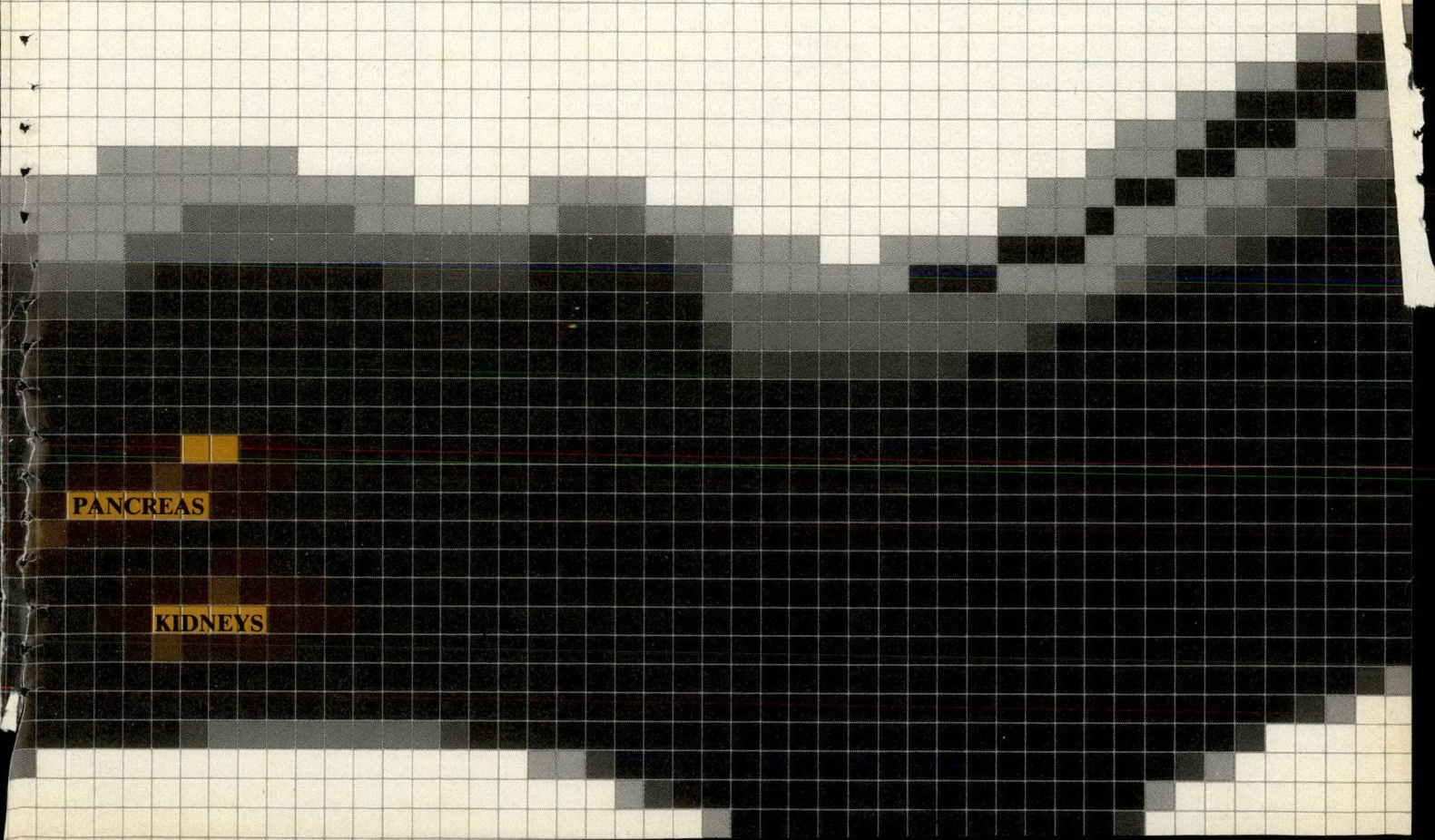
The actions of Solu-Medrol affect all of the body's systems:

- **In the kidney, increased perfusion reverses the anoxic state and improves organ function as evidenced clinically by an increase in urine output.[1]**
- **Improvement in the pulmonary vasculature is demonstrated by a reduction in shunting and an increase in oxygen consumption.[2]**
- **The affinity of haemoglobin for oxygen is reduced permitting increased delivery of oxygen by the blood to the tissues.[3]**
- **A positive inotropic effect is exerted on the heart further increasing the flow of blood.[4]**
- **Pancreatic lysosomes are stabilized halting the production of MDF.[5]**
- **Capillary membranes in the brain are stabilized, and capillary permeability reduced.[6]**

Through its network of protective actions, Solu-Medrol strengthens the chain of organ systems and increases the shock patient's chances of survival.

Solu-Medrol

Upjohn CE 1376.1



patients with positive biopsies in zone 2 had other evidence of inoperability.

Discussion

Carcinoma of the lung is an aggressive neoplasm that metastasizes to lymph nodes early. This is most marked with small cell anaplastic tumours, for which resection is seldom recommended because most patients already have metastases at the time of diagnosis. Tissue diagnosis is therefore mandatory to define cell type and to stage cancer spread. A number of mediastinoscopy procedures have been devised over the last 22 years to accomplish these ends and the present study confirms the value of these procedures.

In performing mediastinal lymph-node biopsies, the main objective was to sample nodes high in the mediastinum and in the subcarinal region. This policy is related to the few positive biopsy specimens obtained from zone 1. Most positive specimens were from zone 3, hence were definitive.

Summary

Seventy-five patients considered for thoracotomy due to cancer of the lung underwent mediastinal lymph-node biopsy through a suprasternal notch incision. The biopsy sites were marked with hemoclips allowing them to be easily located on postoperative chest roentgenograms. The sites were classified and correlated with pathological findings. In 40 patients the biopsy specimens were positive for malignant tumour. Of the entire group, 86% of tumours had metastasized beyond the limits of surgical resectability (zone 3). Twenty-two of the 40 patients with positive biopsy specimens had other evidence of inoperability.

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Right Paraduodenal Hernia

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Right paraduodenal hernias are uncommon. Approximately 50 cases have been reported and 2 more are reported in this paper. The diagnosis of internal hernia should be considered in all patients with abdominal cramps and intermittent small bowel obstruction. The most valuable investigation is roentgenography of the small intestine after barium ingestion; this usually shows a clumping of the intestine, as in a bag, with incomplete rotation of the cecum and ascending colon. Duodenal hernias should be treated surgically even if they are asymptomatic, because they may cause potentially lethal complications such as obstruction, gangrene or bowel perforation.

La hernie paraduodénale droite est une affection rare. Environ 50 cas ont déjà été rapportés et 2 autres sont signalés dans cette publication. Le diagnostic de hernie interne doit être envisagé chez tout patient qui souffre de crampes et d'obstruction intermittente du grêle. L'examen le plus utile est la radiographie de l'intestin grêle après ingestion de barium; ceci met habituellement en évidence une agrégation de l'intestin, comme s'il était dans un sac, avec rotation incomplète du caecum et du côlon ascendant. La hernie duodénale doit être traitée chirurgicalement, même si elle est asymptomatique, car elle peut être la cause de complications létales telles que obstruction, gangrène ou perforation de l'intestin.

Internal hernias are paraduodenal in origin in 30% to 50% of cases. Approximately 75% occur on the left. Right paraduodenal hernia was first described by Treitz;[1] since then, numerous theories concerning the origin of this defect have been proposed.[2-9]

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We report two patients with right paraduodenal hernia, diagnosed preoperatively by roentgenography after barium meal and follow-through examination. We also review the literature with respect to incidence, presenting symptoms and signs, treatment, and morbidity and mortality.

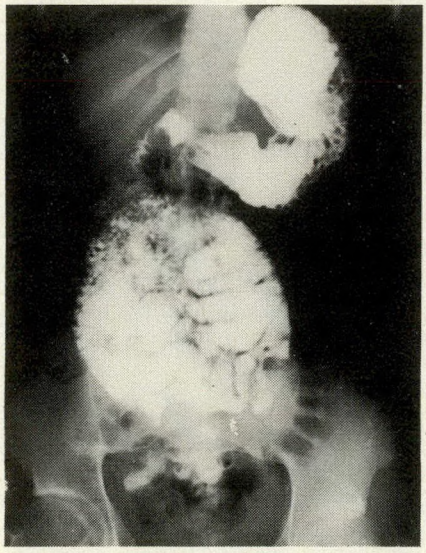

FIG. 1—Case 1. Roentgenogram after barium meal and follow-through. Small bowel appears to be enclosed within a sac.

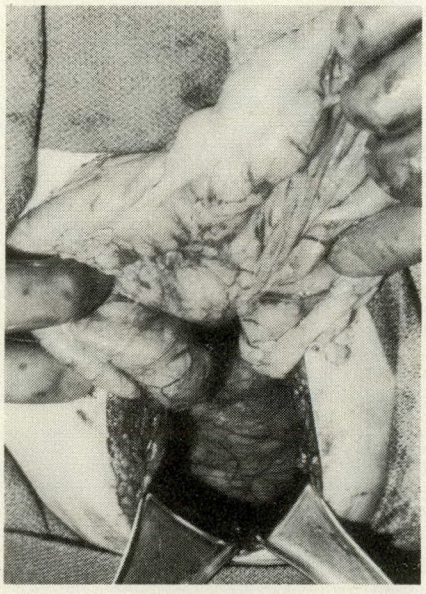

FIG. 2—Case 1. Findings at laparotomy. Transverse colon has been reflected cephalad. Entire small bowel, except for terminal ileum, lies inside large peritoneal sac.

Case Reports

Case 1

A 14-year-old girl had had crampy abdominal pain with occasional nausea for several years. Cramps were most often postprandial. The length of the attacks varied from a few minutes to several hours and on one occasion only, the patient brought up fresh blood. Roentgenography after a barium meal and follow-through examination showed the small bowel as if it were enclosed within an oval sac (Fig. 1). The duodenum was pulled laterally and superiorly. The cecum and ascending colon were incompletely rotated and were lying in the right upper abdominal quadrant.

At laparotomy, the entire small bowel, except for 46 cm of the terminal ileum, was enclosed within the peritoneal sac (Fig. 2). The anterior wall of the sac consisted of the mesentery of the ascending colon.

Ladd's bands were divided, lateral peritoneum was excised, the colon was reflected to the right and the intestine was replaced. The small bowel was thickened and edematous and had enlarged blood vessels, indicating long-standing, incomplete, small bowel obstruction (Fig. 3). The sac was excised and the defect closed with interrupted 3-0 sutures of intestinal chromic catgut. The postoperative course was smooth and the patient was discharged 6 days after the operation.

Case 2

Because of a relapse, this 28-year-old man, who had long-standing ulcerative colitis, was admitted to hospital. He had complained since childhood of crampy abdominal pain with occasional nausea and vomiting. Most of the discomfort was postprandial and attacks lasted occasionally for 1 hour. There was no hematemesis. Since the diagnosis of ul-

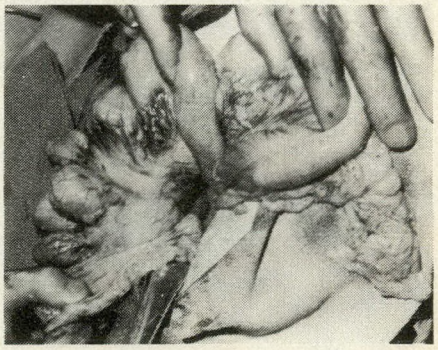

FIG. 3—Case 1. Small bowel is thickened and edematous, with enlarged blood vessels.

cerative colitis had been made, the patient had related most of his cramps and discomfort to that condition.

Roentgenography after barium enema confirmed extensive ulcerative colitis involving the entire rectum and colon, with malrotation (Fig. 4). Abnormal gas distribution in the small bowel was also noted; because of this, roentgenography after barium meal and follow-through examination was carried out and a right paraduodenal hernia was demonstrated (Fig. 5). Most of the loops of small bowel appeared to be enclosed within the sac. This was confirmed during a proctocolectomy. The small bowel was replaced, the sac was excised and the defect closed with 3-0 chromic catgut sutures. A permanent ileostomy was made. Recovery was uncomplicated.

Discussion

More than 50 cases of right paraduodenal hernia have been reported in the English literature since Moynihan's[2] review of autopsy material in 1906. Most of the patients had a long history of gastrointestinal symptoms, nausea and bloating after meals, epigastric and abdominal cramps, inflammation or obstruction of the small bowel. Most patients were adults, with a mean age of 36.6 years. None were younger than 8 years.[3,6,7,10-15] Why this congenital defect does not produce symptoms early in life is unclear. The embryology in the region of the ligament of Treitz was discussed by Berardi.[16] This is where the fixed retroperitoneal duodenum meets the mobile intraperitoneal jejunum, resulting in an appreciable number of variable folds and fossae.

Roentgenography of the small intestine after barium meal is the most valuable investigation. This will show a clumping of the intestine as in a bag, lifting of the axis to the right or left of the midline, the absence of bowel from the pelvis with the terminal ileum outside the sac, a change in bowel calibre at the site of exit from the sac, the presence of the ascending colon behind the mass, incomplete rotation of the cecum and ascending colon, and decreased motility of the entire small bowel.[17,18] Angiography shows the change in direction of the mesenteric vessels as intestinal loops enter and leave the hernial sac.[19]

Treatment of the condition is surgical. Because the leading edge of the hernial sac in the right paraduodenal hernia contains the superior mesenteric artery, one has to be very careful at the time of the operation not to damage it. The contents of the hernial sac are returned to their normal position, adhesions are divided, the superior mesenteric artery is preserved and the defect in the peritoneum is closed. If the sac is large, it should be removed and the defect closed.

Summary

Two cases of right paraduodenal hernia, diagnosed preoperatively, are presented. These hernias may be asymptomatic or cause life-threatening complications.

All paraduodenal hernias, even if asymptomatic, should be considered potentially lethal and capable of causing obstruction, gangrene or perforation of the bowel.

Diagnosis is confirmed by roentgenography after barium meal and follow-through examination.

At the time of operation, care must be taken not to injure the superior mesenteric artery, which is an integral part of the wall of the sac and its orifice.

The diagnosis of internal hernia should be considered in all patients with symptoms of crampy abdominal pain, intermittent small bowel obstruction and vomiting, because a delay in diagnosis may result in increased morbidity and mortality.

I thank Dr. P. Tam for allowing me to include case 2.

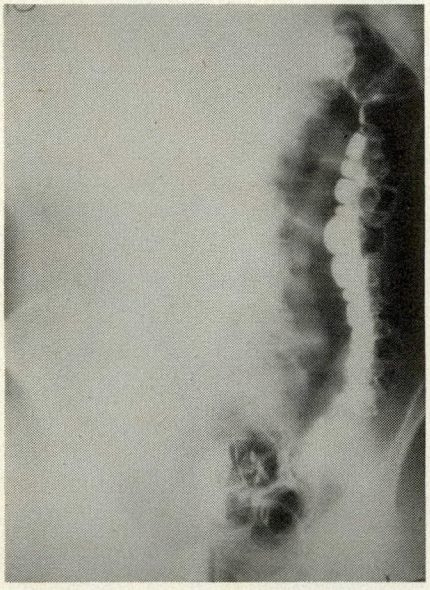

FIG. 4—Case 2. Roentgenogram after barium enema shows malrotation of intestine and long-standing ulcerative colitis.

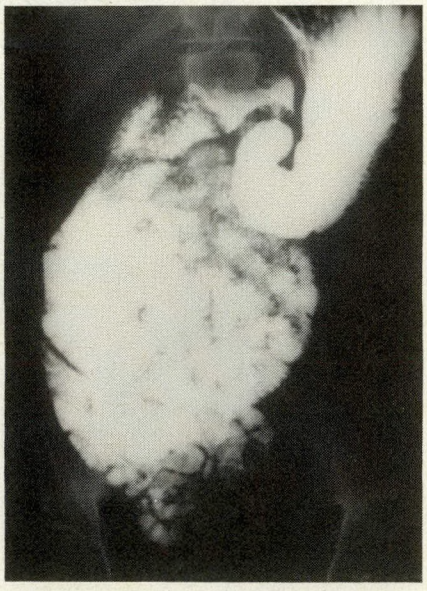

FIG. 5—Case 2. Roentgenogram after barium meal and follow-through demonstrates right paraduodenal hernia.

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Benign Solid Teratoma of the Ovary with Rupture into the Rectum

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The authors present an unusual case of benign, solid, complex teratoma of the ovary with rupture into the rectum. A young woman, investigated for bowel problems, was found to have a prolapsing tumour in the upper rectum. A diagnosis of benign solid teratoma of the ovary was made by histologic examination of the surgical specimen; the tumour had perforated the rectal wall and protruded into the bowel lumen, a most unusual complication for this type of tumour. Pararectal teratomas can arise from either the ovaries or the soft tissues of the sacrococcygeal region. The latter do, on rare occasions, perforate the rectum. The possible mechanisms of rectal perforation by these teratomas are briefly discussed.

Les auteurs présentent un cas de rupture intrarectale d'un tératome bénin et solide de l'ovaire. Lors de l'investigation d'un problème digestif, une tumeur faisant prolapsus fut découverte dans le rectum d'une jeune femme. Le diagnostic ne fut établi que lors de l'examen histologique du spécimen. La tumeur consistait en un tératome solide et bénin de l'ovaire ayant perforé la paroi rectale. Il s'agit d'une complication très inhabituelle de ce type de tumeur. L'origine des tératomes para-rectaux peut être l'ovaire ou les tissus mous de la région sacrococcygienne. Ces derniers ont été décrits comme pouvant perforer à l'intérieur du rectum. Les mécanismes possibles des perforations rectales sont brièvement discutés.

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Rupture of ovarian teratoma into a hollow organ is rare.[1] Few cases of benign cystic teratomas perforating the wall of the rectum have been reported.[2] This paper describes a unique case of a benign, solid, complex teratoma that penetrated the wall of the rectum and protruded into its lumen mimicking rectal tumour.

Case Report

A 26-year-old mother of two children was admitted to the Hôpital du Sacré-Coeur, complaining of pain in the lower right side of the abdomen, which had begun 12 months earlier. The pain was exacerbated by defecation and was associated with tenesmus and the sensation of something prolapsing into the rectum. For a few weeks before admission, the patient had had slight difficulty in passing stools, but she had never noticed any rectal bleeding. Menstruation was regular and there was no vaginal discharge. Examination of the abdomen showed no abnormalities except for slight tenderness on deep palpation of the right iliac fossa.

Routine laboratory investigations gave no abnormal findings. The hemoglobin value was 12.5 g/dl. Roentgenograms after barium double-contrast enema revealed the presence of a well-circumscribed lobulated tumour, about 8 cm in diameter, protruding into the lumen of the upper rectum. This polypoid tumour was confirmed by sigmoidoscopy; it was located 14 cm from the anal margin. Histologic examination of the biopsy specimen showed malpighian cellular metaplasia, but the true nature of the rectal tumour was not recognized.

At laparotomy the right ovary was found to be adherent to the rectal wall and seemed to be in continuity with the intraluminal rectal tumour. The uterus and left ovary appeared normal. En bloc resection of the tumour-bearing segment (12 cm long) of the upper rectum, together with the adherent right ovary and right fallopian tube, was carried out followed by end-to-end anastomosis of the bowel. The postoperative period was uncomplicated and the patient was discharged from hospital 1 week after the operation.

Serial sections of the resected specimen at the junction of the right ovary and the rectal tumour showed that the tumour was actually a solid teratoma of the ovary that had perforated the rectal wall and protruded into the bowel lumen (Fig. 1). On the rectal side of the ovary, the parenchyma was replaced by tumour tissue identical to that of the rectal tumour. It was composed of more or less mature well-differentiated tissues derived from all three germ layers, for example skin (Fig. 2), muscle, fat, bowel

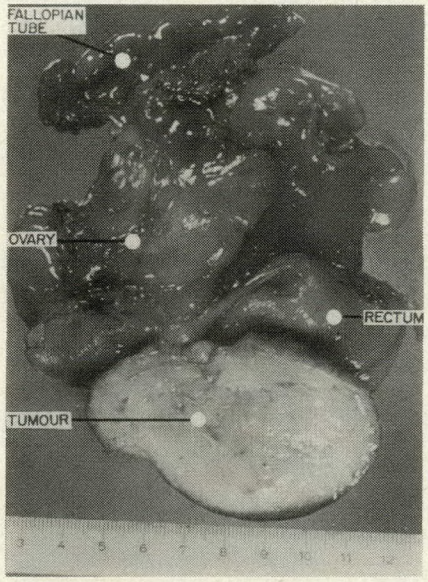

FIG. 1—Cut section of ovarian teratoma with perforation of rectal wall and protrusion into bowel lumen.

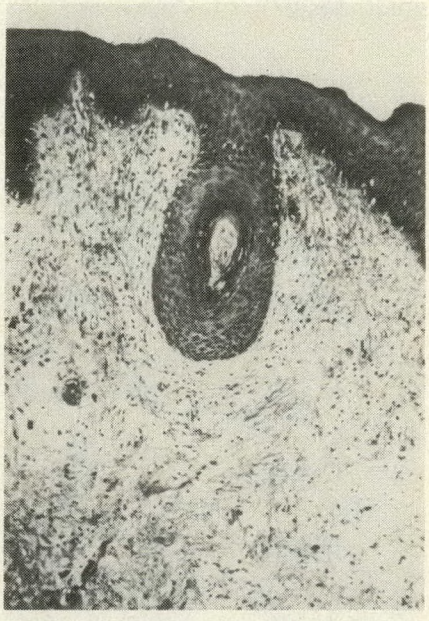

FIG. 2—Surface of polypoid tumour covered by keratinized malpighian epithelial layer with hair follicles (hematoxylin and eosin, reduced by 52% from ×100).

epithelium, respiratory epithelium and eccrine glands (Fig. 3), apocrine glandular structures and meninges (Fig. 4), and nerve fibres. The histologic findings thus described are characteristic of a benign solid teratoma of the ovary.

Discussion

Teratomas of the ovary are usually benign dermoid cysts, but occasionally they are solid lesions. The solid, complex teratoma differs from the dermoid cyst in that it has a more heterogeneous collection of recognizable tissues and organoid structures derived from all three germ layers: ectoderm, mesoderm and endoderm. Almost all cystic ovarian teratomas are benign; only 2% have a malignant component. In sharp contrast, about 20% of solid teratomas show malignant degeneration.[3] Malignant changes may occur in any of the tissues. Immature, solid teratomas may sometimes be accompanied by the dissemination of cellular implants on the peritoneum. Many years ago Peterson,[4] studying a group of such tumours, found that those most likely to show peritoneal dissemination and to recur contained glial tissue. This observation was later confirmed by others.[5-7]

A histologic grading system for solid teratoma of the ovary has been proposed by Thurlbeck and Scully.[8] Based upon the maturity of the component germ-layer elements, the tumours are graded 0 to 3. Grade 3 tumours are the most malignant; they contain large quantities of embryonal immature tissue and the prognosis is poor. Grade 0 neoplasms, to which our case seems to belong, are composed of mature, well-differentiated tissue types and have an innocuous clinical course.

Our case was unusual since the complication in which the solid teratoma of the ovary was involved was so rare. The nature of the rectal tumour remained obscure until it was surgically excised en bloc with the adherent right ovary and the specimen examined microcospically, revealing continuity of the malpighian cell layer of the ovarian tumour on one side with the intrarectal extension of the tumour on the other. This finding confirmed that the rectal teratoma had its origin in the adjacent right ovary.

Teratomas in close proximity to the rectal wall may originate not only from the ovaries but also from the soft tissues of the sacrococcygeal region. Gonadal teratomas are most often found in children or young adults, while those of sacrococcygeal origin tend to be detected in the first few months of life, except for a few that have been recorded in adults.[9] The majority of the sacrococcygeal teratomas present externally, but may have a large internal component. However, a small percentage of these tumours are totally presacral and their presence can only be detected by rectal examination. A few of the sacrococcygeal teratomas, if not resected early in life, may perforate into the rectum;[10] the commonest complications related to these tumours are infection and malignant degeneration.[9]

The possible mechanisms enabling these pararectal teratomas to perforate the bowel wall are thought to be: (a) ischemic pressure necrosis, (b) secondary infection with adhesion to the bowel wall and eventual rupture into the lumen of the rectum and (c) malignant degeneration with direct extension into, and infiltration of, the rectum. Since the tumour in our case was of the mature well-differentiated type with no evidence of malignant change and the histologic sections did not reveal signs of inflammation, the probable reason for rupture of this benign, solid, ovarian teratoma into the rectum was pressure necrosis and devascularization of the bowel wall.

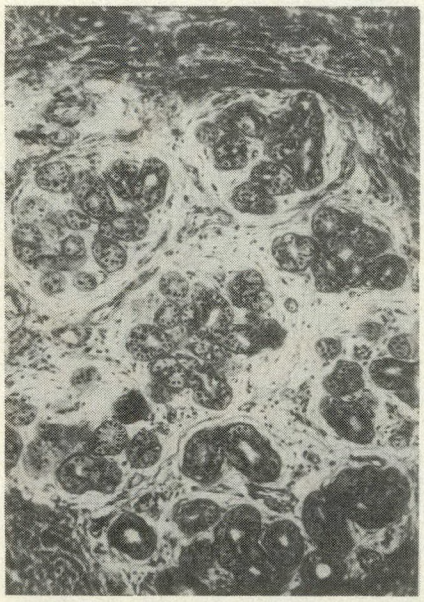

FIG. 3—Eccrine glands (hematoxylin and eosin, reduced by 52% from ×100).

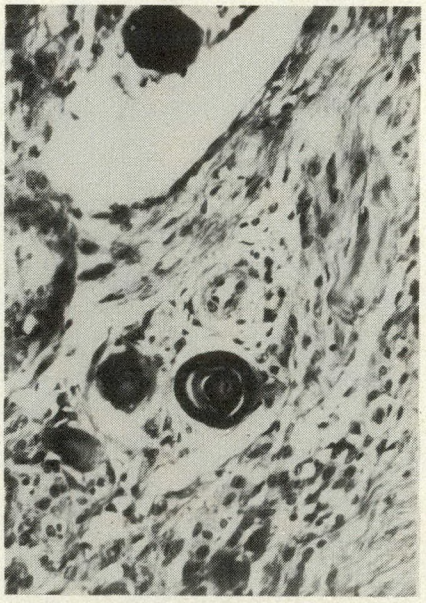

FIG. 4—Meningeal tissue with psammoma bodies (hematoxylin and eosin, reduced by 52% from ×250).

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NOTICES

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Home Study Course in Immunology

The University of Wisconsin is pleased to offer a home study course in immunology. Physicians can enrol at any time and study at their own pace.

The course covers basic concepts about B cells, T cells, neutrophils, macrophages and complement. The concepts are utilized to define a useful clinical approach to patients.

For further information please contact: Home Study-CME, University of Wisconsin, 481 WARF Building, 610 Walnut St., Madison, Wisconsin 53706, or call (608) 263-2853.

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Retroperitoneal Leiomyoma with Periorbital and Peripheral Edema

D.C. Drinkwater, Jr., md, J.O. Lough, md, frcp[c] and R.A. Brown, md, frcs[c]

Removal of a large retroperitoneal leiomyoma from a 51-year-old woman resulted in complete resolution of periorbital edema and pitting edema of the hands and feet from which she had suffered for 8 months. Cardiac, renal and dietary studies gave normal results. The diagnosis of leiomyoma, which is uncommon in the retroperitoneal region, was supported by the findings on light and electron microscopy. The patient remains asymptomatic after 3 years. The association of such widespread edema with a retroperitoneal tumour is rare; the cause is unknown.

L'ablation d'un gros léiomyome rétropéritonéal chez une femme de 51 ans a entraîné la résolution complète d'un oedème périorbitaire et d'un oedème en godet des mains et des pieds, dont elle souffrait depuis 8 mois. Les études cardiaque, rénale et diététique ont donné des résultats normaux. Le diagnostic de léiomyome, dont la localisation rétropéritonéale est rare, a reposé sur les observations de microscopie optique et électronique. La patiente demeure asymptomatique après 3 ans. L'association d'un oedème aussi étendu avec une tumeur rétropéritonéale est rare; la cause en est inconnue.

Periorbital edema and edema of the hands and feet is an unusual manifestation of retroperitoneal leiomyoma. In no recent review has it been reported. The purpose of this paper is to record this rare finding and to note that there was complete resolution of the condition after surgical extirpation of the mass and for a follow-up period of 3 years.

Case Report

A 51-year-old woman was admitted to hospital for evaluation and treatment of an abdominal mass. Six months earlier she had noticed swelling of her hands and feet and around her eyes on rising each morning. At the end of the day the swelling was limited to her lower extremities. A salt-restricted diet, elevation of the legs and use of support stockings had no appreciable effect. She denied any weight loss, fatigue, polydypsia or polyphagia. The cardiovascular system was normal and there was no history of hypertension, or cardiac or renal disease. The vital signs were normal. She was moderately obese. Symmetrical periorbital edema, severe pitting edema of the ankles and feet and mild pitting edema of the hands were noted. A 6 × 8-cm, nontender, firm, nonpulsatile mass was palpated in the midabdomen on the right side. The rest of the abdominal findings were unremarkable. The findings on neurologic examination were normal. There was no lymphadenopathy.

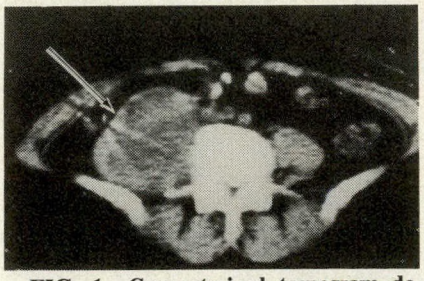

FIG. 1—Computerized tomogram demonstrating right retroperitoneal mass (arrow), immediately adjacent to and contiguous with vertebral bodies.

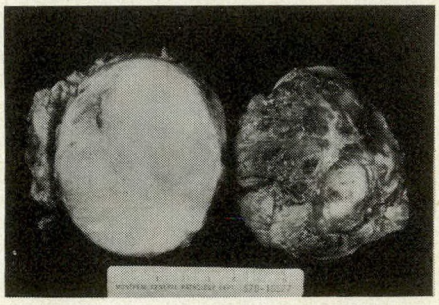

FIG. 2—Circumscribed leiomyoma after removal from right psoas muscle.

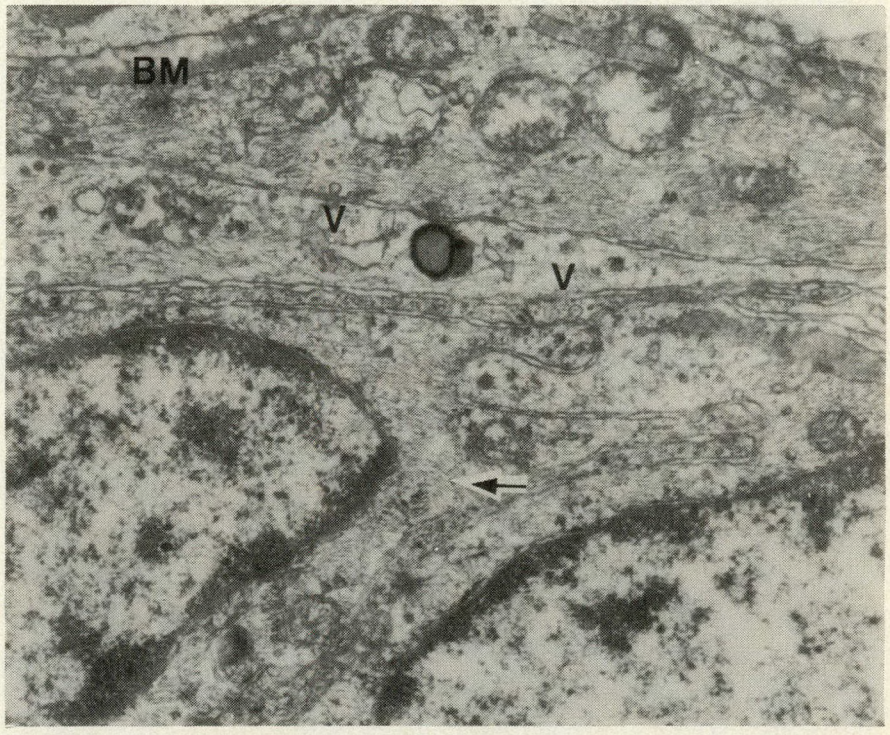

FIG. 3—Electron-microscopic section showing ovoid nuclei with cytoplasmic myofilaments, pinocytic vesicles (V), attachment zones (arrow) and basement membrane (BM), all characteristic of smooth muscle (uranyl acetate and lead citrate stain, reduced by 7% from ×3700).

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The results of routine laboratory investigations were within normal limits. Endocrine tests, however, showed a urine free cortisol value of 115 mg/d (normal 10 to 12 mg/d), 17-hydroxysteroids 2.3 mg/d (normal 2 to 6 mg/d), 17-ketogenic steroids 5.6 mg/d (normal 7 to 12 mg/d), 17-ketosteroids 7.5 mg/d (normal 6 to 15 mg/d) and vanillylmandelic acid 2.2 mg/d (normal 1 to 5 mg/d) on proper diet. Her morning and evening blood cortisol levels were 233 and 83 μg/l respectively (normal 50 to 250 μg/l).

Intravenous pyelography demonstrated that the mass was situated lateral and inferior to the right kidney but did not involve it or the ureter. Ultrasonography confirmed that the 8 × 6-cm mass was noncystic and separate from the kidney. Computerized tomography (Fig. 1) showed a large, fusiform, low-density mass in the right psoas muscle, displacing the caudal portion of the vena cava medially. This was compatible with a leiomyosarcoma or a rhabdomyosarcoma. There was no bone destruction.

At operation a 9 × 7-cm mass was found in the right psoas muscle. Grossly it was well encapsulated, with attachment to the adjacent vertebral bodies of L4 and L5. There was no obstruction of the inferior vena cava and no other organs were involved. Removal of the mass from the psoas muscle was facilitated by previous retrograde catheterization of the right ureter.

Grossly, the mass (Fig. 2), weighing 239 g, was contained within a smooth shiny capsule. The sectioned surface was firm and yellow. There was no necrosis or hemorrhage. Microscopically, the mass was well circumscribed but no definite capsule was noted. There were uniform, interlacing bundles of cells with sausage-shaped nuclei and scanty cytoplasm in a fibrillar stroma. The cells were rarely pleomorphic with only occasional mitoses. Electron microscopy confirmed the diagnosis of leiomyoma by showing myofilament attachment zones, pinocytic vesicles and a basement membrane (Fig. 3).

The perioperative course was uncomplicated and 8 days postoperatively the patient was discharged from hospital. She was on a regular diet and was not taking diuretics. She had no evidence of swelling. Three years later she was asymptomatic and the edema had not recurred.

Discussion

Benign smooth muscle tumour (leiomyoma) of the retroperitoneal region is relatively rare and is less common than its malignant counterpart leiomyosarcoma. In a review by Braasch and Mon[1] of retroperitoneal tumours treated at the Lahey Clinic from 1930 to 1960, only 2 of 101 tumours were leiomyomas. This infrequency was confirmed in a recent study of 100 patients with smooth muscle tumours by Ranchod and Kempson,[2] in which no retroperitoneal leiomyomas were noted.

Peripheral extremity (hands and feet) and periorbital swelling in the absence of renal, cardiovascular or dietary deficiencies has not to our knowledge been described in association with retroperitoneal tumours. Common presenting signs and symptoms of retroperitoneal tumours are abdominal pain, abdominal mass, weight loss, anorexia, nausea and vomiting. Hypoglycemia has been reported in association with fibrosarcomas.[3] An infrequent finding is swelling confined to the lower extremity due to inferior vena caval obstruction; this was reported in 17% of cases in a recent series of primary retroperitoneal tumours by Bose.[4] Perry and associates[5] reported a case of total occlusion of the abdominal aorta by a malignant fibrous histiocytoma, and Rossi and Libertino[6] reported a case of neurocutaneous syndrome associated with a retroperitoneal lymphangioma.

Because of the diffuse nature of our patient's edema, it is unlikely that the cause was obstructive or mechanical. There was also no evidence of a hormonal, renal or dietary deficiency or of origin in nervous tissue. Perhaps future observations will help to clarify the precise mechanism of this unusual association of a retroperitoneal leiomyoma and diffuse edema.

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Correction

In the November 1981 issue, the section in the List of Contents and the flag on page 591 headed "Canadian Association of General Surgeons" should have read "Canadian Association of Clinical Surgeons". The Journal apologizes for this proofreading error to the authors of all papers included in that section and to members of the two associations.

Early Gastric Cancer

C. HEUGHAN, B CHIR, FRCS, FRCS[C], FACS, D. KEPKAY, MD, FRCP[C], A.M. CRUZ, MD AND H. IDIKIO, MB, BS, FRCP[C]

Early gastric cancer confined to the mucosa or submucosa, similar to that described in the Japanese literature, exists in Newfoundland, an area of North America in which gastric cancer is four times more prevalent than on the rest of the continent. If untreated, this early gastric cancer will progress to advanced disease.

The clinical presentation of 10 patients suffering from cancer confined to the mucosa and submucosa of the stomach is described.

The disease presents with acute or chronic bleeding or unexplained dyspepsia; no abnormality of the stomach can be seen on roentgenograms. The diagnosis may be suspected at endoscopic examination. Cytologic studies using touch preparations may be suggestive but the diagnosis should be confirmed by biopsy before operation is performed.

Le cancer précoce de l'estomac confiné à la muqueuse ou à la sous-muqueuse, semblable à ce qui est décrit dans la littérature japonaise, existe à Terre-Neuve, une région d'Amérique du Nord où le cancer gastrique est quatre fois plus fréquent que sur le reste du continent. Non traité, ce cancer précoce de l'estomac évolue vers une maladie de stade avancé.

On décrit le tableau clinique de 10 malades souffrant d'un cancer confiné à la muqueuse ou à la sous-muqueuse gastrique.

La maladie apparaît sous la forme d'un saignement aigu ou chronique ou d'une dyspepsie inexpliquée; aucune anomalie de l'estomac n'est révélée à la radiographie. Le diagnostic peut être soupçonné à l'examen endoscopique. Les études cytologiques peuvent être évocatrices mais le diagnostic doit être confirmé par une biopsie avant de procéder à l'opération.

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The prognosis for gastric cancer in North America is dismal. Only about 50% of patients who have gastric cancer undergo and survive resection and only about 15% are alive after 5 years.

In Japan, by contrast, Yamagata and associates[1] and Kidokoro[2] have reported a 5-year survival rate of over 90% in patients treated surgically for cancer limited to the mucosa or submucosa. Furthermore, in over one third of Japanese patients with carcinoma of the stomach, the disease is diagnosed when it is still confined to the superficial layers. If the biology of gastric cancer in North America is the same as in Japan, the high proportion of early tumours diagnosed in Japanese series must be due to better diagnostic techniques, including the use of mass screening by gastrocamera, double-contrast upper gastrointestinal roentgenography and the liberal use of endoscopy and biopsy. The differences in prognosis and incidence have raised some doubt as to whether cancer of the stomach is the same disease in North America as in Japan.

The chances of North Americans accepting mass screening by gastrocamera are remote, particularly since the incidence of gastric cancer is low compared with that in Japan and is falling. North American practice must, therefore, be directed towards diagnosing mucosal cancer in patients who present with upper gastrointestinal symptoms.

Gastric Cancer in Newfoundland

The majority of the 550 000 inhabitants of Newfoundland are of British or Irish descent.

Pfeiffer and colleagues[3] documented a mortality from gastric cancer in men of 30 per 100 000 in Newfoundland, a figure approximately four times higher than those reported in the United States and mainland Canada, but somewhat lower than comparable figures for Japan, Chile and Iceland. The mortality in Newfoundland shows a notable regional variation and Newfoundlanders who take up residence in mainland Canada are subject to the low mainland rates.

The provincial cancer registry reports approximately 100 new patients per year with gastric carcinoma.

This paper reviews our experience with 10 mucosal cancers seen in one hospital over an 8-year period. In eight patients, the diagnosis of cancer was made before gastrectomy. Pathological examination confirmed the diagnosis of cancer limited to the mucosa and submucosa in all 10 patients.

Patients and Methods

Patient records from the General Hospital in St. John's were reviewed for the period July 1, 1972 to Mar. 31, 1980. The pathologic features of 10 patients having mucosal disease were reviewed. Ages ranged from 43 to 76 years; five patients were in their seventh decade. Six of the 10 were men. Eight patients were diagnosed as having gastric cancer before operation.

Four of the 10 patients presented with bleeding; 3 noted hematemesis or melena and 1 patient had iron deficiency anemia. Four other patients complained of dyspepsia, one other had anorexia and weight loss and one an acute exacerbation of ulcer pain.

All patients but one underwent conventional roentgenography after a barium meal. Eight patients underwent endoscopic examination with conventional equipment. Four to six biopsy specimens were taken from any suspicious lesions and touch preparations were made on ground glass slides, which were immediately sprayed with fixative. We routinely use touch preparation of individual specimens for cytologic examination. This preparation contains fewer red cells than brushings, and abnormal mucosal cells print more readily onto the ground glass than do normal mucosal cells. Both of these features make the study of individual cells easier. Standard criteria for malignancy applied. The mucosal biopsy specimens were then fixed in formalin solution and embedded in paraffin. Serial sections were cut and stained with hematoxylin and eosin for light microscopy.

All patients underwent a conventional gastrectomy with no attempt at aggressive removal of the lymph nodes draining the stomach.

Findings and Discussion

Conventional contrast roentgenography after barium meal did not suggest a diagnosis of cancer in any of the nine patients who had this examination. In four of the nine, gastric ulceration was demonstrated. The other five patients had roentgenograms that either appeared normal or demonstrated a duodenal lesion that was not confirmed by endoscopic examination.

The endoscopic appearance of the lesions was suspicious of cancer in five of nine patients. In nine patients the cytologic examination and biopsy specimens (Figs. 1 to 3) were judged to show malignant tumours and this was confirmed on examination of the resected specimens. The notable features of these lesions were irregular shape and dirty, grey slough in the ulcer base. They were only 4 or 5 mm in size and sometimes contiguous with the edge of a benign gastric ulcer. Distortion of the folds approaching the ulcer has been of little diagnostic value in the acute phase due to surrounding edema. Healing of an ulcer is no guarantee of benignity in these mucosal lesions.

Although no aggressive attempt was made to remove the lymph nodes from the stomach, in one later patient (not included in our group of 10 patients) a single node close to a cancer confined to the submucosa contained metastatic tumour. In none of the 10 patients reported in this series were any lymph nodes affected.

All the tumours were in the distal part of the stomach so total gastrectomy was not necessary either on technical grounds or for reasons of cancer cure. So far no patient has shown evidence of recurrence; the longest follow-up is 6 years.

In 1 of our 10 patients the proximal margin of resection passed through a mucosal cancer. Seven years later he returned with a massive tumour. This clearly illustrates how important it is for the operating surgeon to know the location of the tumour since there is nothing to see or to feel from the serosal surface.

The two growths that were protuberant were sessile, both were less than 1 cm in diameter and appeared to be covered by mucosa. When biopsy was performed both were friable and bled easily.

Eight of the 10 lesions were depressed or ulcerated. This proportion is similar to that reported by Sakita[4] in a series of 421 superficial cancers.

It should be noted that a number of patients not included in this series have shown suspicious or frankly malignant cells on cytologic examination of gastric ulcers. In most, this abnormality has reverted to normal as the lesions healed. Two patients, however, underwent gastrectomy because the malignant appearance of cells on cytologic examination persisted; in neither patient did the resected specimen show any evidence of cancer.

Three of the 10 patients are worthy of special mention. One had a gastrectomy for gastric cancer in 1963. The growth infiltrated the muscle coat; no nodes were involved. Postoperatively, he complained of bloating and pain. Numerous endoscopic examinations and roentgenograms made after barium meal showed bile gastritis and on one occasion a food bezoar was broken up during endoscopy. Another endoscopic examination in 1973 showed an area of slough on the gastric side of the stomach. Cytologic examination and biopsy specimens showed malignant cells, so a revision gastrectomy was performed. The resected specimen confirmed mucosal disease. The patient's symptoms were unchanged when he died in 1976 of a presumed myocardial infarction; no autopsy was performed.

A second patient presented with a 3-week history of anorexia and weight loss. Roentgenography after barium meal suggested linitis plastica, which was confirmed at endoscopic examination. In addition to a deformed aperistaltic antrum, a raised area in the antrum was demonstrated; a biopsy specimen of the raised area showed carcinoma. At laparotomy, the stomach appeared normal and a blind 50% gastrectomy was performed. The resected specimen contained an area of carcinoma confined to the mucosa and submucosa.

The third patient underwent a gastrectomy for cancer. The tumour was confined to the mucosa but the resected margin was not clear of tumour. He was lost to follow-up for 7 years when he was referred again with episodes of dyspepsia and hematemesis associated with alcoholic binge drinking. An extensive adenocarcinoma was found at the suture line and was judged to be unresectable.

We had no problems with postgastrectomy syndromes except for one patient who required revision of his Bilroth II gastrectomy to a Roux-en-Y stoma because of bilious vomiting.

Four patients have been followed up for 3 years or more.

Conclusions

There are very few references to

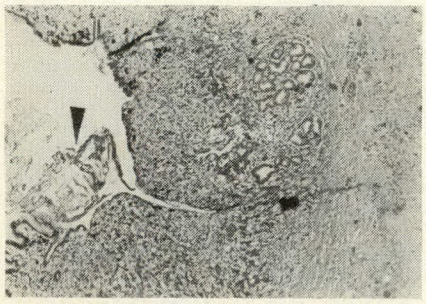

FIG. 1—Gastric ulcer with inflammatory cells at base. At left hand edge is area of cancer (arrow) superficial to muscularis mucosae (hematoxylin and eosin, reduced by 50% from ×50).

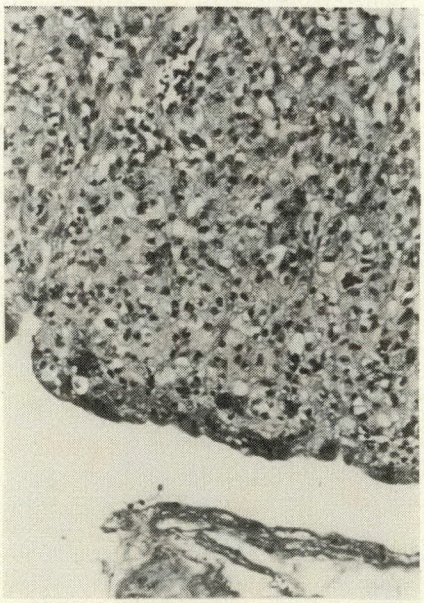

FIG. 2—Higher power view of edge of ulcer shown in Fig. 1 (reduced by 32% from ×200).

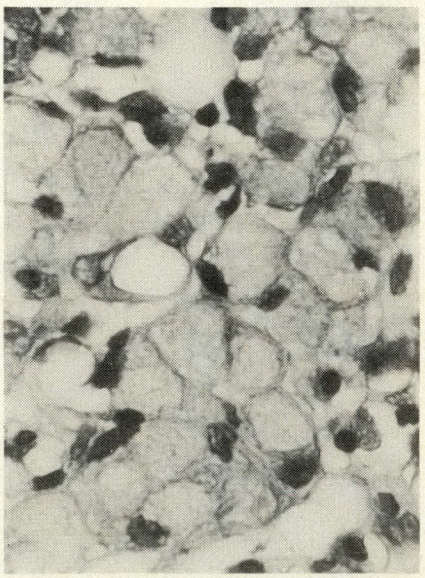

FIG. 3—High power view showing cluster of malignant "signet-ring" cells (hematoxylin and eosin, reduced by 32% from ×500).

the clinical syndrome of early gastric cancer in the North American literature. Hence, we believe it is important to report this small series and to draw some tentative conclusions.

Early cancer should be suspected in any patient over 40 years of age who presents with acute or chronic upper gastrointestinal blood loss or dyspepsia with no radiologically demonstrable cause or with any gastric lesions shown on a roentgenogram regardless of the appearance. The optimal time for endoscopic examination is during a healing phase when the surrounding edema has subsided and interpretation of the touch preparations is more reliable because the changes due to inflammation and regeneration are less marked.

Before operation is carried out the diagnosis should be confirmed by biopsy and in equivocal cases repeated examinations should be performed and specimens taken until a definite answer is obtained. It is likely that the urgency with which suspected cancer is traditionally treated may be inappropriate.

The gastric remnant that is left following partial gastrectomy is subject to the same genetic and environmental influences that induced the original tumour. Therefore, long-term follow-up by regular endoscopic examination is desirable. In our series, geographic, economic and logistic difficulties prevented this.

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Cesarean Section: Recent Trends

MARKUS C. MARTIN, MD, CM, FRCS[C], FACOG, STAN MOYYEN, MD AND MORRIE GELFAND, MD, FRCS[C], FACOG

There has been a rapid increase in the number of cesarean sections performed. At the Sir Mortimer B. Davis-Jewish General Hospital in Montreal, the authors reviewed the records of all cesarean sections performed between Jan. 1, 1973 and Dec. 31, 1979. The rate increased from 10.8% in 1973 to 19% in 1977, due primarily to an increasing trend to diagnose, and perform cesarean section for, dystocia. All breech presentations are also delivered by cesarean section but fewer cesarean sections are being performed for fetal distress. Cesarean section is still a major operation and the procedure is associated with substantial maternal morbidity.

Il y a eu une augmentation rapide du nombre des césariennes. A l'Hôpital Juif-Sir Mortimer B. Davis de Montréal, les auteurs ont étudié les dossiers des césariennes pratiquées entre le 1er janvier 1973 et le 31 décembre 1979. Le taux a augmenté de 10.8% en 1973 à 19% en 1977, et ceci est principalement dû à la tendance grandissante de diagnostiquer les dystocies et à pratiquer dans ces cas une césarienne. Toutes les présentations par le siège sont aussi accouchées par césarienne mais moins de césariennes sont effectuées dans les cas de souffrance foetale. La césarienne demeure une opération majeure et cette intervention est rattachée à une morbidité maternelle importante.

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The European[1,2] and American[3-5] literature has indicated a rapid increase in the number of cesarean sections being performed during the past few years. This has received much scrutiny[6,7] because any deviation from the status quo in patient management requires, at least, a decrease in the risk-to-benefit ratio. With any surgical procedure there is an inherent risk, but with the advent of safer anesthetic procedures this risk has been diminishing. The benefit derived from the increasing rate of cesarean sections as measured by improved perinatal outcome is more difficult to document.[8] In this paper we study the trend in cesarean section rates at the Sir Mortimer B. Davis-Jewish General Hospital in Montreal, compare our rates and indications with other major centres and evaluate the rate of maternal complications associated with cesarean section.

Methods

The records of deliveries from Jan. 1, 1973 to Dec. 31, 1979 at the Jewish General Hospital were reviewed. Two of us (M.C.M. and S.M.) studied all the available charts of patients who underwent cesarean section and collated the appropriate data for the calendar years 1973, 1976 and 1978. The perinatal mortality was assessed for each year from 1973 until 1979. For our definitions, we adopted the commonly accepted terms used by the American College of Obstetricians and Gynecologists.

Findings

During the 7-year period of the study, there were 15 929 deliveries of which 2406 were by cesarean section (Table I). The percentage of cesarean sections performed increased from 10.8% in 1973 to a high of 19% in 1977 (Fig. 1).

Table I—Number of Deliveries and Cesarean Sections by Year

Year	No. of deliveries	No. of cesarean sections (%)
1973	1 719	186 (10.8)
1974	2 361	248 (10.5)
1975	2 342	308 (13.2)
1976	2 409	358 (14.9)
1977	2 394	455 (19.0)
1978	2 334	424 (18.2)
1979	2 370	427 (18.0)
	15 929	2 406 (15.1)

It is not only at our institution, but also across North America, that notable changes are occurring in the rate of cesarean sections performed. In 1975, the Mayo Clinic paper[9] showed a minimal rise with an absolute rate of 3.7%. But thereafter numerous papers, all showing much more marked increases in the rate, rapidly changed the accepted norms.

What is most striking about our data is the lack of correlation between our rising cesarean section rate after 1974 and our stable perinatal mortality (Fig. 1). Minkoff and Schwarz[10] noted a similar absence of correlation at their institution after 1972. This has been further confirmed by the upper New York state group[11] who noted that the number of cesarean sections performed correlated with the perinatal mortality in 1968/9, but not in 1977/8.

Public versus Private

The number and percentages of deliveries and cesarean sections among private and public patients in 1978 are shown in Table II. The overall rate was 18%; 64% were primary and 36% repeat cesarean sections. Among public patients the cesarean section rate was 23.3%, 85% of which consisted of primary procedures. Among the private sector the total rate was 18% but the primary cesarean sections accounted for only 63%.

Anesthesia

In 1978, the majority of cesarean sections were done under general anesthesia. However, epidural analgesia was used in more than 25%. This was a substantial increase over our 1973 figures, in which less than 5% of patients had epidural anesthesia (Table III).

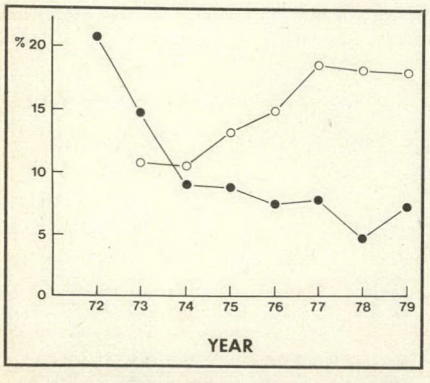


FIG. 1—Percentage of all deliveries performed by cesarean section (white circles) and perinatal mortality per 1000 infants weighing over 1000 g (black circles), from 1973 to 1979.

Age

Fig. 2 illustrates the changing patterns from 1973 to 1978 in the ages of women who had a primary cesarean section. The most striking feature was the increase in cesarean sections among multiparous patients, shattering the misconception that such women are immune to the need for cesarean section. Furthermore, among the multiparous women, the average age was increased. In 1978 the largest group of women who underwent cesa-

Table II—Number and Percentage of Deliveries and Cesarean Sections among Public and Private Patients in 1978

Type of patient	No. of deliveries (%)	No. of cesarean sections (%) Total	Primary	Repeat
Public	86 (3.7)	20 (23.3*)	17 (85)	3 (15)
Private	2 248 (96.3)	404 (18.0*)	254 (63)	150 (37)
	2 334 (100.0)	424 (18.2*)	271 (64)	153 (36)

*% of all deliveries performed by cesarean section.

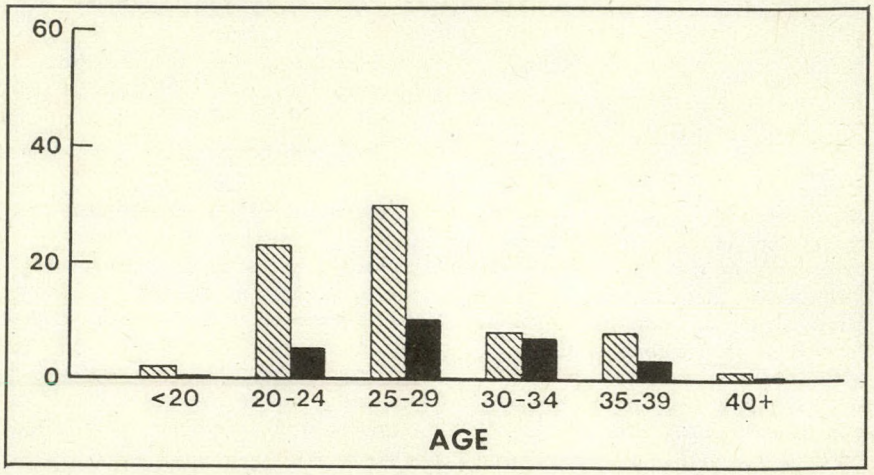


Fig. 2a

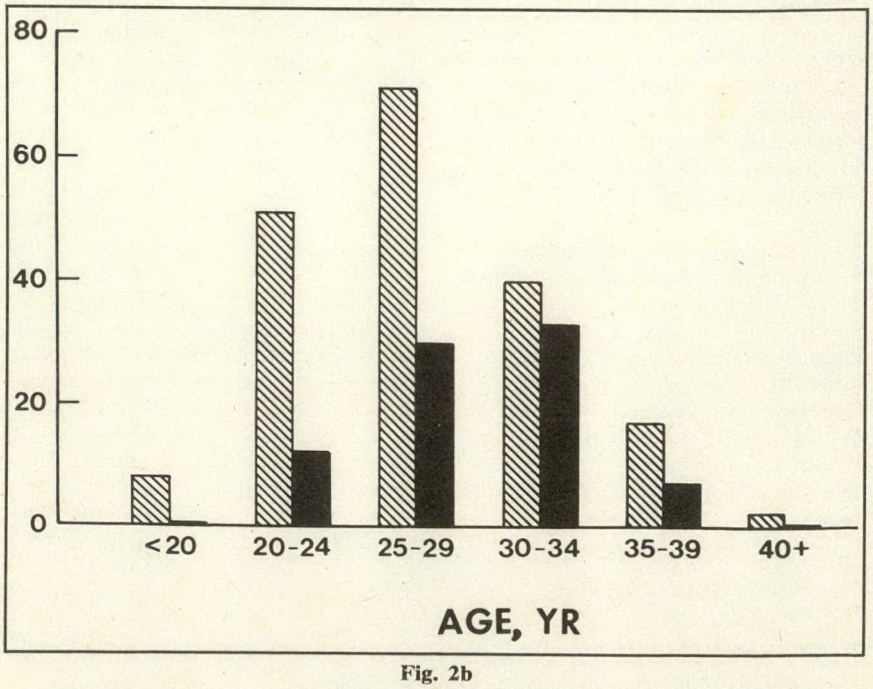


Fig. 2b

FIG. 2—Number of primary cesarean sections performed by patient age, (a) in 1973, (b) in 1978. Hatched bars = primiparous, solid bars = multiparous.

Table III—Types of Anesthesia Used in 1973 and 1978

Type of anesthesia	No. of cesarean sections (%) 1973*	1978
General	163 (94.2)	304 (71.7)
Epidural	8 (4.6)	120 (28.3)
Local	2 (1.2)	—
Total	173 (100.0)	424 (100.0)

*13 charts could not be found.

rean section was in the age range 30 to 34 years.

Indications

The indications for primary cesarean section in 1973, 1976 and 1978 are shown respectively in Tables IV, V and VI.

Our commonest indication was dystocia, which was responsible for over 30% of all cesarean sections. Among primiparous patients it was responsible for over 50% of all sections.

Table IV—Indications for Cesarean Section in 173 Patients, 1973*

Indication	Primiparous, no. (%)	Multiparous, no. (%)	Total, no. (%)	% of all deliveries
Repeat	0 (0)	76 (100)	76 (43.9)	4.4
Primary	72 (74.2)	25 (25.8)	97 (56.1)	5.6
Dystocia	44 (61.1)	9 (36)	53 (30.6)	3.1
Breech	5 (6.9)	3 (12)	8 (4.6)	0.5
Cord prolapse	1 (1.4)	0 (0)	1 (0.6)	0.1
Fetal distress	9 (12.5)	5 (20)	14 (8.1)	0.8
Placenta previa	3 (4.2)	4 (16)	7 (4.0)	0.4
Abruptio placentae	5 (6.9)	1 (4)	6 (3.5)	0.3
Previous surgery	3 (4.2)	0 (0)	3 (1.7)	0.2
Miscellaneous	2 (2.8)	3 (12)	5 (2.9)	0.3

*13 charts could not be traced.

Table V—Indications for Cesarean Section, 1976

Indication	No. of cesarean sections (%)	% of all deliveries
Repeat	104 (29)	4.3
Primary	254 (71)	10.5
Dystocia	120 (33.5)	5.0
Cephalopelvic disproportion	72 (20.1)	3.0
Lack of progress	48 (13.4)	2.0
Breech	41 (11.5)	1.7
Cord prolapse	3 (0.8)	0.1
Fetal distress	54 (15.1)	2.2
Placenta previa	2 (0.6)	0.1
Abruptio placentae	2 (0.6)	0.1
Toxemia	8 (2.2)	0.3
Previous surgery	2 (0.6)	0.1
Miscellaneous	22 (6.1)	0.9

Table VI—Indications for Cesarean Section, 1978

Indication	Primiparous, no. (%)	Multiparous, no. (%)	Total, no. (%)	% of all deliveries
Repeat	0 (0)	153 (100)	153 (36)	6.6
Primary	189 (69.7)	82 (30.3)	271 (64)	11.6
Dystocia	106 (56.1)	24 (29.3)	130 (30.7)	5.6
Breech	35 (18.5)	25 (30.5)	60 (14.2)	2.6
Cord prolapse	0 (0)	2 (2.4)	2 (0.5)	0.1
Fetal distress	26 (13.8)	9 (11.0)	35 (8.3)	1.5
Placenta previa	4 (2.1)	7 (8.5)	11 (2.6)	0.5
Abruptio placentae	1 (0.5)	1 (1.2)	2 (0.5)	0.1
Previous surgery	3 (1.6)	1 (1.2)	4 (0.9)	0.2
Miscellaneous	14 (7.4)	13 (15.9)	27 (6.4)	1.2

Our repeat cesarean section rate was phenomenally high in 1973 — almost 44%. However, more recently it has been in the 30% to 35% range, which is much closer to the acceptable rate in the obstetrical literature.[12]

In 1973, breech presentation was a minor indication, being responsible for less than 5%. In 1976 it was responsible for 11% of cesarean sections and by 1978 it accounted for almost 15% of cases. Again these figures compare well with those in the literature.[12]

Fetal distress traced an interesting pattern during the 1970s. In 1973 it was responsible for 8.1% of all sections, but in 1976 coinciding with the increase in electronic fetal monitoring there was a dramatic doubling of the percentage, to 15.1. In 1978, as a result of increasing expertise in fetal monitoring, we are back to a rate of 8.3%.

The Canadian PAS study of 1976[13] reported that one third of cesarean sections were due to dystocia, 28% were repeat and only 5.6% were due to fetal distress.

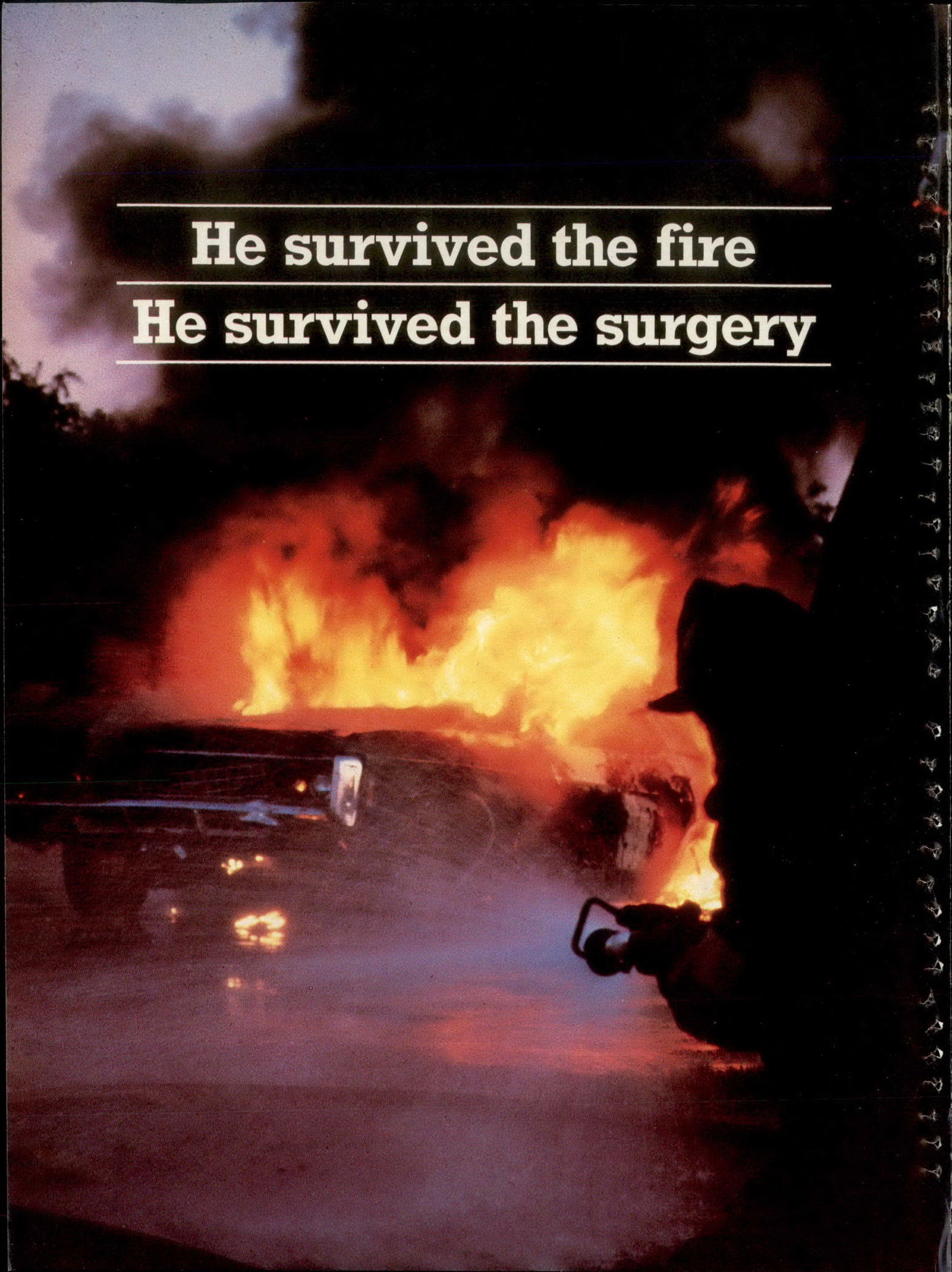
There has been no change with respect to the minor indications such as placenta previa, previous surgery and abruptio placentae. They accounted for approximately 10% of the cases in 1973 and in 1978.

The most remarkable finding has been the rise in the percentage of infants delivered by primary section; in 1973 the percentage was only 5.6, in 1976 it was 10.5 and in 1978 it was 11.6. This correlates with the three main indications for cesarean section, which also rose rapidly during this period.

Maternal Complications

Overall, maternal death is extremely uncommon. At our institution no death was reported in 1973 or in 1978.

Maternal morbidity, however, was common, with infections constituting the largest portion. Endometritis and urinary tract infections were predominant among women who had primary cesarean section, compared with those who underwent elective repeat cesarean section (Table VII). In 1973, urinary tract infection developed in over 25% of women who had cesarean section, but in 1978 it occurred in only 5% (Table VIII). The frequency of endometritis also decreased, from 16% to 7%. Thus, a definite trend in reduced febrile morbidity has made this major operative procedure much more palatable to the professional and general population.


He survived the fire
He survived the surgery

Discussion

Analysis of the short- and long-term trends for cesarean section at our institution showed us that after an initial increase in the mid 1970s. we have stabilized the frequency of cesarean sections performed at just under 20%. There was an unexplained increase in dystocia as an indication for cesarean section and all our breech presentations are now managed by cesarean section.

Because the increased number of cesarean sections performed at our institution has not resulted in decreased perinatal mortality, we must reassess the value of the procedure, as others are doing.[10] One of the many factors has been the substantial decline in forceps application thereby increasing the already broad category of dystocia. The recent National Institutes of Health study[13] reflected this concern, particularly with respect to the group of infants weighing over 2500 g for which cesarean section does not appear to increase the survival rates. This report also recommended that the outcome of breech presentation after cesarean section be reassessed and that vaginal delivery of a term infant in the breech position is still an acceptable obstetrical choice under certain conditions.

We must deal with the factors that influence the health of the mother as well as that of the fetus. The complications that we found confirm that the increase in cesarean sections performed has resulted in a proportional increase in morbidity and potential mortality.

Table VII—Maternal Complications in 173 Patients, 1973*

Complication	No. of cesarean sections		
	Primary	Repeat	Total (%)
Fever (≥38°C)	0	4	4 (2.3)
Endometritis	19	9	28 (16.2)
Urinary tract infection	33	15	48 (27.7)
Anemia	8	1	9 (5.2)
Wound infection	2	0	2 (1.2)
Thromboembolic disease	1	0	1 (0.6)
Bowel ileus	1	0	1 (0.6)
Pyelonephritis	1	0	1 (0.6)
None	32	47	79 (45.7)

*13 charts missing.

Table VIII—Maternal Complications, 1978

Complication	No. of cesarean sections		
	Primary	Repeat	Total (%)
Fever (≥38°C)	8	14	22 (5.2)
Endometritis	19	11	30 (7.1)
Urinary tract infection	12	9	21 (5.0)
Anemia	0	5	5 (1.2)
Wound infection	5	1	6 (1.4)
Thromboembolic disease	1	2	3 (0.7)
Bowel obstruction	1	0	1 (0.2)
Pneumonia	3	1	4 (0.9)
Postop. hemorrhage	1	0	1 (0.2)
None	221	110	331 (78.1)

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SESAP III Question

628. At the time of abdominal operation, a suspected intraoperative vesical injury is best detected by

(A) diminished return of urine from a urethral catheter
(B) presence of bloody urine during surgical procedure
(C) distention of the bladder with a solution of indigo carmine dye during operation
(D) inspection of the bladder
(E) intraoperative intravenous pyelogram (IVP)

For the incomplete statement above select the one answer that is best of the five given.

For the critique of Item 628 see page 101 of this issue.

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Mania Operativa: an Uncommon, Unrecognized Cause of Limb Amputation

G.A. HUNTER, MB, FRCS, FRCS[C] AND A.B. KENNARD, MB, BS

Mania operativa is an obsession with pain and disability and the seeking of relief from this pain by repeated surgical procedures. The authors report eight patients in whom a minor injury was followed by multiple operations, culminating in amputation of the upper or lower limb, at increasingly higher levels, in an unsuccessful attempt to relieve the patient's pain. They believe these patients had mania operativa.

There are many varieties of psychogenic pain, which present the surgeon with a problem in both diagnosis and management. The authors discuss identifiable factors in the patient, the surgeon and society. By calling attention to this condition, they hope to avoid unnecessary multiple surgical procedures on such patients.

La "mania operativa" est une obsession de la douleur et de l'invalidité, et la recherche du soulagement de cette douleur par le recours à des interventions chirurgicales répétées. Les auteurs décrivent huit malades chez qui une blessure banale a été suivie d'opérations multiples se terminant par l'amputation d'une membre supérieur ou inférieur, à un niveau de plus en plus élevé, dans une tentative infructueuse pour soulager la douleur du patient. Ils croient que ces malades souffraient de "mania operativa".

Il existe plusieurs types de douleurs psychogènes qui posent au chirurgien un problème de diagnostic aussi bien que le traitement. Les auteurs discutent les facteurs identifiables chez le malade, le chirurgien et dans la société. En attirant l'attention sur cette affection, ils espèrent éviter pour ces patients des interventions chirurgicales inutiles multiples.

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You will readily understand that when these patients, attacked with a "mania operativa passiva" find themselves unfortunately in the presence of surgeons affected with an analagous, though this time active, madness "mania operativa activa", the most fantastic operations may result from this unlucky collision. Amputations have been done.

J.M. CHARCOT[1]

Although Charcot[1] in 1889 was referring to cases of hysterical hip disease, which had often led to amputation, it was the German surgeon Stromeyer,[2] according to Chertok,[3] who introduced the term "mania operativa activa" in 1873. Stromeyer recorded a series of operations performed on patients suffering from psychogenic pain: painful symptoms in the knee led to amputation at the level of the thigh or to disarticulation of the hip joint. Involvement of the hand led to amputation of the forearm or the upper arm and even to disarticulation of the shoulder joint but without relieving the pain.

In this paper, we report eight patients, seen at an amputee clinic, in whom a minor injury was followed by multiple surgical procedures, culminating in amputation, at increasingly higher levels, in an unsuccessful attempt to relieve the patient's pain. We believe that the condition in these patients merits a positive diagnosis of mania operativa, that is, an obsession with pain and disability and the seeking of relief from this pain by repeated surgical procedures — in these cases amputation of the upper or lower limb.

Case Reports

Case 1

A 33-year-old woman struck her right hand on a table. Roentgenograms revealed no fracture or dislocation. Because of pain in the hand, carpal tunnel release was followed by tenolysis of the extensor tendons within a year of the accident. Skin necrosis developed after the second operation, necessitating a split-thickness skin graft and an unsuccessful skin pedicle flap to the dorsum of the hand. Two years after her accident, she requested a below-elbow amputation, which was carried out in an attempt to relieve unremitting pain in the hand. Thirteen years later, she still has stump pain and is unable to wear a prosthesis. She also had a history of multiple abdominal operations, finally resulting in removal of her right kidney.

Case 2

A 19-year-old man with a weak left leg due to poliomyelitis suffered a minor crush injury to the left foot. Roentgenograms of the injured foot showed no fracture or dislocation. To relieve the patient's persistent pain, the left big toe was fused. This was followed by fusion of the first metatarsal and medial cuneiform bones. One year later a Syme amputation was carried out but, at the patient's request, this was revised, initially to a below-knee and 6 years later to an above-knee amputation. This man was noted to be a chronic alcoholic with a poor work record.

Case 3

A 26-year-old man, immature and unemployable, twisted his right ankle. Roentgenograms revealed no fracture. Because of continuing pain, the Achilles tendon was first injected and later explored, but no abnormality was found.

Lumbar sympathectomy failed to relieve the patient's foot pain, and, at the patient's request, a below-knee amputation was carried out. The patient still complains of pain in the stump and is unable to wear a prosthesis.

Case 4

A fracture of the terminal phalanx of the left little finger was sustained by this 30-year-old woman. Six months later she requested amputation of the finger to relieve her pain. Subsequent revision was performed at a transmetacarpal level and during the course of these procedures multiple sinuses were explored. At that time it was suggested that these wounds had been self-inflicted. Finally, at the patient's request, a below-elbow amputation was carried out. Further operation was necessary to heal multiple sinuses and skin fistulas. The wound has healed but she cannot tolerate a prosthesis. Review of her history indicated that she had suffered from depression, anorexia nervosa and drug addiction.

Case 5

A 33-year-old man sustained a minor laceration to his right fifth finger. The wound failed to heal and 9 months later amputation of the finger was carried out at the patient's request. This procedure was followed over the next 9 years by transmetacarpal amputation, ray resection, fusion of the wrist and eventually a below-elbow amputation because of

pain and recurrent failure of the wound to heal. This patient was a drug addict and had attempted suicide on three occasions. A number of references were made on the patient's chart to the possibility of self-inflicted wounds.

Case 6

Although there was no radiologic evidence of a fracture, this 30-year-old man who had twisted his right ankle continued to complain of pain in his foot. Two attempts at fusion of the ankle and subtalar joints failed to relieve the pain. A lumbar sympathectomy was followed by a below-knee amputation at the patient's request 10 years after the injury, and two further revisions of his stump have been carried out in an attempt to relieve persistent pain. He was noted to be a drug addict, anxious and insecure.

Case 7

This 28-year-old chronic alcoholic sprained his right ankle. After conservative treatment for 6 years failed to relieve the pain, a tenodesis was carried out. Over the next 15 years 14 bone and soft-tissue operations around the foot were carried out, culminating in a Syme amputation which was subsequently revised to a below-knee amputation. The patient still complains of stump and phantom pain and is still requesting further surgery.

Case 8

A 29-year-old man fell 12 feet, suffering a dorsal dislocation of the first right tarsometatarsal joint. Closed reduction was carried out, but 6 years later the joint was fused because of continuing pain.

A Syme amputation followed by supracondylar and above-knee amputations failed to alleviate the patient's pain or obtain satisfactory prosthetic fitting. He was noted to have a sociopathic personality and he has not worked since his accident.

Discussion

Although this type of patient is fortunately uncommon in medical practice, it should be remembered that there are many varieties of psychogenic pain which present a problem in both diagnosis and management.

Mania operativa is a pattern of behaviour, the underlying psychopathology of which is diverse and which includes the following conditions: (a) Munchausen syndrome, (b) SHAFT syndrome, (c) polysurgery and polysurgical addiction, (d) phantom limb sensation and painful phantom and (e) reflex sympathetic dystrophy.[4]

● Munchausen syndrome. Since Asher's original description[5] there have been several reports of this syndrome,[6] but none have included limb amputation as a complication of surgical treatment.

● SHAFT syndrome (the chronic pain syndrome).[7,8] In this syndrome the patient submits to and demands surgery to meet needs, whether financial or psychological, hence the acronym representing *s*ad, *h*ostile, *a*nxious *f*rustrating patients who *t*enaciously cling to the health care system. Wallace and Fitzmorris[7] reported on two such patients whose pain in the upper extremity culminated in digital and above-elbow amputations.

● Polysurgery and polysurgical addiction. Menninger[9] considered that the neurotic patient is unconsciously transferring dependence to the surgeon, who is seen as a strong, incisive and ruthless father figure.

In addition to these syndromes, the picture can be clouded, as it was in our patients, with associated factors such as alcoholism, drug addiction, self-mutilation, hypochondriasis and sociopathic personality.

There must be identifiable factors to account for this rare but serious problem, which may be more common than is recognized. We will discuss some factors with regard to the patient, the surgeon and society.

The Patient

The patient may suffer from preexisting or post-traumatic mental disease and often holds a grudge against society, hospitals and doctors. Drug addiction may contribute to a masochistic desire for self-mutilation, in itself a partial suicide attempt.

Repeated hospital visits fulfil a desire to become the centre of interest and attention in the dramatic role of a patient. Since all these patients were seen in the Workmen's Compensation Board Hospital and Rehabilitation Centre, this syndrome may be due to a simple desire not to work, coupled with secondary financial gain. It should be noted, however, that financial compensation to Board patients never equals the patient's former income and permanent disability payments are relatively small, by today's standards, even for limb amputation.

The Surgeon

If one accepts an excessive number of surgical procedures performed on one patient as one of the categories for defining "unnecessary surgery", it should be noted that orthopedic surgeons have been cited as those who perform the highest percentage of unnecessary surgery.[10]

Most surgeons are poorly trained in psychiatric medicine and naively believe that amputation will cure pain in these patients.[11] When faced with failure, the situation arouses bewilderment, contempt and anger. Anger may incite latent sadistic tendencies,[9] and the entire cycle is repeated as the patient and surgeon regard each other as being either incompetent or psychologically disturbed.

If one is to blame the patient for hoping to gain financially from amputation, it should be remembered that in a fee-for-service system the surgeon may have secondary motives for involving himself in repeated surgical procedures.

Society

Deceiving the medical profession is not a criminal offence or grounds for commitment. Universal health care, which in the minds of the public is "free", encourages many diverse opinions and consultations; often the surgeon has insufficient information on the patient to realize the problem before making a decision about further surgical procedures.

Conclusion

When a patient presents in a depressed, even hostile, state, with longstanding bizarre pain after a trivial injury and has a turbulent social history, possibly including drug addiction, we recommend that the surgeon obtain the old records and arrange a psychiatric consultation before proceeding with primary or secondary amputation of a limb, often at the patient's request. Such procedures are harmful to the patient and costly to society.

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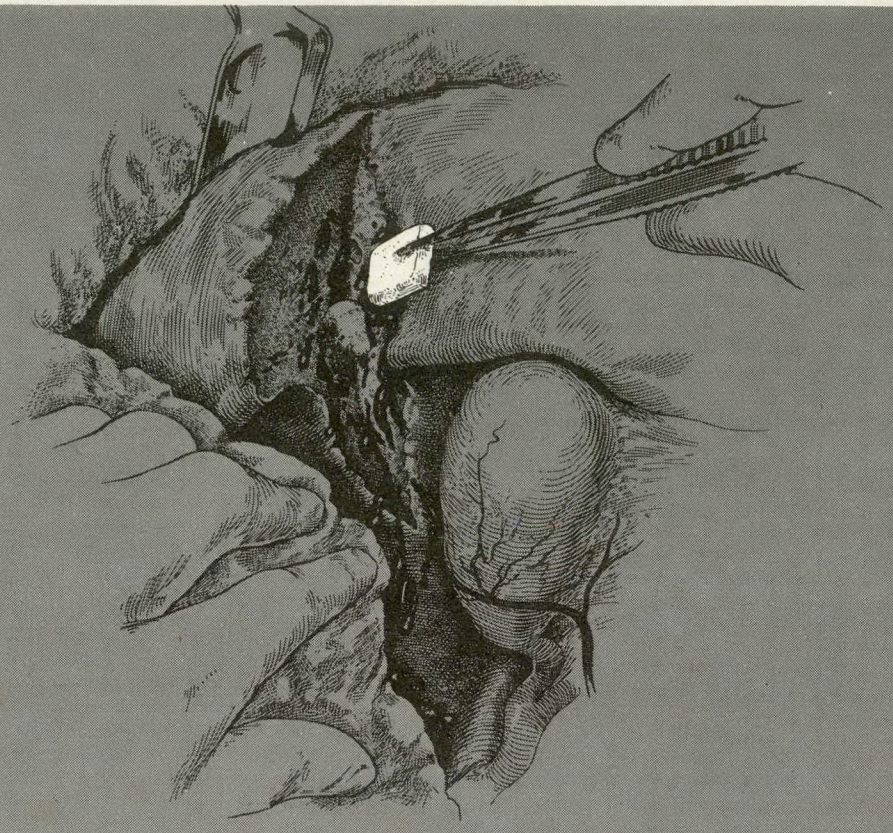
Gelfoam

used by a generation of physicians in hepatic surgery, haemorrhoidectomy, cholecystectomy and decubitus ulcer



still the only absorbable haemostat that meets all these criteria:

absorbed completely in four to six weeks

safe as a permanent packing in any tissue; won't interfere with bone regeneration, cause cyst formation or excessive scar tissue

effective dry or moistened with thrombin solution, isotonic sodium chloride or antibiotic

non-irritating, naturally-occurring, neutral pH; may be cut, molded, or sutured in place when necessary

stimulates natural clotting and healing of disrupted tissue

Management of Ulnar Artery Aneurysm in the Hand: a Case Report

R.D. MARTIN, MD, FRCS[C] AND R.T. MANKTELOW, MD, FRCS[C]

Despite the common occurrence of trauma to the hand, arterial aneurysms in this area are rare. The authors describe the symptoms, signs and microvascular treatment of a true aneurysm of the ulnar artery in the palm of an 18-year-old youth. Although there is no clear evidence that vascular restoration is needed after resection of the aneurysm, the authors believe that reconstruction of the ulnar artery using microvascular techniques will ensure that blood supply to the digits is adequate.

En dépit de la fréquence des traumatismes de la main, les anévrysmes artériels dans cette région sont rares. Les auteurs décrivent les symptômes, les signes et le traitement d'un anévrysme vrai de l'artère cubitale dans la paume d'une jeune homme de 18 ans. Bien qu'il n'y ait pas de preuve évidente qu'une restauration vasculaire soit nécessaire après la résection de l'anévrysme, les auteurs croient que la reconstruction de l'artère cubitale par microchirurgie permettra d'assurer un apport sanguin adéquat aux doigts.

The first report of an arterial aneurysm in the hand was made by Guattani in 1772.[1] Although the hand is highly vascular and is frequently subjected to trauma, only 52 cases of true aneurysms have been described; 30 of those were aneurysms of the ulnar artery.[2-6] In this report we describe the clinical and pathologic features, and treatment of another case. Because of new developments in microvascular surgery, the treatment of this condition must be re-examined.

Case Report

An 18-year-old left-handed boy had for 3 months had episodes of lancinating pain in his right hand over the volar aspect of the base of the little and ring fingers. On several occasions he had experienced coolness, pallor and numbness in either his index or long fingers for periods ranging from 5 to 10 minutes. These episodes seemed unrelated to position, activity or temperature change and involved only his right hand. He was an accomplished musician who usually played the guitar for 3 hours each day but the symptoms of coolness and numbness prevented this. Several weeks before admission he noticed a small, painless lump in the proximal hypothenar area. He gave no history of trauma to his hands.

The right upper extremity appeared normal except for a pulsating mass, 2 cm in diameter, in the hypothenar eminence. The mass was firm, not tender and fairly mobile, with no associated thrill or bruit. The distal circulation was normal at the time of examination, as were motor and sensory functions.

Occluding the radial artery at the wrist slightly diminished the pulsation in the mass but did not adversely affect circulation distally. When the ulnar artery was occluded, there was still good circulation to all fingertips but much less pulsation in the hypothenar mass. Other findings on physical examination and results of routine laboratory tests were normal.

Arteriography was done to outline the aneurysm and associated vessels (Fig. 1). This study supported the diagnosis of an aneurysm of the distal portion of the ulnar artery at its junction with the superficial palmar arch.

At operation, with a pneumatic tourniquet in place, the aneurysm with proximal and distal vessels was easily dissected free from surrounding tissues. There was no fibrosis around the aneurysm. Proximal and distal vessels appeared to be normal (Fig. 2).

The aneurysm was resected leaving a gap of 2 cm in the ulnar artery, which was reconstructed using a reverse vein graft. Superficial vein, 2 mm in diameter, was taken from the dorsum of the hand and end-to-end microvascular anastomosis done with 10-0 nylon sutures (Fig. 3). Following release of the clamps, there was good flow through the anastomoses. Digital occlusion of the radial artery was continued for 15 minutes to encourage flow through the reconstructed vessel.

The resected aneurysm was in fact larger than it appeared on the arteriogram because the lumen was partially occluded by thrombus. The sac had a fairly thick wall and microscopic examination proved that it was a true aneurysm (Fig. 4). There were no postoperative complications and the patient was discharged from hospital 5 days after the operation. The Allen test performed 2 weeks later gave a negative result and the patient was free of symptoms.

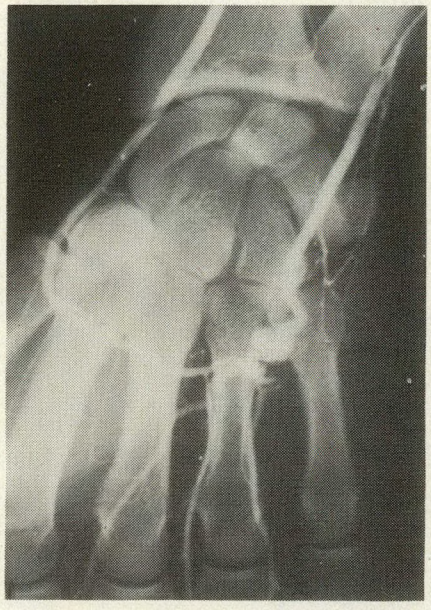


FIG. 1—Arteriogram of right hand showing smooth-walled circular dilatation at junction between ulnar artery and superficial palmar arch.

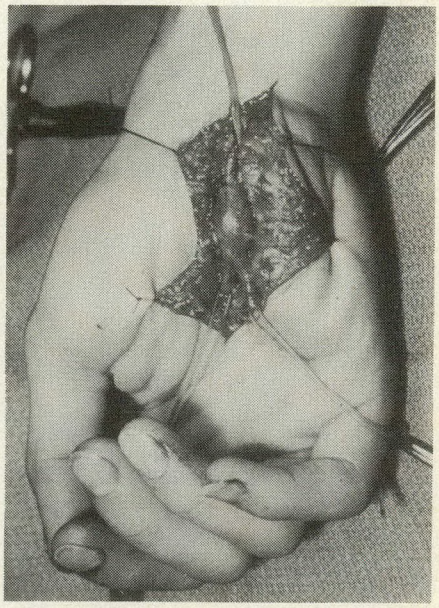


FIG. 2—Aneurysm at operation.

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Discussion

Peripheral artery aneurysms most commonly result from direct trauma due to a penetrating injury that disrupts all three layers of the vascular wall. Arterial flow is usually maintained past the obstruction and the blood lost through the vessel wall is contained by surrounding tissues and becomes a pulsating hematoma. In a few weeks there is central liquefaction of the hematoma and a fibrous capsule develops. This is a false aneurysm. True aneurysms have a sac, formed by dilation of the whole arterial wall. Thus, the true aneurysm contains elements of internal elastic lamina and smooth muscle, which can be demonstrated under the microscope. True aneurysms may be traumatic, mycotic, arteriosclerotic, idiopathic or congenital.

In 1976, Chapuis and associates[7] reviewed the world literature and found only 47 cases of unilateral true aneurysms in the palm. There have been two reports of bilateral palmar ulnar artery aneurysms.[8,9] However, the incidence of damaged ulnar arteries in the palm is much higher.[10] In 1970, Conn and colleagues[11] suggested the term hypothenar hammer syndrome to describe patients with vascular changes in the palm resulting in pathologic changes in the ulnar artery. Minor repetitive trauma causes vasospasm and intimal damage that may lead to vessel thrombosis or aneurysm formation.

There are three stages in the pathophysiology of the hypothenar hammer syndrome. First, minor repetitive trauma causes distal vasospasm, which remains reversible for a time. Second, greater or more prolonged injury occurs in which damage to the vessel intima may result, followed by thrombosis and vascular occlusion, with distal spasm. Third, more severe trauma occurs in which the tunica media is injured with resultant weakness and aneurysm formation with distal vasospasm and distal embolization. Hypothenar hammer syndrome is best understood through an appreciation of the anatomical relations of the ulnar artery and superficial palmar arch and the hamate bone (Fig. 5). Here, just distal to Guyon's canal, the vessel lies unprotected as it courses over the transverse carpal ligament and carpal bones. A force applied to the artery on its palmar and ulnar aspect will crush it against the unyielding hook of the hamate. Most true palmar aneurysms have been located in this segment of the artery.[12]

Symptoms are caused by local irritation of the hypothenar eminence by the aneurysm and by distal ischemic change in the fingers, including coolness, pallor, ulcers and gangrene. The ischemic changes may be caused by vasospasm, emboli or vascular insufficiency. Neurologic changes may be related to direct pressure of the aneurysm on the ulnar nerve. The intermittent numbness and coolness of the fingers in our patient was likely due to vasospasm of the distal digital arteries or embolization from the aneurysm, which was partially occluded by thrombus.

Surgical resection is indicated for symptomatic arterial aneurysms of the palm. Surgical resection produces a local sympathectomy and removes the source of embolization. Opinions differ on the need for restoring vessel continuity after resection. Most of the literature deals with hypothenar hammer syndrome in which the condition was more often thrombosis than aneurysm.[10-14] Millender and associates[13] mentioned reanastomosis as a possibility but thought it unnecessary. Smith[12] stated that "collateral circulation is always sufficient" and that "no attempt need be made to restore continuity of the divided ends of the artery". Conn and associates,[11] concerned about placing incisions in the palm, preferred sympathectomy.

Given and associates[14] reported their experience with two groups of 47 patients having ulnar artery thrombosis. One group was treated mainly by resection and ligation. Of these, 60% had excellent or good results while 40% remained unimproved. An-

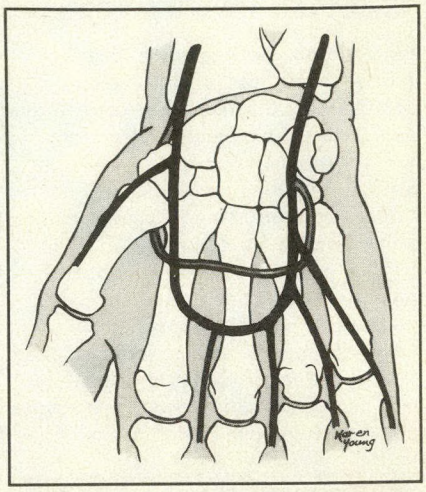

FIG. 5—Normal anatomic relations between ulnar artery and hook of hamate bone.

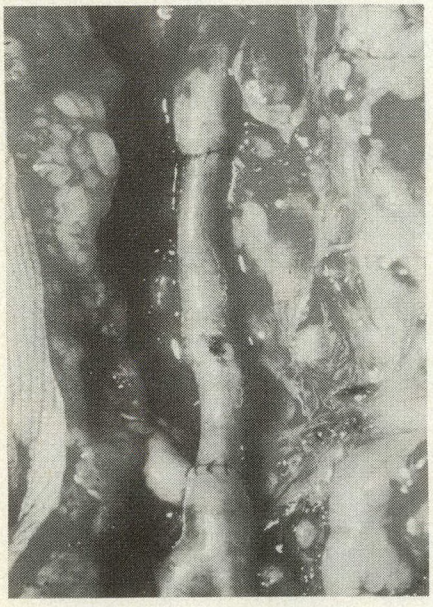

FIG. 3—Vein graft in place.

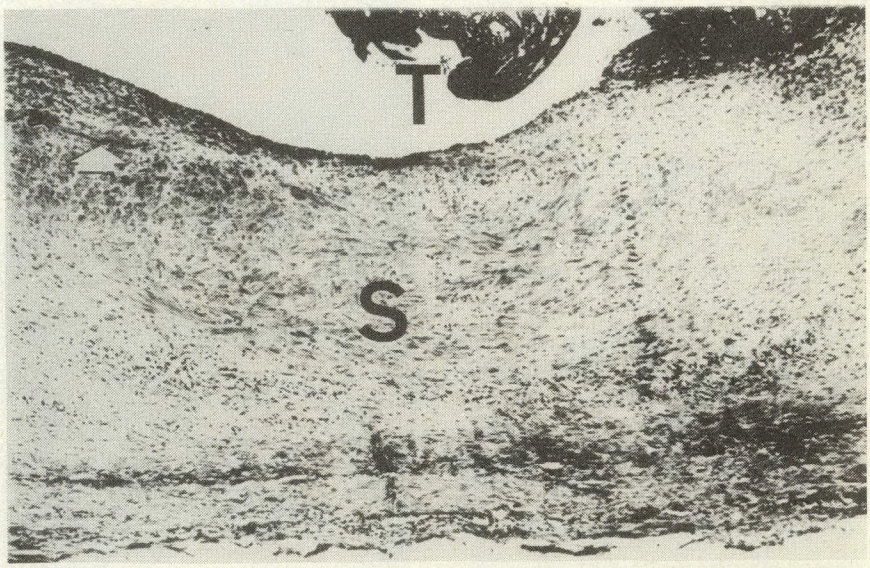

FIG. 4—Section through aneurysm showing smooth muscle and elastic fibres identifying true aneurysm. Arrow points to internal elastic lamina. T = thrombus in lumen, S = smooth muscle (reduced by 19% from ×40).

other group underwent resection and vein graft reconstruction. In this group 89% had excellent or good results with only 11% being unimproved. On the basis of these results they advised that an attempt should be made to re-establish normal flow.

There is no clear evidence to support the need for vascular restoration. Following resection, the presence of good back flow from the distal end may indicate that reconstitution of vessel continuity is unnecessary. Patients who do not have good back flow should have the vessel reconstructed. Even when the circulation appears satisfactory through other routes, an interposition vein graft gives greater assurance that the supply is adequate and that a vascular reserve is available.

Conclusion

True aneurysms in the hand are uncommon. They are usually the result of closed trauma over the hypothenar area and have an understandable anatomical basis. When they are symptomatic, surgical resection is indicated and microsurgical reconstruction should be considered.

We thank Dr. M. Silver, department of pathology, University of Toronto, for the histologic interpretation.

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Nouvelle méthode simplifiée d'implantation d'électrodes épicardiques temporaires

Y.F. Glock, md,* J.M. Herreros, md† et F.J. Teijeira, md‡

Les auteurs présentent une nouvelle méthode simplifée d'implantation d'électrodes épicardiques temporaires réalisable extemporanément, en per-opératoire, à partir d'une électrode standard. L'étude comparative avec l'électrode standard montre à l'étage auriculaire comme à l'étage ventriculaire, une amélioration des seuils myocardiques, tant au niveau du milliampérage que du voltage ($P < 0.05$ à l'étage auriculaire et $P < 0.005$ à l'étage ventriculaire).

Au 7e jour, cette mise en place d'électrode apparaît plus fiable que l'électrode standard et montre une dégradation moindre de ses caractéristiques ($P < 0.05$).

The authors present a new simplified method for implanting temporary epicardial electrodes, which can be carried out extemporaneously during operation from a standard electrode. The modified electrode showed an improvement over the standard electrode in the myocardial thresholds with respect to milliamperage as well as voltage at both atrial and ventricular levels ($P < 0.05$ for atrial and $P < 0.005$ for ventricular). On the 7th day after placement the modified electrode appears to be more reliable than the standard electrode and demonstrates less degeneration of its threshold and current characteristics ($P < 0.05$).

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Les demandes de tirés-à-part doivent être adressées au Dr F.J. Teijeira, Département de chirurgie cardio-vasculaire et thoracique, Université de Sherbrooke, Sherbrooke, PQ J1H 5N4

L'implantation d'électrodes épicardiques temporaires est systématique pour la plupart des équipes chirurgicales. A l'étage ventriculaire, elle permet de contrôler les troubles de conduction auriculo-ventriculaire et les bradyarythmies avec fibrillation auriculaire; à l'étage auriculaire, elle rend possible le diagnostic de certains troubles rythmiques supra-ventriculaires par enregistrement d'un électrogramme auriculaire, et elle autorise le traitement des arythmies auriculaires en l'absence de fibrillation auriculaire.[1-8]

La stimulation auriculaire, conservant une systole auriculaire, améliore les index et débit cardiaques.[9]

Le seuil de l'électrode épicardique temporaire augmente significativement en période postopératoire quand une électrode standard est utilisée.[10,11] Cette augmentation du seuil peut être réduite si la partie dénudée de l'électrode est exclusivement intra-myocardique.[11-13] Nous proposons une nouvelle technique d'implantation d'électrodes épicardiques temporaires à partir d'une électrode standard qui, à cet avantage, associe la simplicité technique. Nous avons étudié dans les jours postopératoires, les caractéristiques de cette électrode comparées à celles d'une électrode standard.

Patients et méthode

Chez 14 patients ayant subi une chirurgie cardiaque (12 pontages aorto-coronariens et 2 remplacements valvulaires mitraux) nous avons implanté des couples d'électrodes (0-Flexon 2597.63; Davis & Geck, Willowdale, Ont.) à la face diaphragmatique du ventricule droit, une électrode placée selon la technique standard et la seconde modifiée selon notre technique (figs. 1 à 3).

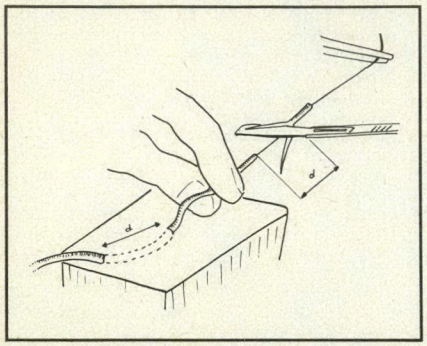


FIG. 1—Confection du harpon: l'électrode standard est dénudée de façon à confectionner un "harpon" de Teflon sur une longueur (d) inférieure ou égale au trajet intra-myocardique.

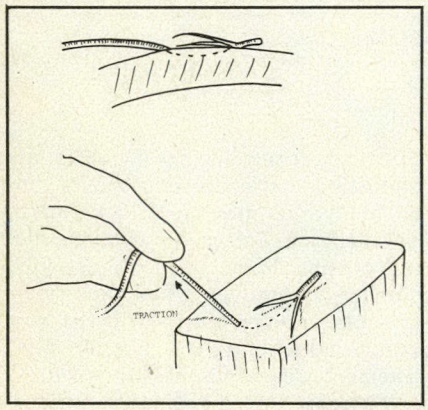


FIG. 2—Mise en place de l'électrode par traction douce: la zone dénudée est exclusivement intra-myocardique.

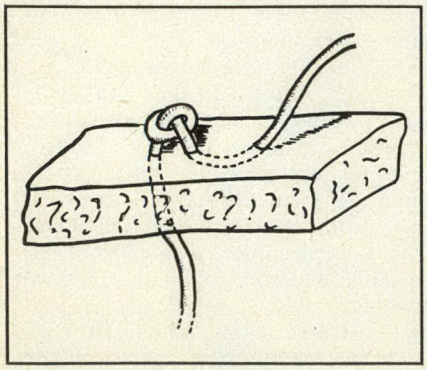


FIG. 3—Artifice de fixation de l'électrode par elle-même à la peau.

L'implantation d'un couple d'électrodes standard et modifié a été pratiquée à l'étage auriculaire chez 11 patients (10 pontages aorto-coronaires, 1 remplacement valvulaire mitral).

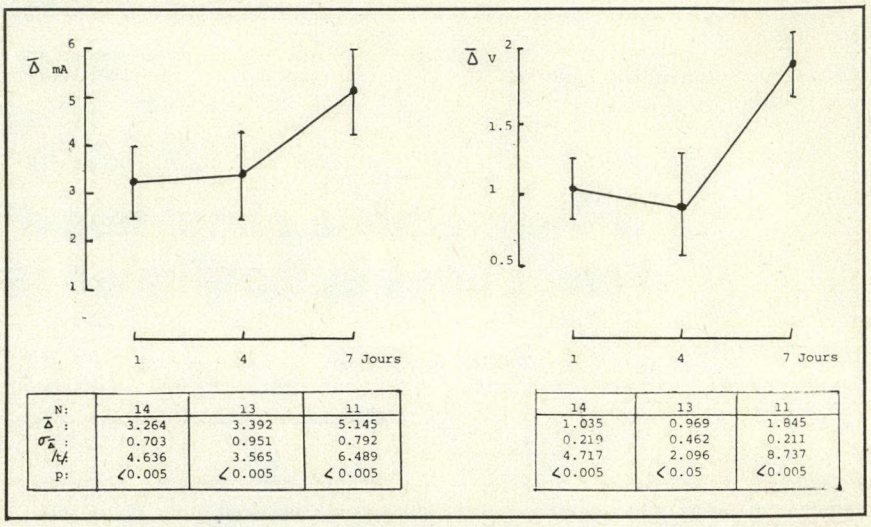
Pour permettre une comparaison des caractéristiques de l'électrode (seuil [volt], courant noté [mA]): a) les caractéristiques de chaque électrode d'un couple ont été mesurées par rapport à une électrode souscutanée commune de référence, et b) chaque couple d'électrodes a été implanté dans une aire myocardique de 2 cm^2 afin d'éviter le biais lié aux variations de seuil inhérent aux différentes zones de tissu myocardique. Ces mesures ont été recueillies à l'aide d'un analyseur (Medtronic 5300, Medtronic Inc., Minneapolis, Minn.) à la 6e heure, et les 4e et 7e jours post-opératoires.

Nous avons comparé les moyennes des différences observées entre l'électrode standard et l'électrode modifiée par le test de Student (significatif, $P < 0.05$).

Les mesures comparatives faites le 1er jour sur 14 couples d'électrodes ventriculaires fonctionnelles et 11 couples d'électrodes auriculaires fonctionnelles, ont été répétées au 7e jour sur 11 couples d'électrodes ventriculaires et 9 couples d'électrodes auriculaires fonctionnelles, ceci en raison de la dysfonction de l'électrode standard au 7e jour dans les autres cas.

Résultats

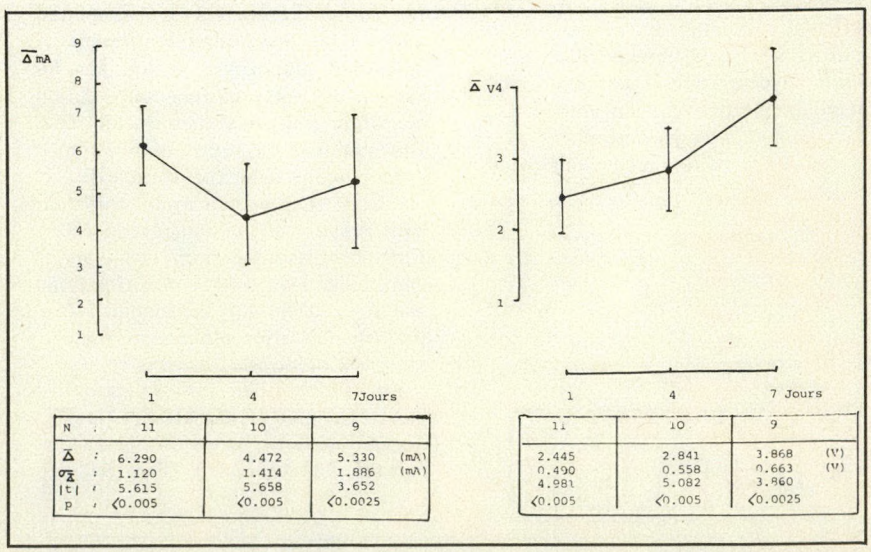
A l'étage ventriculaire, l'étude de



N:	14	13	11
$\bar{\Delta}$:	3.264	3.392	5.145
$\sigma_{\bar{\Delta}}$:	0.703	0.951	0.792
/t/	4.636	3.565	6.489
p:	<0.005	<0.005	<0.005

14	13	11
1.035	0.969	1.845
0.219	0.462	0.211
4.717	2.096	8.737
<0.005	<0.05	<0.005

FIG. 4—Evolution de la moyenne ($\bar{\Delta}$) des différences d'ampérage et de voltage entre l'électrode standard et l'électrode modifiée à l'étage ventriculaire au 1er, 4e et 7e jour ($P < 0.005$). N = nombre, $\sigma_{\bar{\Delta}}$ = erreur type de la moyenne, t = valeur absolue du t de Student.



N :	11	10	9	
$\bar{\Delta}$:	6.290	4.472	5.330	(mA)
$\sigma_{\bar{\Delta}}$:	1.120	1.414	1.886	(mA)
|t| :	5.615	5.658	3.652	
p :	<0.005	<0.005	<0.0025	

11	10	9	
2.445	2.841	3.868	(V)
0.490	0.558	0.663	(V)
4.981	5.082	3.960	
<0.005	<0.005	<0.0025	

FIG. 5—Evolution de la moyenne ($\bar{\Delta}$) des différences d'ampérage et de voltage entre l'électrode standard et l'électrode modifiée à l'étage auriculaire au 1er, 4e et 7e jour ($P < 0.05$).

la moyenne des différences de courant récurrent observées est significative à la 6e heure, au 4e et au 7e jour ($P < 0.005$) où elle est respectivement de 3.26 ± 0.70 mA, 3.39 ± 0.95 mA et 5.14 ± 0.79 mA. Elle se fait toujours dans le sens d'un milliampérage minimum pour notre électrode modifiée. On constate qu'elle augmente avec le temps du 1er au 3e jour de façon significative ($P < 0.05$) (fig. 4).

En ce qui a trait au voltage requis, les constatations sont identiques (fig. 4). La moyenne des différences au 1er jour (1.03 ± 0.21 V) au 4e jour (0.96 ± 0.46 V) et au 7e jour (1.84 ± 0.21 V) est significative ($P < 0.05$) en faveur de l'électrode modifiée qui montre le voltage le plus bas. Cette différence est accusée entre le 1er et le 7e jour de façon significative ($P < 0.05$).

A l'étage auriculaire, les constatations sont superposables (fig. 5). La moyenne des différences de milliampérage entre l'électrode standard et l'électrode modifiée est significative ($P < 0.05$), ceci à la 6e heure (6.2 ± 1.1 mA), au 4e jour (4.9 ± 1.4 mA) et au 7e jour (5.3 ± 1.8 mA). Il en est de même des voltages requis dont les valeurs sont successivement de 2.44 ± 0.49 V au 1er jour, de 2.84 ± 0.5 V au 4e jour et de 3.36 ± 0.66 V au 7e jour. L'ablation des électrodes au 7e jour s'est toujours faite sans aucun problème.

Discussion

De nombreux auteurs insistent sur la nécessité de l'implantation postopératoire des électrodes épicardiques temporaires à l'étage auriculaire[1,2,6-9] et à l'étage ventriculaire.[3-5,10-13]

Nos résultats comme ceux des autres auteurs[10-13] objectivent une augmentation du milliampérage myocardique dans la phase postopératoire dans l'électrode standard, ce qui représente un danger létal en cas de dysfonctionnement, ou un inconfort du fait de la stimulation diaphragmatique liée à la nécessité d'un voltage plus fort. Cette majoration du seuil est liée à la fuite électrique due à la partie dénudée extra-myocardique baignée par les fluides sero-sanguins péricardiques.[10,11] Elle peut être diminuée par l'enfouissement intra-myocardique de la partie dénudée de l'électrode. L'électrode épicardique temporaire de Yokoyama et Wada[13] représente un modèle différent d'électrode alors que celle d'Aris et collaborateurs,[11] celle de Katsumoto[12] et la nôtre sont réalisables extemporanément à partir de l'électrode standard. Les résultats électriques sont superposables à ceux observés par ces auteurs.[11-13] La fiabilité de notre électrode par rapport à l'électrode standard est supérieure. Au 7e jour, 100% des électrodes modifiées sont fonctionnelles contre 81% des électrodes standards ventriculaires et 76% des électrodes standards auriculaires. Notre simplification technique réside dans l'absence de points de fixation à adjoindre tant au niveau du myocarde que de la peau. Notre électrode est arrimée à la peau et au coeur par elle-même et son ablation se fait toujours sans problème.

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SESAP III Critique

ITEM 628

The instillation of any dye helps to detect a bladder injury. Indigo carmine is preferred because tissue-staining is reduced. Decreased urine flow from the urethral catheter, or the presence of bloody urine, is suggestive of some trauma, but is not diagnostic. Identifying the bladder and searching for a hole is not always reliable. An intraoperative intravenous pyelogram may be helpful in suspected ureteral injuries, but intravesical indigo carmine is a simpler procedure in this instance.

C

Reference

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Surgical Management of Pulmonary Metastases

G.A. PATTERSON, MD, FRCS[C], T.R.J. TODD, MD, FRCS[C], R. ILVES, MD, FRCS[C], F.G. PEARSON, MD, FACS, FRCS[C] AND J.D. COOPER, MD, FRCS[C]

Between 1969 and 1979 at the Toronto General Hospital, 78 patients were assessed for possible resection of pulmonary metastases, assuming that the primary tumour was controlled and no other known metastatic foci were present. Primary tumours were renal in 16 patients, colorectal in 15 and breast in 10; 11 had sarcoma, 5 melanoma and 21 had miscellaneous primary cancers. Metastases were resected in 64 patients. Thirteen patients did not undergo resection since additional information indicating inoperability was provided by whole lung tomography in 6, mediastinoscopy in 4 and thoracotomy in 3. One patient was considered medically to have inoperable disease.

There was one death postoperatively and major complications were encountered in six patients. Follow-up was possible in 62 of the 64 patients who underwent resection. Actuarial survival at 2 and 5 years was 63% and 42% respectively. Of 12 patients who had a disease-free interval of less than 12 months, only 3 are alive (mean survival 37.6 months). Of 48 patients with a disease-free interval longer than 12 months, 24 are alive (mean survival 55.1 months). Six of 14 patients with primary tumour of the colorectum are alive a mean of 40 months (range from 6 to 80 months) after resection; the other 8 survived a mean of 22 months (range from 5 to 61 months). Of 14 patients with renal tumours, only 3 are alive; 11 patients died, having survived a mean of 22.5 months (range from 3 to 59 months).

This review supports resection of pulmonary metastases in selected patients, particularly those with a disease-free interval of longer than 12 months.

Au Toronto General Hospital, entre 1969 et 1979, 78 malades ont été évalués sur la possibilité de réséquer des métastases pulmonaires, en supposant que la tumeur primaire était jugulée et qu'aucun autre foyer métastatique connu n'était présent. La tumeur primaire était d'origine rénale chez 16 patients, colorectale chez 15 et mammaire chez 10; 11 avaient un sarcome, 5 un mélanome et 21 avaient divers cancers primaires. Des métastases ont été réséqués chez 64 malades. Treize patients n'ont pas subi de résection à cause de l'information additionnelle obtenue par tomographie pulmonaire chez 6, par médiastinoscopie chez 4 et par thoracotomie chez 3 indiquant que la tumeur était inopérable. Chez un malade, la maladie a été considérée médicalement comme étant inopérable.

Il y a eu un décès postopératoire et des complications majeures ont été rencontrées chez 6 patients. Les suites thérapeutiques sont disponibles pour 62 des 64 patients qui ont subi la résection. Les taux de survie, à 2 et 5 ans calculés par la méthode actuarielle ont été respectivement de 63% et 42%. Des 12 patients qui avaient eu un intervalle exempt de maladie de moins de 12 mois, seulement 3 sont vivants (survie moyenne de 37.6 mois). Des 48 malades qui avaient eu une période exempte de maladie de plus de 12 mois, 24 sont vivants (survie moyenne de 55.1 mois). Six des 14 patients porteurs d'une tumeur du côlon ou du rectum sont vivants, 40 mois en moyenne (écart de 6 à 80 mois) après la résection; les 8 autres ont survécu 22 mois en moyenne (écart de 5 à 61 mois). Des 14 malades qui avaient une tumeur rénale, seulement 3 sont vivants; 11 sont décédés après avoir survécu durant une moyenne de 22.5 mois (écart de 3 à 59 mois).

Cette étude soutient la résection des métastases pulmonaires chez des patients choisis, particulièrement chez ceux qui ont été exempts de maladie pendant plus de 12 mois.

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Traditionally patients with pulmonary metastases were thought to have widespread unresectable disease. However, in 1935, Farrell[1] demonstrated that many patients who died of pulmonary metastases had no other metastatic foci. Subsequently, in 1939, Barney and Churchill[2] reported the first excision of a metastatic pulmonary nodule resulting in long-term survival. Several reports followed advocating resection of pulmonary metastatic lesions.[3-6] This approach is not universally accepted. Therefore, we have analysed our experience at the Toronto General Hospital between Jan. 1, 1969 and Dec. 31, 1978 in managing patients with pulmonary metastatic nodules.

Patients and Methods

Study Population

Seventy-eight patients (37 men, 41 women; mean age 53.3 years) were considered for resection of their pulmonary metastatic lesions. Criteria for consideration included: (a) no evidence of residual primary tumour and (b) no initial evidence of other metastatic foci. The type of primary tumour is shown in Table I. Of the 78 patients, 47 were asymptomatic but had an abnormal chest film. In the other 31 patients the commonest symptom was cough (24 cases). A solitary pulmonary metastasis was present in 47 patients while 31 had multiple metastatic tumours.

Diagnostic Investigations

The 10-year period of this review

Table I—Type of Primary Tumour

Tumour type	No. of patients
Renal	16
Colorectal	15
Sarcoma	11
Breast	10
Melanoma	5
Cervical	5
Adenoid cystic	4
Endometrial	2
Bladder	2
Testicular	2
Ovarian	2
Pancreatic	1
Thyroid	1
Adamantinoma	1
Hemangiopericytoma	1
Total	78

accounts for a certain variability in the investigations employed. Fifty-four patients had whole lung tomography; 11 were found to have additional lesions not apparent on routine roentgenography.

Percutaneous aspiration needle biopsy was attempted in 34 patients. A malignant neoplasm was diagnosed in 26 (76%) and the tumour type specifically identified in 20 of them (77%). In the other eight patients the results were negative mainly because of technical failure producing an inadequate sample for cytologic examination.

Forty-two patients underwent mediastinoscopy; in 37 patients no metastases were found. Mediastinoscopy gave a positive result in five patients: in three of seven patients with metastatic breast carcinoma who underwent this procedure, in one patient with metastatic adrenal carcinoma and in one with metastatic leiomyosarcoma.

Patients with Inoperable Metastases

Fourteen patients did not undergo resection since additional information was gained during their investigation that precluded resection. In six of them multiple additional metastases were discovered by whole lung tomography. Positive findings on mediastinoscopy eliminated four others from consideration for resection (three with breast carcinoma and one with adrenocortical carcinoma). Three patients were found to have extensive or inoperable disease at thoracotomy and the chest was closed without resection. One elderly patient had refractory congestive heart failure.

Resection Group

Sixty-four patients underwent resection of 110 tumours (Table II). In three patients sternotomy was performed for excision of bilateral tumours and the remainder underwent thoracotomy. Fifty-three had a single thoracotomy and 8 had bilateral thoracotomies. Of the latter, three patients had synchronous bilateral thoracotomies and five had staged procedures. There were 53 wedge resections (including enucleation), 52 lobectomies and 2 pneumonectomies.

Table II—Number of Tumours Resected per Patient

No. of patients	No. of tumours resected
38	1
15	2
5	3
3	4
3	5
64	110

Results

Six patients had major complications. Four had respiratory failure and one of them required re-exploration for postoperative bleeding. Empyema with subsequent bronchopleural fistula developed in one patient. A sternal osteomyelitis and dehiscence occurred in another. There was one death postoperatively.

Twenty-nine of the 62 patients followed up are alive, 3 to 156 months after resection; only 6 of them have recurrent metastatic disease. Thirty-three patients died; 29 had definite metastatic disease at the time of death. In 23 of the 29 death was thought to be due to the metastatic disease. The 2- and 5-year actuarial survival rates for the entire group were 63% and 42% respectively (Fig. 1). For patients with a disease-free interval longer than 12 months the comparable figures were 69% and 42% but for those with a disease-free interval of less than 12 months the rates were only 40% and 20% respectively. Disease-free interval was defined as the interval between effective control of the primary disease and presentation with pulmonary metastases. In 24 patients with multiple tumours, an actuarial survival of 67% and 40% at 2 and 5 years, respectively, did not differ from the actuarial survival of

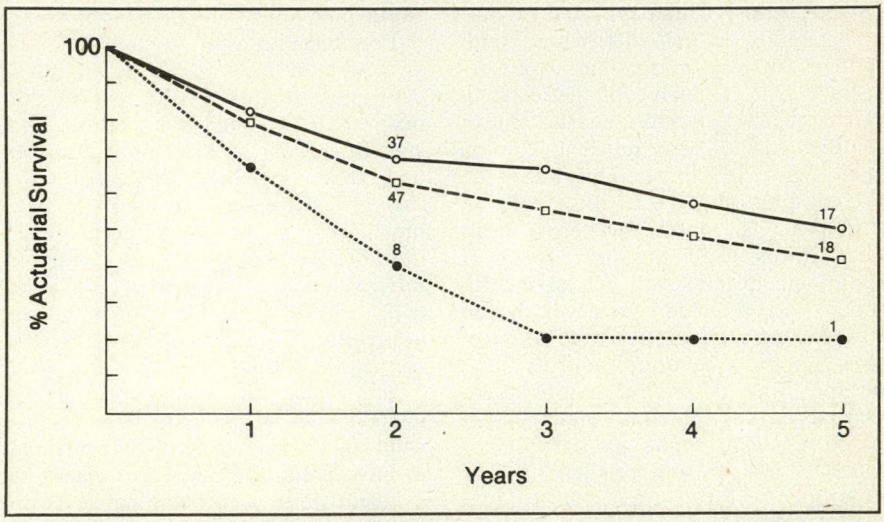

FIG. 1—Actuarial survival following resection of pulmonary metastases for entire group (squares), including those with disease-free interval (DFI) of less than 12 months (black circles) and those with DFI longer than 12 months (white circles). Numbers on curves represent numbers of patients alive and available for analysis in succeeding period.

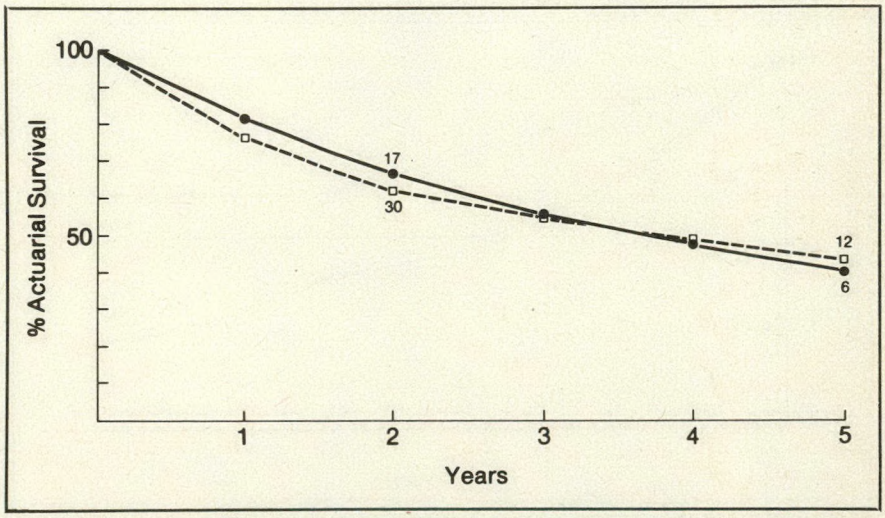

FIG. 2—Actuarial survival of patients with single (squares) and multiple (circles) pulmonary metastases. Numbers on curves represent numbers of patients alive and available for analysis in succeeding period.

40 patients with single tumours (62% and 43%) (Fig. 2). When individual primary tumour types are considered, 10 patients with sarcoma had a better survival than 14 patients with primary colorectal or 14 patients with renal tumours, although patients with colorectal tumours fared better than those with renal carcinoma (Fig. 3).

Discussion

Since the successful excision of a renal secondary tumour more than 40 years ago by Barney and Churchill,[2] the removal of pulmonary metastatic tumours has been considered acceptable under certain circumstances. The availability of more effective adjuvant therapy has also altered the philosophy towards this group of patients.[7] Several series[3,6,8] have reported favourable results in patients whose pulmonary metastatic tumours were resected. The majority of patients in our series were asymptomatic, abnormalities having been noted at routine radiologic assessment. This has been the finding of others.[3] In many of our patients routine posteroanterior chest films were the only form of radiologic examination before the tumour was resected. However, when whole lung tomography was used, it was found to be quite helpful; 20% of the time additional lesions were discovered. Significant management decisions were made as a result of the new information provided by tomography. This is especially true in recent years since sternotomy and excision of bilateral lesions have become more popular.

We could not assess the role of computerized axial tomography since the equipment was available only in the later years of the study. However, this procedure has been shown in several reports[9,10] to be more accurate than whole lung tomography in identifying additional pulmonary metastases. In one study, computerized axial tomography defined additional lesions in 35% of patients who had undergone routine tomographic assessment.[10] Unfortunately neither standard nor axial tomography can differentiate benign from malignant processes. In the study of Schaner and associates,[9] 60% of the additional lesions discovered by axial tomography were ultimately found to be benign. In our view computerized axial tomography is a sensitive but not specific study, which should be carried out in any patient before a presumed metastatic pulmonary nodule is removed.

Percutaneous aspiration needle biopsy has been used increasingly in recent years as a diagnostic tool. In our hospital it provided an accurate and specific means of determining histology. The morbidity associated with the procedure is restricted for the most part to easily managed pneumothoraces.[11] When expert cytologic interpretation of samples is available, it is a most worthwhile aid in the investigation of patients with pulmonary metastatic disease.

The value of mediastinoscopy is unclear. Of 42 patients who underwent mediastinoscopy, 5 were found to have positive mediastinal nodes. As a result four were eliminated from consideration for resection. In the majority of patients with small peripheral tumours mediastinoscopy gave negative results. Moreover, in all patients with colorectal, renal and sarcomatous tumours who underwent mediastinoscopy the findings were negative. The only tumour type for which mediastinoscopy appeared to be valuable was primary breast cancer. Therefore, mediastinoscopy appears to be an appropriate procedure in situations where there are central or large multiple tumours or where metastatic nodules from primary breast cancer are suspected.

Median sternotomy was used in only three patients in this series, although several patients who underwent bilateral thoracotomy might have been better served by median sternotomy. In recent years we have found that sternotomy for bilateral disease is a favourable approach. The relative number of wedge resections and enucleations has also increased. In the early years of this review lobectomy was performed for lesions that would now be managed by wedge resection. Thus, the ratio of wedge resections to lobectomy reported in this series is not representative of our current practice.

Some authors[4,6] have advocated using the tumour doubling time to define more accurately the biologic nature of the specific metastases. They have reported increased survival in patients whose tumour doubling times exceeded 40 days. Tumour doubling time was available in only a few of the patients reported here and usually we did not use doubling time to select patients for resection. Although McCormack and Martini[6] found no correlation between disease-free interval and survival, we found a direct relation (Fig. 1).

The actuarial survival figures from our series compared favourably with those in the literature.[3,6,8] We were surprised to find that patients with primary renal tumours had a shorter survival than those with colorectal tumours. Our findings support those of Joseph and colleagues[5] who thought that multiplicity of tumours was less important than their biologic nature. We found no difference in actuarial survival between patients with single as opposed to multiple tumours.

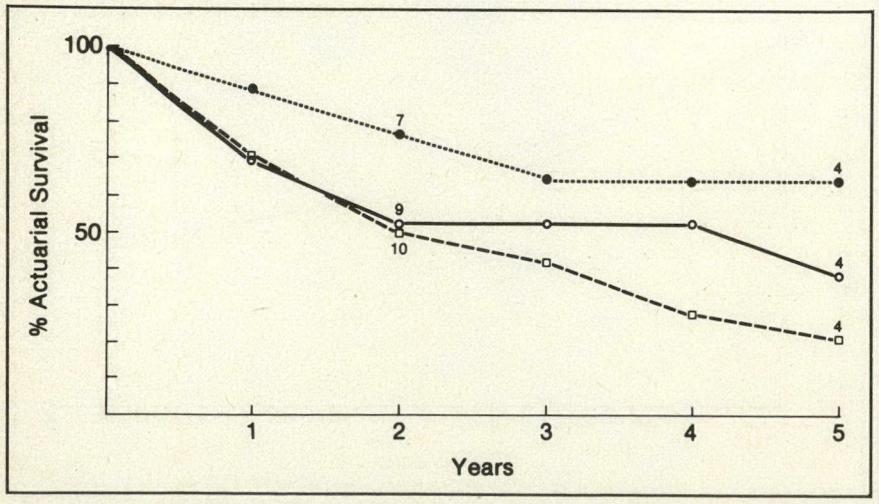

FIG. 3—Actuarial survival by tumour type. Black circles = sarcomas, white circles = colorectal tumours and squares = renal tumours. Numbers on curves represent number of patients alive and available for analysis for succeeding period.

Conclusions

The results reported here are no doubt influenced by additional forms of treatment (chemotherapy or radiotherapy) received by many of the patients. Although the relative merit of these additional therapeutic measures cannot be assessed, the role of surgery can be examined by this retrospective analysis. There is a clear

place for resection in those patients who have pulmonary metastatic disease in the presence of a controlled primary, and no evidence of active metastatic disease elsewhere. This is particularly true when the disease-free interval is at least 12 months. Such resections can be carried out with acceptable morbidity and mortality and provide a reasonable prognosis in the majority of cases. It is particularly difficult to assess whether the reasonable survival provided reflects the surgical intervention or the biology of the tumour. It is strictly impossible to conduct appropriate randomized trials as the individual tumour–host relation is a completely controlled variable. However, we have demonstrated that resection carries a low risk, extirpates the tumour and is associated with a reasonable survival.

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All initial communications should be addressed to the Coeditors, PO Box 8650, Ottawa, Ont. K1G 0G8 and marked The Canadian Journal of Surgery.

Manuscripts of original articles and other contributions, including a limited number of case reports, should be submitted in triplicate, *in English or French, with a covering letter requesting consideration for publication. They should be typed on one side of plain paper, double spaced with wide margins. Common measurements should be expressed according to Système international d'unités if possible.*

Illustrations (e.g., photographs of clinical material, radiographs, photomicrographs, graphs and diagrams), in triplicate, *must be in the form of glossy, unmounted and untrimmed prints, not larger than 20 X 25 cm. A legend must be supplied for each: the legend(s) should be typed on a page separate from the text of the article. For a roentgenogram submit a print rather than the original; for a photomicrograph include details of the stain and magnification in the legend. Lettering identifying parts of the illustration should be large enough to remain visible when the illustration is reduced in size for publication. A patient must not be recognizable unless the patient's written consent has been obtained; facial features may require blocking. Colour work can be published only at the author's expense. If an illustration is taken from a source other than the author's, letters of permission from the publisher and original author for reproduction of the illustration must be obtained.*

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References should be cited by number in the text, in order of occurrence, and listed at the end of the article in the style used in this issue of the Journal. In general, references to journals should follow the style used in this issue.

An abstract, in both English and French, about 125 words long, should accompany each article, on a separate page.

Authors will receive a copy of the edited manuscript for approval before publication but will not receive galley proofs.

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Toute communication initiale doit être adressée aux corédacteurs, CP 8650, Ottawa, Ont. K1G 0G8 sous la mention: "Le journal canadien de chirurgie".

Les textes originaux des articles et des autres communications y compris un nombre limité de rapports sur des cas spéciaux doivent être rédigés en triplicata , *en français ou en anglais, et accompagnés d'une lettre demandant leur publication dans le Journal. Veuillez les dactylographier sur une seule face d'une feuille non réglée avec double interligne et grandes marges.*

Les principales unités de mesure doivent être exprimées selon le Système international d'unités si c'est possible.

Les illustrations telles que des photographies d'appareils cliniques, des radiographies, des photomicrographies, des graphiques et des diagrammes, en triplicata, *doivent être fournies sous la forme d'épreuves sur papier glacé sans montage, les bordures intactes, d'un format ne dépassant pas 20 X 25 cm. Chaque illustration doit être munie d'une légende dactylographiée sur une page séparée du texte de l'article. S'il s'agit de radiographie, envoyez une copie et non l'original. S'il s'agit d'une photomicrographie, indiquez le contraste et l'échelle de l'agrandissement. Les lettres qui servent à identifier les éléments d'une illustration doivent être d'une dimension suffisante afin de demeurer visibles lorsque les nécessités de l'impression imposent une réduction de l'image fournie.*

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Il faut que les tableaux soient conformes au format rectangulaire du Journal et rédigés sur des feuilles séparées du texte, un tableau par feuille.

Les références doivent être citées dans le texte au moyen d'un chiffre et groupées dans l'ordre à la fin de l'article selon la manière de faire adoptée par ce Journal. Les références à des périodiques doivent être conformes à celles dans cette revue.

Un résumé, en français et aussi en anglais, qui ne doit pas dépasser 125 mots doit accompagner chaque article sur une feuille séparée.

A titre d'approbation, un exemplaire du manuscrit rédigé sera envoyé à l'auteur mais non les épreuves.

BOOK REVIEWS

ACUTE DISORDERS OF THE ABDOMEN. Diagnosis and Treatment. V.I. Sreenivas. 200 pp. Illust. Springer-Verlag New York Inc., New York, 1980. $13.95, paperbound. ISBN 0-387-90483-2.

The author discusses conditions causing the acute abdomen in a concise, clear and concentrated fashion. The first part of the book outlines the steps of clinical investigation; the majority of the book discusses specific conditions that may require surgical intervention and the book concludes with a discussion of urologic and medical conditions that may simulate conditions for which surgical treatment is imperative. Each discussion follows the classical format of etiology, pathogenesis, signs and symptoms, laboratory investigations and radiologic or other investigations. Where appropriate, illustrative roentgenograms have been included. These are of high quality and clearly show all the pertinent findings.

This has been accomplished in 195 pages and the book has the advantage of "one author" evenness of presentation. If there is any criticism, it would be that information is so concise that it is not easy to read about a number of conditions and sort out all the pertinent details.

This book is particularly suited to the needs of clinical clerks, junior residents and family practitioners who are faced early in their career, or infrequently, with patients suffering from abdominal pain of perplexing origin. At $13.95 it is an excellent buy and should be in every emergency department and in the library of medical students and junior residents. It is a good book.

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MANUEL DU TRAITEMENT ORTHOPÉDIQUE DES FRACTURES. Des membres et des ceintures. R. Borgi, J. Butel, R. Seringe, F. Fassier et G. Frere. 171 pp. Illust. Masson, Paris, 1981. Prix non mentionné. ISBN 2-225-67420-5.

The small size of this book is deceiving in the sense that the amount of information contained in it is valuable, even excessive; many methods described have never been used on this continent and others are rarely used at present, even in Europe. This makes the book in some parts little more than a list of methods available for a particular fracture. The authors state clearly for each fracture which method they prefer, but in some the technique could have been elaborated. The book will give the uninitiated a complete listing of all the methods for the closed treatment of fractures. It may be useful for the experienced orthopedist who occasionally wishes to resort to infrequently used techniques and for whom few instructions plus his own experience would allow the use of the methods without further consultation. The intermediate resident or orthopedist will have to use the bibliography for detail on the techniques before attempting some of them. This bibliography, at the end of each chapter, is quite complete and pertinent.

I enjoyed reading this book and agree entirely with the prologue by Professor Merle d'Aubigné that the authors have made a good effort to provide an inventory of the closed methods for treating fractures, and that it is important to remind orthopedists that fractures should be treated by the simplest method that gives the best result with the fewest complications.

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OPERATIVE TECHNIQUES IN VASCULAR SURGERY. Edited by John J. Bergan and James S.T. Yao. 310 pp. Illust. Grune & Stratton, Inc., New York, 1980. $54. ISBN 0-8089-1334-4.

Devoted to the technical aspects of vascular surgery, "Operative Techniques in Vascular Surgery" is based on a symposium organized by Drs. Bergan and Yao. The book is comprehensive and includes

sections on surgery of the aorta and its branches, cerebral revascularization, surgery of the upper extremity, femoral and infrageniculate arterial bypass, reoperation for graft complications, extra-anatomical bypass, portal hypertension and direct venous reconstructive surgery. The numerous contributors are all eminent surgeons, well known for the contributions they have made in the specific area they present. For example, who is more qualified to write about thoracoabdominal aortic aneurysms than E. Stanley Crawford, or carotid surgery than Jesse E. Thompson or the LeVeen shunt than Harry H. LeVeen? Moreover, this book has an international flavour including chapters by H.H.G. Eastcott and R.M. Greenhalgh from London, and by Henner Müller-Wiefel from Dusseldorf.

This book is basically a technical atlas and as such consists of a series of illustrations with a complementary text. Since each contributor was obviously responsible for his own illustrations, there is a wide discrepancy in type and quality, but in general they are clear and well annotated. The accompanying text is concise and appropriate.

Almost all techniques currently used in vascular surgery are described. Although the experienced vascular surgeon may find relatively little that is new, it does afford him the opportunity to reinforce his experience and compare his techniques with those of recognized authorities. Furthermore, even the very experienced surgeon will pick up a trick or two that may allow him to simplify a procedure. This book will prove invaluable to the resident in training and to the novice vascular surgeon and indeed should be considered a must for every vascular trainee. It represents a 1980 state of the art collection of vascular surgical techniques.

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STATUS OF THE CURABILITY OF CHILDHOOD CANCERS. The University of Texas System Cancer Center M.D. Anderson Hospital and Tumor Institute 24th Annual Clinical Conference on Cancer. Edited by Jan van Eys and Margaret P. Sullivan. 329 pp. Illust. Raven Press, New York, 1980. $31.50. ISBN 0-89004-478-3.

Among pediatric diseases, cancer is the leading cause of death. This book is a compilation of papers presented on the subject at a recent symposium held at the M.D. Anderson Hospital and Tumor Institute in Houston, Texas. The authors are recognized leaders in their respective fields; half of them are from the M.D. Anderson Hospital.

The working papers are divided into four sections. The first deals with definition of biologic and functional "cures", the role of supportive therapy in attaining current cure rates and a discussion of statistical methods. The second section addresses the contributions of surgery, chemotherapy and radiotherapy to improved survival rates in patients with solid tumours. The lack of appreciable improvement in the treatment of brain tumours and metastatic neuroblastoma in children over 1 year of age is notable. The third part deals with the leukemias and lymphomas. Salient features include an overview of Hodgkin's disease and the influence of front-end prognostic factors (those present in children with acute lymphoblastic leukemia *at diagnosis* that help categorize them as being at low or high risk for relapse). These factors include leukocyte count, the presence or absence of central-nervous-system leukemia, of a thymic mass on the chest film and of thymus-derived (T cell) or bursa-derived (B cell) surface markers on bone-marrow lymphoblasts. The final section deals with the physical and neuropsychologic sequelae in long-term survivors, including the spectre of a second malignant lesion. The risks of genetic aberrations in the offspring of survivors and methods of preventing cancer are discussed. While there is some overlap and repetition of subject matter, this book highlights the advances in survival made with standardized protocol studies, the value of a multidisciplinary approach to treatment and the need for minimizing therapy in selected cases to preserve the physical and psychologic integrity of long-term survivors.

This book will be useful to any health professional interested in the management of cancer in children. It summarizes the current state of the art with regard to childhood cancers.

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Neurosurgery Postgraduate Course

The 12th Annual Neurosurgery Postgraduate Course and the 6th Annual Neurosurgical Nurses' Conference will be held on June 3 and 4, 1982 in San Francisco, California. The course will provide an update on selected, often controversial, topics in clinical neurosurgery. The lectures will be presented by a distinguished visiting faculty: Fred Epstein, Irvin Kricheff, Leonard Malis and Robert Spetzler. Selected faculty from the University of California at San Francisco will also participate.

Cerebral and spinal neoplasms, cerebrovascular disease and recent clinically relevant advances in the neurologic sciences will be covered in depth. In addition to the didactic sessions, there will be luncheon discussions between small groups of registrants and individulal members of the faculty on a variety of neurosurgical problems.

This program is presented by the department of neurological surgery of the University of California School of Medicine at San Francisco. It is sponsored by Extended Programs in Medical Education and will meet the criteria for 16 hours of ACCME/AMA/CMA Category 1 (formal) continuing education credit for physicians. The program is also approved for nursing credit.

For further information, please write: Extended Programs in Medical Education, University of California School of Medicine, Room 569-U, Third and Parnassus, San Francisco, CA 94143, or call (415) 666-4251.

Conference on Total Hip Joint Replacement

Sponsored by the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases with assistance from the National Institutes of Health Office for Medical Applications of Research, a consensus development conference on total hip joint replacement will be held Mar. 1 to 3, 1982 at the Masur Auditorium, Building 10, National Institutes of Health in Bethesda, Maryland.

The conference is designed to conduct a scientific evaluation of the safety and effectiveness of total hip joint replacement procedures. Key questions to be addressed are: What are the indications and contraindications for total hip joint replacement? What are the current scientific principles guiding selection of materials, devices, and procedures? What is the short- and long-term prognosis with respect to medical status and functional activity after total hip joint replacement? What are the problems related to revision surgery for total hip joint replacements? What advances in science and technical skill lie in the future for total hip joint replacement?

On the first two days of the conference, experts in the procedures for total hip joint replacement will present data on safety and efficacy. A consensus panel, comprising specialists and generalists, will consider the evidence presented and issue a draft statement

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responding to the key conference questions. On the third day, this draft statement will be read to the conference audience and comments and questions invited.

For program information write to: Stephen L. Gordon, Ph.D., Director, musculoskeletal diseases program, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, Westwood Building, Rm. 405, Bethesda, MD 20205, or call (301) 496-7326.

For administrative information write to: Mr. Peter Murphy, Prospect Associates, 11325 Seven Locks Rd., Ste. 220, Potomac, MD 20854, or call (301) 983-0535.

CLASSIFIED ADVERTISING

As a further service to its readers the *Canadian Journal of Surgery* is pleased to accept suitable classified advertisements. The deadline is 1 month before issue date. Regular classified rates (for each insertion): $31.00 for the first 40 words or less, additional words 30¢ each, to maximum of 150 words (additional $12.00 for frame). Special Display under 75 words, 2¼″ ×2″, $75.00. $5.00 charge (first insertion only) for CJS box numbers. Display rates available on request.

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—S82-005

CLINICAL FELLOWSHIP

Ewart Angus Surgical Intensive Care Unit, Wellesley Hospital, Toronto. Available July 1, 1982 for a period of one year in a multidisciplinary acute surgical unit with 600 admissions per year. Duties will include patient care and clinical research in a strong academic and teaching unit with all types of patient population excepting cardiac surgery. Reply to: **Dr. D.P. Jones, Director, Surgical ICU, Suite 219, E.K. Jones Building, 160 Wellesley St. E., Toronto, Ont. M4Y 1J3. (416) 966-6656.** —S81-019

GENERAL SURGEON — FRCS(C), wide experience in trauma, vascular and GI endoscopy seeks position in solo or group practice. Reply: **Box S101, CJS.** —S82-001

ACADEMIC APPOINTMENT: ONT. — Applications are invited for a full-time position in the Department of Urology at Queen's University. The successful applicant will have responsibility for teaching in an established postgraduate program involving clinical practice and administration. There are excellent opportunities for basic and clinical research. Please send curriculum vitae with names of three referees to: **Dr. A. Morales, Acting Head, Department of Urology, Queen's University, Kingston, Ontario, Canada K7L 2V7.** —S82-004

OTOLARYNGOLOGIST: ONT. — required for peripheral general hospital — Metropolitan Toronto. Full-time staff appointment. Please send particulars to: **Dr. M. Charendoff, Head, Department of Surgery, c/o Medical Staff Office, North York Branson Hospital, 555 Finch Ave. W., Willowdale, Ont. M2R 1N5.** —S82-003

CRITICAL CARE FELLOWSHIP — Surgical Intensive Care Unit, University Hospital, University of Saskatchewan, Saskatoon, Saskatchewan. One year, renewable once, for physicians who are eligible for the Royal College Certification Examination in General Surgery or Anesthesia. Experience offered in: Surgical critical care multidisciplinary unit in multiple trauma, open-heart surgery, major complications following general surgical procedures, neurosurgical post-op care and infections in critically ill patients. Competitive salary. Opportunities for clinical research available. Positions open from January 2, 1982. Send curriculum vitae to: **Jaime C. Pinilla, MD, FRCS(C), Director, Surgical Intensive Care Unit, Department of Surgery, University Hospital, Saskatoon, Sask. S7N 0W0.** —S82-002