1-1-1989

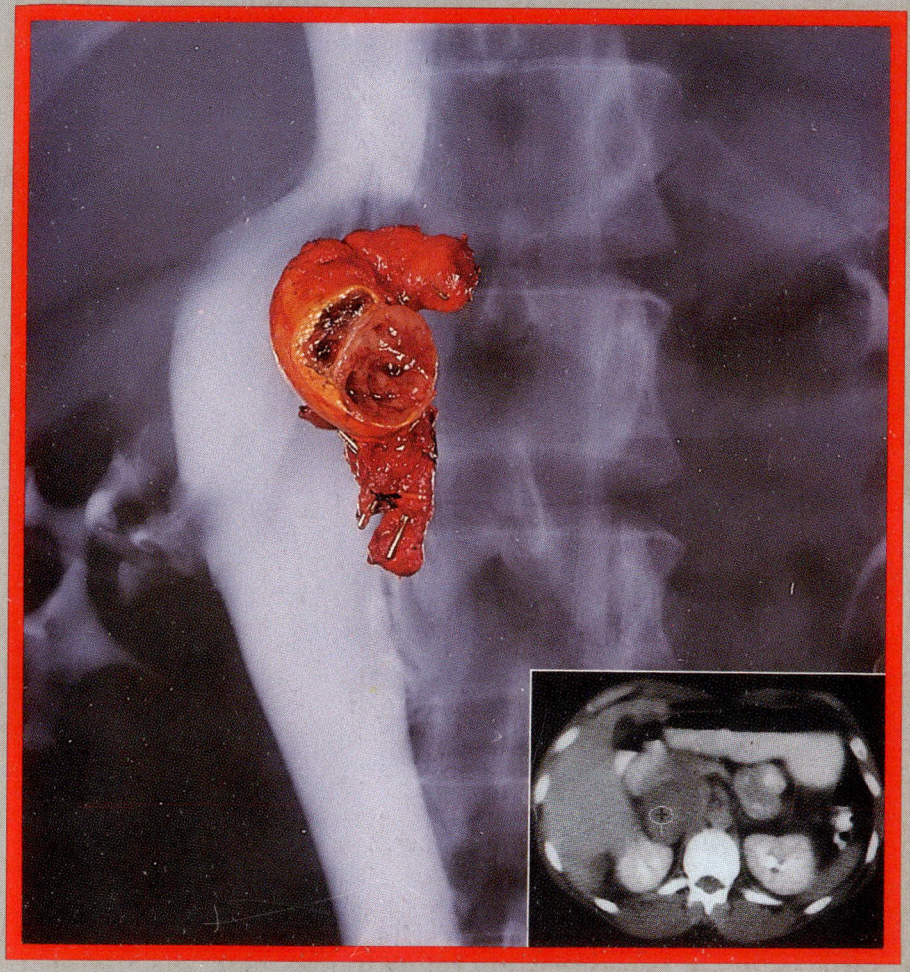
Volume 32, issue 1

Canadian Medical Association

CJS

The Canadian Journal of Surgery
Le journal canadien de chirurgie

Vol. 32, No. 1, January 1989 Janvier



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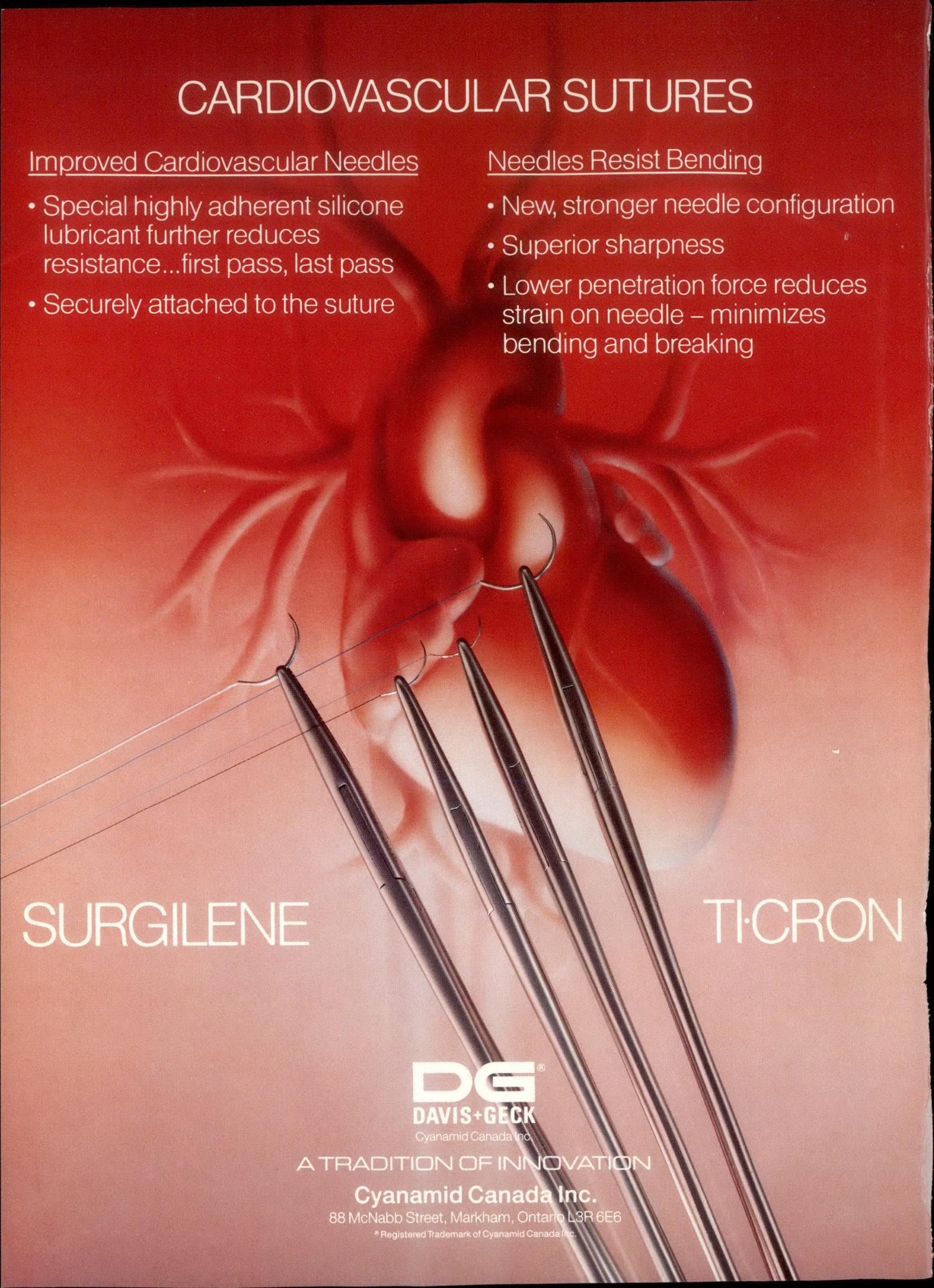

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The Canadian Journal of Surgery
Le journal canadien de chirurgie

Vol. 32, No. 1, January 1989 Janvier
ISSN 0008-428X

Cover picture

A recurrent retrocaval right adrenal pheochromocytoma superimposed on its venacavogram and shown in cross-section by computed tomogram (see editorial, pages 3 and 4).

An Adrenalin Rush

Nis Schmidt, MD, MSc, FRCSC

Member, Editorial Board, Canadian Journal of Surgery. Clinical Professor, Department of Surgery, University of British Columbia, St. Paul's Hospital, Vancouver, BC

Managing a surgical problem of the adrenal gland can get one's adrenalin going. The presentation, pathophysiology, pathological features, investigation and treatment of adrenal disease are fascinating and challenging. Admittedly, adrenal tumours are uncommon in clinical practice — benign nonfunctioning tumours occur unexpectedly in 0.6% of computed tomography series[1] and in only 1.4% to 8.7% of autopsy series,[2] and adrenocortical carcinomas appear in 0.0006% to 0.00017% of annual cancer registries.[3,4] Certainly, these rates indicate that the numbers of cases will be small.

In this issue (pages 51 to 55), Bautista and colleagues describe three cases of a fascinating adrenal tumour that is benign, nonfunctional and may be bilateral. Myelolipomas of the adrenal gland are real tumours in that they are discovered as an adrenal mass. Bautista and colleagues present an interesting debate regarding etiology in their development as a tissue composed of hematopoietic and fatty elements. The real question for the clinician on discovering a tumour of the adrenal gland is what to do with it; fortunately most adrenal tumours found incidentally are nonfunctional and benign. But these must be proven, and therein lies the challenge.

The widespread use of ultrasonography and computed tomography has fortuitously uncovered many previously unsuspected adrenal lesions and at the same time eliminated the use of many invasive and potentially harmful diagnostic procedures. Gone are the days of retroperitoneal air insufflation, and the use of adrenal gland arteriography for tumour diagnosis is decreasing. For patients who present with a clinical syndrome of hypertension, Cushing's syndrome or virilization, and endocrinologic investigation indicates a tumour, the

The Canadian Journal of Surgery
1867 Alta Vista Dr.
Ottawa, Ont. K1G 3Y6

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The Canadian Journal of Surgery is published by the Canadian Medical Association and sponsored by the Royal College of Physicians and Surgeons of Canada. The establishment of editorial policy is the responsibility of the Royal College. The objectives of the Journal, endorsed by the Council of the College, are: (1) to contribute to the effective continuing education of Canadian surgical specialists, using innovative techniques when feasible, and (2) to provide Canadian surgeons with an effective vehicle for the dissemination of their observations in the area of clinical research.

Published every 2 months by the Canadian Medical Association, PO Box 8650, Ottawa, Ont. K1G 0G8. Printed by RBW Graphics, 1749-20th Street E, Owen Sound, Ont. N4K 5R2. Postage is paid at Owen Sound. Second-class mail registration No. 5375. Second-class postage paid at Lewiston, NY (USPS no. 002417). US Postmaster will send address changes to: CJS, PO Box 1172, Lewiston, NY 14092. US Office of Publication: Lewiston, NY 14092. *Subscription rate for Canada and USA is $32.00 per year ($16.00 per year for trainees in surgery in Canada only), for all other countries $37.00 per year. Single copies (current issue) are available at $5.00 each, back issues at $6.00 each.*

Detailed instructions to contributors, in English and French, appear on page 14 of the January 1989 issue.

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treatment is clearly surgical. When adrenal tumours are discovered in the absence of clinical syndromes, careful biochemical investigation is necessary to uncover subclinical pheochromocytoma or androgen/estrogen-producing tumours suggesting malignancy.

Tests basic to this investigation include measurement of plasma concentrations of cortisol, aldosterone, epinephrine, norepinephrine, testosterone and estrogen, levels of vanillylmandelic acid, catecholamines, 17-hydroxycorticosteroids, 17-ketosteroids and dehydroepiandrosterone sulfate. Dexamethasone and metyrapone suppression tests are used to distinguish between pituitary Cushing's disease and adrenal adenomas or carcinomas causing Cushing's syndrome. Collaboration with an endocrinologist is important because interpretation of the results of these tests can be confusing and subject to error. Radionuclide scanning may also help in locating and distinguishing pheochromocytomas and aldosterone-producing Conn's adenomas. Adrenal venous samplings may be important to discriminate between the two glands, particularly in uncommon conditions of bilateral adrenal adenomas associated with clinical syndromes or in adrenal hyperplasia and hyperfunction.

Because an adrenal tumour can be malignant, its pathological features may be of more concern to the surgeon than the presentation and pathophysiology. Although malignant adrenal tumours supposedly start small and increase in size, few adrenal tumours less than 6 cm in diameter are malignant. Adrenal tumours 4 cm or greater in diameter, functioning or not, must be considered for surgical removal. When the tumour is less than 4 cm in diameter, has been carefully evaluated and is clearly nonfunctional, it should be followed up closely. If no changes occur on ultrasonography or computed tomography over 12 to 18 months, the tumour is probably unimportant. A tissue diagnosis will give the best assurance that it is benign.

Fine-needle aspiration biopsy with good radiologic control has proven effective and safe. Simple cysts can be aspirated; bloody fluid indicates the need for surgical removal. Benign cytologic patterns can be recognized and cortical adenoma, nodular hyperplasia, myelolipoma and pheochromocytoma diagnosed. Biopsy of functioning adrenal tumours associated with clinical syndromes is usually not necessary. Primary adrenocortical and secondary carcinomas, functioning or not, have been diagnosed and a few fungal infections of the adrenal glands identified using fine-needle aspiration biopsy.

When the clinical picture, history, physical examination, biochemical investigation and possible pathological findings are established, a surgical approach can be formulated, dictated mainly by the type of syndrome and tumour suspected. I prefer to approach Conn's tumours and benign unilateral nonfunctioning tumours through the flank. A bilateral flank or posterior approach is used in bilateral adrenalectomy for Cushing's disease. Pheochromocytomas need an anterior approach to permit scrutiny for multiple tumours and to eliminate the possibility of a malignant tumour. Larger, more complex tumours and those that are likely malignant may require extensive exposure and possible vascular bypass; for these I prefer a long midline laparotomy incision with extension to a midline sternotomy.

Surgery in the investigation of adrenal clinical syndromes and tumours can be challenging, particularly in the planning and performance of procedures that technically may be demanding. What appeared to be potentially serious may prove to be an innocent benign nonfunctional tumour, like a myelolipoma, requiring simple removal, much to the relief of surgeon and patient. Results can be extremely satisfying, since postoperative recovery from these endocrine syndromes can be dramatic.

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A Plea for Standard Methods of Reporting Studies on Lower Extremity Ischemia

Nathan M. Sheiner, MD, FRCSC

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In this issue (pages 48 to 50) is an article by my colleagues Laurendeau and Lassonde entitled "Above-knee femoropopliteal reconstruction with polytetrafluoroethylene: a good alternative to saphenous vein bypass". I do not intend to criticize the article, debate the selection of patients for surgery or the conclusions of the authors, but rather to point out that this and most other reports in the vascular surgery literature cannot be assessed appropriately because there is a complete lack of standardized reporting practices. For example, in their article Laurendeau and Lassonde claim that of the 64 femoropopliteal bypasses performed, 34 were for ischemic problems with rest pain and trophic changes and 30 for claudication alone. There is no objective categorization of the severity of claudication as could be achieved by treadmill testing in a vascular laboratory, nor is there any attempt to further categorize ischemic rest pain or trophic changes. As a result it is virtually impossible to compare this group of patients with others reported in the literature.

In terms of outcome, the only criterion noted in this article appears to be graft patency, though it is well known that patency does not necessarily imply success. Furthermore, there are instances in which graft occlusion occurs but does not result in limb loss, even when the bypass grafting is performed for so-called "limb salvage". Consequently, it is essential that patients be placed into standardized categories and that success be gauged by a shift into a higher category accompanied by an improvement in the ankle–brachial index. There must be objective criteria for determining patency, and a distinction should be made between primary and secondary patency rates. There should also be a standardized technique for identifying and grading those features that modify outcome, such as diabetes, smoking history, hypertension, hyperlipidemia and cardiac disease, in addition to a standardized method of assessing and reporting runoff. The reporting of deaths and complications should also be standardized as should results by life-table analyses; this can be done in either table or graph form. In Laurendeau's paper, results are reported by life-table analysis, but there is no notation of the number of grafts at risk or the standard deviation in each period.

Aware of the importance of standardizing reporting methods, the joint councils of the Society for Vascular Surgery and the North American Chapter of the International Society for Cardiovascular Surgery appointed an ad hoc committee to deal with this issue. The first report,[1] issued by a subcommittee, deals with reporting in lower extremity ischemia. In this report, terms are defined and criteria presented for uniformly gauging severity of disease, the findings of diagnostic studies, the types of therapeutic intervention and their outcome. The authors conclude: "We feel confident that most readers will appreciate that precisely defined and uniformly adopted reporting practices will allow us to better understand the data presented in the articles we read, be able to compare them with reliance, depend more confidently on their conclusions, and base our practices on the more solid foundations of fact and the proper perspectives they will provide."

Although acceptance of the recommendations in this report will result in considerably more work for vascular surgeons and necessitate the use of computers, the potential gains are enormous. Local, regional and national vascular societies should accept these recommendations, or at least their broad principles and insist that they be followed when presentations are made at their meetings.

Reference

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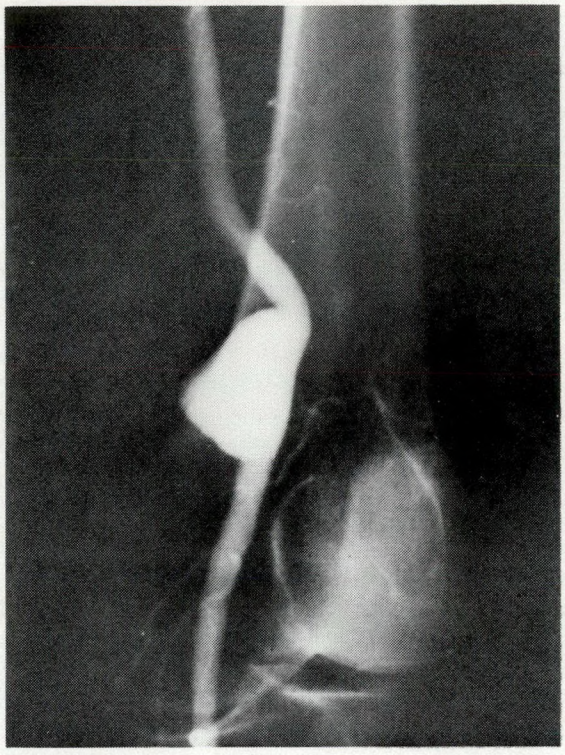
SESAP V Question



Item 218

The arteriogram of a 74-year-old man is shown above. Which of the following statements about this lesion is NOT true?

(A) The incidence of bilaterality is 35% to 70%

(B) It may be associated with ischemic symptoms in the toe even in the presence of good pedal pulses

(C) Spontaneous rupture may occur

(D) Abdominal aortic aneurysms occur in 30% to 50% of cases

(E) This disease is seen with equal frequency in both sexes

For the critique of Item 218 see page 68.

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CORRESPONDENCE

Contributions to the Correspondence section are welcome. They should be typewritten and double spaced.

Primary Omental Torsion

To the editors. Primary torsion of the greater omentum is a rare cause of abdominal pain. Since it was first described by Eitel[1] in 1899, fewer than 250 cases have been reported.[2] It occurs when a segment of omentum twists on its vascular pedicle, producing congestion, ischemia and eventual necrosis of the distal segment. Since the condition is rarely diagnosed preoperatively, its presence must be recognized at laparotomy. It should be distinguished from the more common secondary omental torsion, caused by attachment of the free edge of the omentum to cysts, tumours, inflammatory foci, postoperative wounds or scarring, and to internal or external hernias.

We recently treated two such patients. Both had tenderness and guarding in the right lower quadrant of the abdomen, diagnosed as acute appendicitis preoperatively.

At laparotomy, the appendix appeared normal in both patients and was removed. There was approximately 250 ml of serosanguineous fluid in the peritoneal cavity in one patient, and further exploration revealed a 10 × 15-cm mass in the right upper quadrant. The mass comprised an edematous, cyanotic piece of greater omentum with areas of necrosis. By twisting on itself, an attached pedicle caused infarction of the distal segment which was easily excised. Pathological examination confirmed a normal appendix and necrosis of omentum.

In the second case, a smaller 3 × 3.5-cm segment of infarcted omentum was found and excised. Again, pathological examination confirmed the diagnosis. Both patients made smooth recoveries and were discharged after 5 days.

In an extensive review of primary omental torsion by Mainzer and Simoes,[3] the commonest preoperative diagnosis was acute appendicitis (82%), followed by acute cholecystitis (12%). An abdominal mass was palpable in approximately 50% of the patients.

The finding of sterile serosanguineous fluid in the peritoneal cavity is almost universal.[3,4]

The etiology of primary omental torsion is unknown; however, in 1951, Leitner and colleagues[5] classified possible predisposing and precipitating factors. The former included anatomical variations in the omentum, obesity and redundancy of omental veins leading to kinking and twisting around the shorter, more tense arteries. Precipitating factors are those causing displacement of the omentum; they include trauma, violent exercise and hyperperistalsis with resultant increased passive movement of the omentum.

Treatment is resection of the infarcted segment; if it is not excised, the mass becomes atrophied and fibrotic and, on rare occasions, autoamputated. Associated morbidity and mortality are extremely low.

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Immediate Thrombosis of Carotid Endarterectomy

To the editors. In the September 1988 issue of the Journal (pages 368 to 371), Egan and Walker documented symptomatic thrombosis of carotid endarterectomy in 5 of 325 procedures (1.5%). Four of the five patients were symptomatic within 2 hours and one within 9 hours after operation. Although they indicated that the condition will be recognized only in patients with symptoms, the authors cited one reference[1] in which asymptomatic postoperative thrombosis, documented by digital subtraction angiography, was found in 1.2% of patients.

In a series of 864 carotid endarterectomies, in which all patients were monitored in the recovery room by ocular pneumoplethysmography (OPG-Gee), 26 patients were considered to have early thromboses, all of which were confirmed by immediate reoperation without interval arteriography.[2] These thromboses were *symptomatic* on the side appropriate in 9 patients; they were *asymptomatic* in 17 patients.

Although direct testing and other

forms of indirect noninvasive testing are difficult to apply in the recovery room, the OPG-Gee is a simple, economical procedure for identifying thrombosed carotid repairs, both *symptomatic* and *asymptomatic*.

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Dilatation and Curettage

Mark E. Boyd, MD, FRCSC

The most important role of dilatation and curettage is in the evacuation of retained products of conception; its diagnostic value is mostly limited to the detection of cancer of the endometrium. The procedure is associated with a number of complications, the majority of which occur during dilatation of the cervix. Vabra curettage is suggested as an alternative to diagnostic dilatation and curettage; it is efficient, is associated with fewer complications and is less expensive. Hysteroscopy is a useful supplement to Vabra curettage, especially in diagnosing focal lesions.

L'indication principale de la dilatation et du curetage est l'évacuation des restes des produits de conception; son intérêt diagnostique se limite à la détection des cancers de l'endomètre. L'intervention est associée à un certain nombre de complications, dont la majorité survient durant la dilatation du col. Le curetage par la méthode Vabra est recommandé comme alternative à la dilatation et au curetage diagnostiques; il est efficace, comporte moins de complications et est moins coûteux. L'hystéroscopie complémente bien le curetage Vabra, surtout pour diagnostiquer les lésions focales.

As a result of new understanding of its diagnostic and therapeutic worth and concerns over its cost, dilatation and curettage (D & C) is no longer the mainstay of gynecologic practice. In this review, the value of D & C will be discussed and the surgical technique described; the diagnosis and avoidance of complications will be emphasized. Alternatives to D & C for diagnosing gynecologic conditions will be suggested.

Indications

The most important diagnostic use of D & C is in cancer of the endometrium, presenting as postmenopausal, intermenstrual or excessive menstrual bleeding. The only patients at high risk of harbouring the disease are those with postmenopausal bleeding (8%).[1,2] It is surprising, therefore, to find that the majority of D & Cs are performed on women under 34 years of age when cancer of the endometrium is almost nonexistent.[3] The procedure is not a perfect diagnostic tool; initial curettage fails to identify 10% of endometrial cancers and repeat curettage is often necessary for a definitive diagnosis.[3,4] Dilatation and curettage infrequently establishes other causes of abnormal bleeding.[1] Information regarding ovulation and its timing may be important in the investigation of infertility; although ovulation can be confirmed by progesterone assays, its timing depends on histologic examination of the endometrium.

There are important, albeit limited, therapeutic uses for curettage. It is curative when bleeding is caused by retained products of conception or submucous polyps, but unexpected discovery of the former has declined as preoperative pregnancy tests have become more sensitive.

Curettage may also be useful in cases of acute vaginal bleeding not associated with pregnancy. The hemorrhage is arrested by removing endometrium, which is rich in prostaglandins, and by causing thrombosis of endometrial arterioles and sinuses. Endometrial disease is found in only one-third of such cases.[2]

In all other circumstances, D & C is unlikely to have any therapeutic effect,[1,5] particularly in patients who complain of menorrhagia.[6] In selected cases, medical curettage, using progesterone to initiate withdrawal bleeding, would be a more logical alternative.

Surgical Technique

Preoperatively, routine perineal shaving, catheterization and enemas are not necessary; detailed hormone studies are not worthwhile, but pregnancy tests should be done.[1] The size and position of the uterus and adnexa are confirmed by pelvic examination. Local anesthesia is known to be safer than general anesthesia, and efforts should be made to use it in the operation.[7]

The anterior lip of the cervix is grasped with a single-toothed tenaculum and downward tension is exerted; the degree of mobility determines the feasibility of vaginal hysterectomy and this should be recorded.

If cancer of the endometrium is

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Accepted for publication May 10, 1988

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suspected, endocervical curettage is indicated. The endocervix is first sampled, using a Kevorkian curet, care being taken to avoid the lower uterine segment. Firm pressure on the curet is necessary. The pathologist will wish to see endocervical stroma in the specimen which is collected on a separate Tulfa pad. Although endocervical curettage is done to diagnose extension of cancer of the body of the uterus into the cervix (thus marking the progression of endometrial cancer from stage I to stage II), the information gathered is often unreliable. Tumour fragments in the endocervix correlate best with a large tumour in the body of the uterus or with involvement of its lower segment but not with cervical invasion. One-half of the cases diagnosed preoperatively as stage II on endocervical curettage are found to be stage I when the operative specimen is examined.[8] Conversely, 13% of cases initially classified as stage I are found to be stage II.[8-10] The stage of endometrial cancer is altered by extension to the endocervix and although this finding should change the choice of therapy, it seldom does.

The length of the uterine cavity, used in staging endometrial cancer, is estimated with a sound. The procedure is made easier and safer when the angle between the uterus and cervix is obliterated by downward tension on the cervix. If it catches in an endocervical crypt the instrument may be impossible to insert, in which case a slightly larger probe, capable of bypassing the crypt, should be used.

The cervix is then dilated. Most complications associated with D & C occur at this time. It is imperative that there is minimal thrust on the dilators which should be held by the finger tips in a pencil grip. The dilatation should allow the passage of only the smallest curet — a no. 7 Hegar — not nos. 10 to 12 Hegar as advocated in the past.

It has been proposed that the uterine cavity should now be explored with Randall stone forceps to remove any polypoid lesions present.[11] Searching for polyps in this manner is inefficient and is supported only by a single, uncontrolled 30-year-old paper.[12,13] In order to pass stone forceps, the cervix must be dilated to an inappropriate and dangerous degree.

The curettage is done with a sharp curet exploring the anterior and posterior walls, the cornua and the fundus. Despite the seeming thoroughness of the curettage, later examination will show that only half the endometrium has been sampled.[3,14] Accurate histologic diagnosis cannot be made from gross examination of the tissue, and even frozen-section examination can be misleading.[14,15] In 6% of cases the sample of endometrium is such that the pathologist is unable to give a histologic diagnosis.[1]

Complications

The frequency of major complications is similar to that with which endometrial cancer is found.[1,2] Perforation is the most serious complication, caused by improper dilatation of the cervix;[16] this begins when the proper axis between the cervix and uterus is not found and a false passage is created.

Perforation of the pregnant uterus with a suction curet is particularly dangerous and necessitates laparotomy.[7] If the perforation is in the cervix, the uterine artery may be torn, and the ensuing hemorrhage into the broad ligament can be massive.[17] If the fundus of the pregnant uterus is perforated with a dilator, the curettage may be completed under laparoscopic control.

In the nonpregnant uterus, the fundus is usually perforated and there is seldom excessive intraperitoneal hemorrhage. When perforation is diagnosed, the procedure is discontinued and the patient closely observed for 3 to 4 hours. The D & C can be repeated later.

Laceration of the whole thickness of the cervix is caused by use of too large a dilator and is diagnosed by the sudden release of resistance to the instrument. Substantial vaginal or retroperitoneal hemorrhage may follow; the injury is best managed by laparotomy since vaginal manipulations are unsatisfactory.

There is some suggestion that D & C contributes to infertility.[18] A long-term ill effect is cervical incompetence.[19] An unusual complication is obliteration of the endometrial cavity by postoperative adhesions (Asherman's syndrome), most often a sequel to curettage of a postpartum uterus.

Complements and Alternatives to Dilatation and Curettage

Endometrial Cytologic Examination

Endometrial cytologic techniques do not ensure a definitive diagnosis, therefore they are not an alternative to D & C. They can, however, be used in screening when curettage is not justified; for example, in high-risk asymptomatic women (estrogen users) or symptomatic low-risk patients (premenopausal women with irregular bleeding).

The cytologic sample may be obtained directly by aspiration, lavage, brush or direct smear techniques.[20,21] Two appropriate instruments are the EndoPap and Endocyte.[22,23] These techniques allow endometrial cancer to be diagnosed in 94% of cases with a false-positive rate of 8%.[24] In 10% of cases no diagnosis was possible because the specimen was too small and in 50% there was failure to diagnose endometrial hyperplasia.[24]

Endometrial Biopsy

Definite determination of endometrial disease depends on direct biopsy of the endometrium rather than cytologic smears. Endometrial biopsy is an incomplete curettage, customarily done with a small curet and without anesthesia. Since its introduction some 40 years ago its efficacy, compared with that of D & C, has been questioned.[25] Reported series attest to its accuracy (91% to 92%) in diagnosing cancer of the endometrium.[25,26] However, these studies have been criticized for failing to indicate the percentage of cases in which endometrial biopsy was not possible and for failure to perform control curettage.[27]

In recent years, the technologic aspects of endometrial biopsy have been refined, as exemplified by the development of the Vabra curet (Berkeley Medevices Inc., Berkeley, Calif.). This disposable suction device allows thorough curettage without dilatation of the cervix. The procedure is more expensive than endometrial biopsy, but in a fairer cost comparison with D & C it is only 10% of the cost.[29] Its diagnostic value has compared favourably to D & C.[3,28,29] The procedure is 96% to 98% accurate in diagnosing cancer of the endometrium and 95% in the diagnosis of benign disease.[29] Also, it is associated with fewer complications. Its main weakness is a failure to diagnose endometrial or fibroid polyps, a shortcoming also noted with D & C.[1,29,30]

The sensitivity and specificity of endometrial biopsy and Vabra curettage compared with D & C are unavailable because information on the true incidence of endometrial cancer and the diagnostic error of the D & C is lacking. A problem in comparing Vabra curettage with D & C is that the former may remove the lesion and thus hinder the diagnostic accuracy of the latter.[3]

Hysteroscopy

Hysteroscopy is the definitive method of diagnosing abnormal uterine bleeding caused by focal lesions, especially submucous fibroids, but it is equally efficient in diagnosing endometrial cancer.[5,11]

Hysteroscopy is done with distension (panoramic hysteroscopy) or without distension (contact hysteroscopy) of the uterine cavity. Both require expertise and are subject to disruption because of technical problems. It has been suggested that hysteroscopy be used routinely before endometrial biopsy to detect lesions that may be missed by curettage and then to direct the curet toward a lesion.[31] Curettage is a necessary supplement to hysteroscopy since a histologic diagnosis cannot be made with this technique and biopsy through the instrument is unsatisfactory.[5]

Summary

Dilatation and curettage has changed from one of the most frequently used to one of the least frequently used procedures in gynecology. It is a useful diagnostic tool for detecting endometrial cancer but its therapeutic value in controlling uterine hemorrhage is limited. Complications relate to dilatation of the cervix. Under local anesthesia Vabra curettage supplemented by hysteroscopy is the most attractive alternative to D & C.

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Fate of the Gallbladder With Cholelithiasis After Endoscopic Sphincterotomy for Choledocholithiasis

D. David Lamont, MD; Ronald B. Passi, MD, FACS, FRCSC

Endoscopic sphincterotomy is the treatment of choice for choledocholithiasis after cholecystectomy. Its role has been expanded to treat choledocholithiasis in patients with gallbladders still in place. The authors report their experience with endoscopic sphincterotomy, with emphasis on the safety of the procedure, in high-operative-risk patients with choledocholithiasis and gallbladder in situ. Stones were successfully removed in 72 of 75 patients (96%); 1 required an emergency operation and 2 an elective one. Complications included bleeding, pancreatitis and cholangitis; there were no associated deaths. Follow-up of 54 of the patients, who had associated cholelithiasis at the time of endoscopic sphincterotomy, showed that 14 died of causes unrelated to the biliary tract. Of the others, 14 underwent cholecystectomy for failure of endoscopic sphincterotomy (2), acute cholecystitis (4) or persistent biliary tract symptoms (8). The other 26 patients were well after a mean follow-up of 30.4 months; 1 had mild biliary tract symptoms. Ultrasonography in 16 of the 26 patients showed persistent cholelithiasis in 12. Life-table analysis revealed a 15% probability of acute cholecystitis within 5 years of endoscopic sphincterotomy.

La sphinctérotomie endoscopique est le traitement de premier choix de la cholédocholithiase post-cholécystectomie. Son rôle s'est étendu au traitement de la cholédocholithiase chez les patients qui ont conservé leur vésicule biliaire. Les auteurs commentent l'utilisation qu'ils ont faite de la sphinctérotomie endoscopique et ils soulignent l'innocuité de cette technique chez les patients à risque élevé souffrant de cholédocholithiase et ayant conservé leur vésicule. Des calculs purent être retirés chez 72 patients sur 75 (96%); 1 nécessita une opération d'urgence et 2, une intervention différée. On compta parmi les complications une hémorragie, une pancréatite et une cholangite; il n'y eut aucun décès relié à l'intervention. Suite d'observation de 54 patients qui souffraient aussi de cholélithiase au moment de la sphinctérotomie endoscopique, révèle que 14 sont décédés de causes étrangères à l'affection des voies biliaires. Parmi les autres, 14 ont subi une cholécystectomie, soit après échec de la sphinctérotomie endoscopique (2), soit pour cholécystite aiguë (4) ou à cause de la persistance des symptômes biliaires (8). Après un suivi moyen de 30.4 mois, les 26 autres patients étaient en bonne santé; 1 présentait de légers symptômes biliaires. Les analyses actuarielles révèlent un risque de 15% de cholécystite aiguë dans les 5 ans qui suivent une sphinctérotomie endoscopique.

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Presented at the 92nd annual meeting of the Canadian Association of Clinical Surgeons, eastern division, Toronto, Ont., May 6, 1988

Accepted for publication July 5, 1988

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Endoscopic sphincterotomy (ES) was introduced in 1974 as a method of treating choledocholithiasis.[1,2] Its success rate now exceeds 90%, which is comparable to that of choledochotomy.[3] The complication and death rates are less than 10% and 3% respectively, which are superior to the rates for choledochotomy.[4–6] Endoscopic sphincterotomy is now the treatment of choice for retained or recurrent common-duct stones after cholecystectomy. As a result of experience, the role of endoscopic sphincterotomy has expanded to include the management of choledocholithiasis with gallbladders in place. It is also used in patients with ascending cholangitis and selectively in early gallstone pancreatitis.[7] Interest is now focused on whether the gallbladder can safely remain in situ after endoscopic sphincterotomy.[8–12] This question centres on two groups of patients — those with primary common-duct stones and no gallbladder disease and those with both common-duct stones and cholelithiasis. We report on the clinical follow-up of 75 patients with gallbladders in situ after endoscopic sphincterotomy performed for choledocholithiasis; 54 had associated cholelithiasis.

Patients and Methods

Between January 1981 and August 1987, 363 endoscopic sphinc-

terotomies were performed at University Hospital, London, Ont., for the management of choledocholithiasis or its complications. Seventy-five high-operative-risk patients (48 men, 27 women) had their gallbladders left in place. Coronary artery disease and poor pulmonary function were the most commonly encountered risk factors (Table I). The patients ranged in age from 32 to 98 years (mean 74.3 years). The indications for endoscopic sphincterotomy were: obstructive jaundice (38), cholangitis (24) and pancreatitis (5). Eight sphincterotomies were performed at the time of diagnostic endoscopic retrograde cholangiopancreatography when common-duct stones were identified. The technique used in this study has been described previously.[13]

Complete follow-up was obtained for all 75 patients, either from their referring physician or by direct personal contact. The period from endoscopic sphincterotomy to follow-up ranged from 5 to 68 months (mean 31.8 months). The causes of death were determined from death certificates or autopsy.

Life-table analysis was performed on the data from 52 patients in whom cholelithiasis was documented at the time of endoscopic sphincterotomy and who underwent recent ultrasonography.

Table I. Conditions in 75 High-Risk Patients Who Underwent Endoscopic Sphincterotomy

Disease/condition	No. of patients
Coronary artery disease	29
Chronic obstructive pulmonary disease	20
Myocardial infarction	3
Cerebrovascular accident	3
Miscellaneous	20

Results

The common bile duct was successfully cleared in 72 patients (96%). The procedure could not be completed in one uncooperative patient who was mentally retarded. He underwent elective cholecystectomy 2 days later. One patient had large common-duct stones that could not be extracted and were removed surgically 1 week later. The third failure was in a patient who had a large stone impacted in the ampulla; ascending cholangitis developed after the procedure and he underwent emergency cholecystectomy and duct decompression. This case represents the only cholecystectomy performed in a patient without documented cholelithiasis.

In the 75 patients there were three complications (4%): a minor hemorrhage that did not require transfusion, a mild pancreatitis and an ascending cholangitis that required cholecystectomy and duct exploration. There were no associated deaths.

The follow-up after endoscopic sphincterotomy ranged from 2 weeks to 43 months (mean 16.7 months) in 16 patients who died. No death was related to sphincterotomy or biliary sepsis. The causes were myocardial infarction (six patients), carcinoma of the lung (three), chronic obstructive lung disease (two), carcinoma of the prostate (one) and mesenteric infarction (one). Although death was reported as due to carcinoma of the gallbladder in three, this was confirmed in only one. All patients who died had their gallbladders in situ.

Table II. Summary of Outcome in 75 Patients With Gallbladders In Situ After Endoscopic Sphincterotomy (ES)

Outcome	With gallstones (n = 54)	Without gallstones (n = 21)
Death	14	2
Cholecystectomy	14	1
For failed ES	2	1
For acute cholecystitis	4	–
For persistent symptoms	8	–
Alive and well	26	18

Patients With Acalculous Gallbladders

Of the 75 patients, 21 (mean age 73.9 years) had no documented evidence of cholelithiasis at the time of endoscopic sphincterotomy. Follow-up in this subgroup ranged from 5 to 68 months (mean 33.6 months). Two of the 16 deaths occurred in this group. One patient underwent cholecystectomy for failure of endoscopic sphincterotomy; the remaining 18 are well with no further biliary tract symptoms.

Patients With Cholelithiasis

Fifty-four patients (mean age 75 years) had documented cholelithiasis at the time of endoscopic sphincterotomy. The follow-up in this subgroup ranged from 5 to 68 months (mean 30.4 months). Fourteen of the 16 patients who died were in this subgroup. Of the remaining 40 patients, 14 (35%) underwent cholecystectomy, in 2 cases, as noted earlier, for failure of endoscopic sphincterotomy. Four patients suffered from acute cholecystitis, an average of 4 months after endoscopic sphincterotomy. Eight patients who had persistent biliary tract symptoms were medically rehabilitated before elective cholecystectomy, which was performed a mean of 3 months after the procedure (Table II). Twenty-six patients with their gallbladders in situ remain well and all but 1 are asymptomatic.

Ultrasonography in 16 of the 26

patients revealed persistent cholelithiasis in 12, but no stones in 4; these may represent false-negative results, but the stones could have passed from the gallbladder into the duodenum through the sphincterotomy (Fig. 1).

By life-table analysis the probability of a patient having acute cholecystitis within 5 years of endoscopic sphincterotomy was found to be 15% (Fig. 2).

Discussion

Recent emphasis has been placed on the fate of the gallbladder after endoscopic sphincterotomy.[8-12] Most patients who undergo the procedure, leaving the gallbladder in situ, are elderly and high operative risks.

Because of altered gallbladder kinetics and free intestinal reflux into the biliary system, it has been suggested that there is an increased risk of acute cholecystitis developing after endoscopic sphincterotomy, even without cholelithiasis.[11] Tanaka and colleagues[11] presented a long-term follow-up report on 91 patients who underwent endoscopic sphincterotomy with acalculous gallbladders left in situ. None of these patients suffered from acute cholecystitis. This is in keeping with an earlier study by Choi and associates[14] who reported on 271 patients with acalculous gallbladders followed up for 7 years after endoscopic sphincterotomy; 2 suffered from cholecystitis. Our results are in keeping with those in the literature, and it is apparent that endoscopic sphincterotomy is indeed the treatment of choice for primary common-duct stones. The acalculous gallbladder can safely be left in situ.

The management of the calculous gallbladder is more controversial. Tanaka and colleagues[11] reported 16 of 31 patients (51%) with cholelithiasis who had acute cholecystitis after endoscopic sphincterotomy and advocated cholecystectomy whenever feasible. However, the incidence of acute cholecystitis after endoscopic sphincterotomy in patients with gallstones has been reported as 6.2%.[8] Rosseland and Solhaug[12] reported a follow-up study of 77 patients, 10 (12.9%) of whom had acute cholecystitis, but only 7 required cholecystectomy. They believed that the gallbladder which contains stones can safely be left in situ after endoscopic sphincterotomy in elderly high-risk patients.

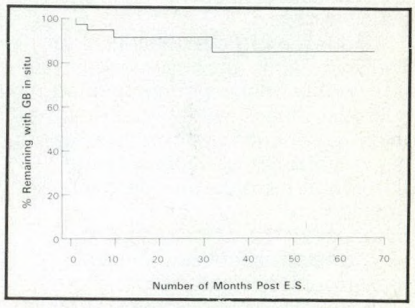

FIG. 2. Life-table analysis performed on patients with associated cholelithiasis, revealing probability of acute cholecystitis in this group. GB = gallbladder, E.S. = endoscopic sphincterotomy.

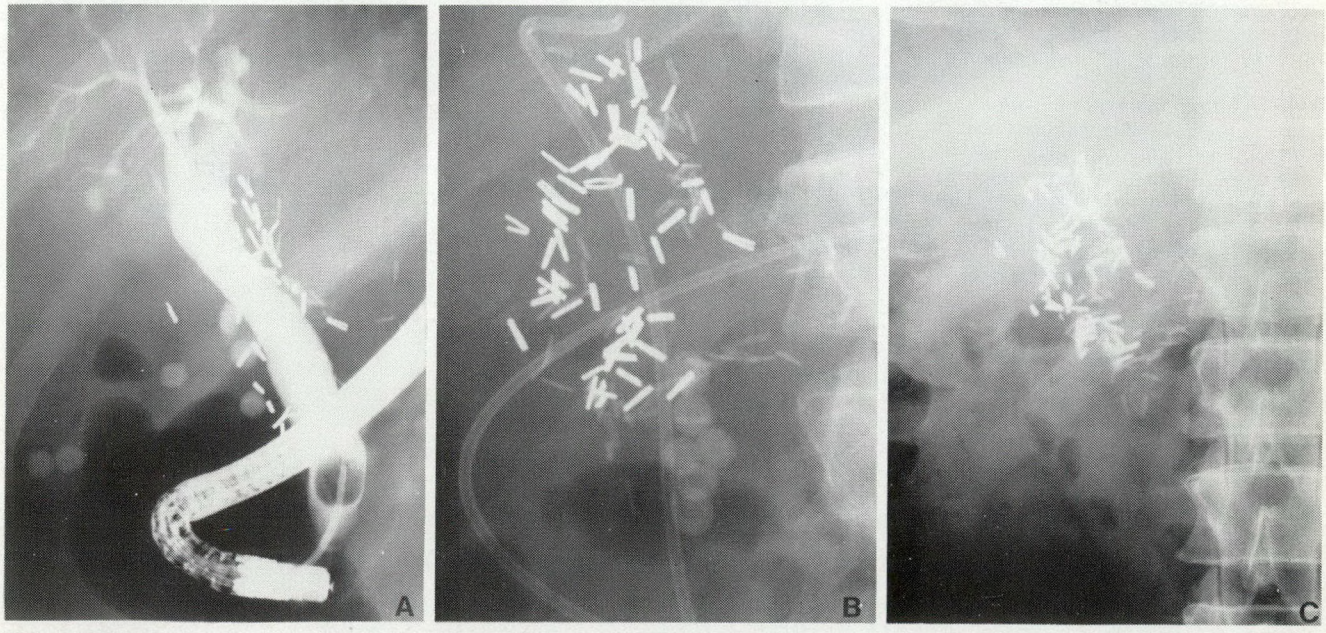

FIG. 1. Patient was 53-year-old man who had cirrhosis and previous placement of portacaval shunt. He underwent endoscopic sphincterotomy for management of ascending cholangitis. Initial x-ray film at endoscopic sphincterotomy (A) reveals radiopaque stones in gallbladder. X-ray film 5 days later (B) shows that stones had migrated to common duct alongside nasobiliary catheter. Follow-up x-ray film 3 weeks later (C) shows no evidence of stones, suggesting that they had passed.

Our results are in agreement with those of Rosseland and Solhaug. In our series, the common duct was successfully cleared in 96% with a 4% rate of complications; only one complication was serious and required operative intervention.

Life-table analysis revealed a 15% probability of acute cholecystitis developing within 5 years of endoscopic sphincterotomy. This is lower than the reported 29% death rate with acute cholecystectomy and duct exploration.[15] Duron and associates[5] have shown that endoscopic clearance of the bile duct before cholecystectomy in the elderly reduces the operative mortality associated with duct exploration from 21% to 6%.

We believe that in elderly high-risk patients, endoscopic sphincterotomy is the treatment of choice for common-duct stones or their complications and that the calculous gallbladder can safely be left in situ. These patients are likely to die of underlying medical conditions before acute cholecystitis develops, but should it do so, common-duct exploration will not be required at the time of cholecystectomy, thus putting them in a lower-risk category.[4,5]

The unanswered question is whether it is safe to manage younger, healthy patients with cholelithiasis in a similar manner. Further studies are required in this area.

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Strictureplasty in Crohn's Disease

Richard E. Silverman, MD, FRCSC; Robin S. McLeod, MD, FRCSC; Zane Cohen, MD, FRCSC

Strictureplasty may eliminate or decrease the extent of resection required in patients who have obstructing Crohn's disease of the small bowel. The authors performed 36 strictureplasties at 16 operations in 14 patients. Additional bowel resection was carried out in 13 of the 16 procedures. Early complications included wound infection in one patient, upper gastrointestinal bleeding in one and presumed suture-line leak, treated conservatively, in a third patient. At the end of the follow-up period (mean 16.1 months), 10 patients were asymptomatic and 4 had symptomatic recurrences; 2 of these required reoperation. A number of preoperative factors and operative techniques may have contributed to the favourable results.

La stricturoplastie peut éliminer ou réduire l'étendue de la résection que nécessitent les patients souffrant d'obstruction intestinale causée par la maladie de Cröhn de l'intestin grêle. Les auteurs ont pratiqué 36 stricturoplasties au cours de 16 opérations chez 14 patients. Des résections intestinales additionnelles ont été effectuées durant 13 de ces 16 interventions. Parmi les complications précoces, on compte une infection de plaie chez un patient, une hémorragie gastrointestinale haute chez un autre et une fuite présumée au point d'anastomose chez un troisième, laquelle fut traitée de façon conservatrice. A la fin de la période de surveillance des suites opératoires (16.1 mois en moyenne), 10 patients étaient asymptomatiques alors que 4 présentaient une récidive des symptômes; 2 de ces derniers nécessitèrent une deuxième intervention. Un certain nombre de facteurs préopératoires, de même que les techniques opératoires utilisées, peuvent avoir contribué à ces résultats favorables.

Goals of surgery for Crohn's disease are to treat complications and relieve symptoms. After an initial small-bowel resection or subsequent ileocolic resection to remove all visibly diseased bowel, 10-year rates of recurrence associated with reoperation range from 30.5% to 53%.[1,2] Indeed, there is histologic evidence that Crohn's disease may affect the entire gastrointestinal tract from the outset.[3,4] These factors dampen any enthusiasm for performing radical bowel resection for cure. Conservative surgery is especially applicable to two groups of patients: those who have previously undergone small-bowel resection and present with recurrent disease of an obstructive nature and those who have diffuse disease and multiple small-bowel strictures. In these patients, removal of the involved areas of intestine may lead to an iatrogenic short-bowel syndrome.

Strictureplasty for small-bowel strictures was pioneered by surgeons in India who successfully used the technique in both tuberculous and Crohn's lesions.[5] Lee and Papaioannou[6] advocated strictureplasty as a cornerstone of their policy of minimal surgery in patients having diffuse obstructive Crohn's disease. Their encouraging preliminary results led to subsequent recent reports[7–9] attesting to the safety and efficacy of the procedure. In this paper we review our experience with strictureplasty between October 1985 and March 1988 in the management of 14 patients who had Crohn's disease.

Patients and Methods

The 14 patients (3 female, 11 male) underwent 16 operative procedures in which 36 strictureplasties were performed. Their average age was 28.1 years (range from 17 to 44 years). As a whole, they had a relatively long history of Crohn's disease, with a mean time from diagnosis of 9.7 years (range from 1 to 27 years). Ten patients had previously undergone a total of 20 bowel resections. The indication for strictureplasty in all cases was recurring obstructive symptoms refractory to medical therapy.

Thirty strictures were short (1 to 7 cm) and were treated by a Heineke–Mikulicz procedure using interrupted 3-0 Vicryl sutures (Fig. 1).

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Presented at the 92nd annual meeting of the Canadian Association of Clinical Surgeons, eastern division, Toronto, Ont., May 6, 1988

Accepted for publication July 5, 1988

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The six longer strictures (7 to 12 cm) were treated by a Finney-type strictureplasty and also sutured with 3-0 Vicryl (Fig. 2). Only 3 operations consisted of strictureplasty alone; the remaining 13 consisted of strictureplasty and small-bowel resections in 9, ileocolic anastomotic resection in 2, proctectomy in 1 and small- and large-bowel resection in 1. We used a Foley catheter with the balloon inflated to 2 cm diameter to calibrate the small-bowel lumen internally in order to define strictures that were not readily apparent. The catheter was introduced into the first enterotomy site and passed proximally and distally to evaluate the entire small bowel.

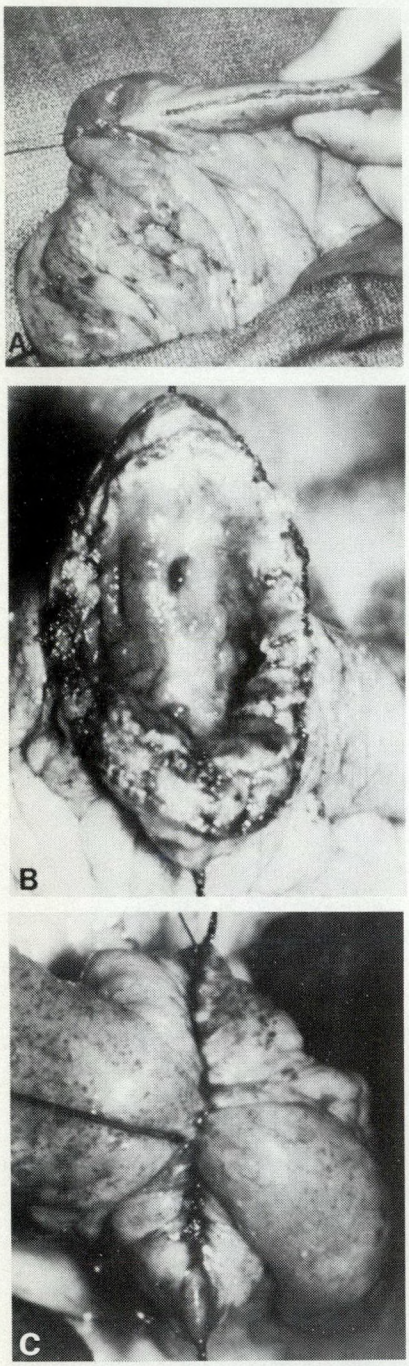

FIG. 1. Heineke–Mikulicz strictureplasty. Strictured area is opened along antimesenteric border with cautery (A). Stay sutures are placed and incision is oriented transversely (B). Interrupted 3-0 Vicryl is used to close strictureplasty (C).

Results

The mean postoperative hospital stay was 12.6 days (range from 9 to 24 days). Complications occurred early after operation in three cases. One patient had a wound infection. Another, on coumadin therapy for preoperative deep wound thrombosis, had an upper gastrointestinal hemorrhage which responded to conservative measures. The third patient complained of localized lower abdominal pain and tenderness 9 days after five strictureplasties and a bowel resection were performed; a presumptive diagnosis of a suture-line leakage was made and he was given broad-spectrum antibiotics and total parenteral nutrition infusion. His symptoms resolved within 48 hours.

The follow-up ranged from 1 to 29 months (mean 16.1 months). Nine patients had an excellent result and were asymptomatic, though five of them required maintenance drug therapy to control residual disease (Table I). Two patients required reoperation for obstructive symptoms, 3 and 8 months postoperatively. One had extensive small-bowel and colonic disease treated by resection and strictureplasty. Three months later a discrete stricture of the ileocecal valve was resected; it had likely been present but undiagnosed at the time of the original operation. The second patient had a resection and strictureplasty for extensive jejunoileitis. Eight months later, at laparotomy for recurrent obstructive symptoms, a more proximal stenosis was treated by strictureplasty. Two, who had recurrent symptoms due to active disease, were being managed medically. The remaining patient had no gastrointestinal symptoms but remained unwell due to unrelated medical problems.

Eleven of the 14 patients gained a substantial amount of weight postoperatively (range from 3.2 to 22.7 kg, mean 9.8 kg); the others had no change in weight or minimal weight loss. Serum albumin levels and total lymphocyte counts did not change greatly after surgery (Table II).

Discussion

Lee and Papaioannou[6] delayed publication of their results of strictureplasty in cases of Crohn's disease because of doubts about its safety and long-term benefits. In fact, on a follow-up of 8 to 42 months, none of their patients suffered a leak or other major complication, and only one had recurrent obstructive symptoms. In a recent review, Alexander-Williams and Haynes[10] updated their results in 52 patients with 148 strictureplasties. They found an 11% rate of "painful episodes" suggestive of a contained leak and a 6% rate of enterocutaneous fistula, which is comparable to that seen after bowel resection for Crohn's disease. In addition, 23% of their patients required further surgery, usually for strictures developing elsewhere in the alimentary

tract. Fazio and Galandiuk[9] described three patients with extensive small-bowel Crohn's disease who underwent 12 strictureplasties. There were no postoperative leaks or symptom recurrences after 6 months' follow-up. Whelan and colleagues[8] performed 15 strictureplasties on three patients. Two recovered without complications and remained well on follow-up. The third had symptoms suggestive of a leak which healed on conservative management, but after 12 months this patient needed reoperation for recurrence of an enterovesical fistula.

Kendal and associates[11] reported on nine patients who had 13 operative procedures and 45 strictureplasties. A high complication rate was noted in those with diffuse disease, including three who had enterocutaneous fistulas and four who required early reoperation (2 to 6 months postoperatively) for recurrent obstructive symptoms.

Our experience is further evidence of the safety and utility of strictureplasty. Of 16 operations, only 1 was associated with a sutureline leak which responded to conservative measures. At last follow-up, 10 of our patients were free of symptoms. Two of four with recurrent symptoms had improved on a medical regimen and two had undergone reoperation at 3 and 8 months respectively. These latter two continued to fare poorly, due to diffuse small-bowel and gastroduodenal Crohn's disease in one and to Crohn's colitis in the other.

An additional benefit has been the ability to maintain patient comfort without using steroids. Only one of nine patients who required prednisone preoperatively needed it postoperatively. Maintenance drugs included Pentasa in five patients and a course of azathioprine in three patients with ongoing disease.

We used a Foley catheter to identify stenotic areas not appreciated by external palpation. As in one of our patients, the ileocecal valve may be the site of an isolated narrowing, so the entire small bowel should be carefully evaluated.

In our opinion a number of therapeutic maneuvers could have contributed to the effectiveness of strictureplasty in this series.

- An adequate trial of medical therapy preoperatively may decrease the number of strictureplasties performed because of resolution of stenoses caused by inflammatory edema.
- Many of these patients, initially hospitalized with marked weight loss and nutritional depletion, benefit from the use of total parenteral nutrition or an elemental diet, as in eight of our patients, for 10 to 14 days before surgery and thus may have fewer complications.
- The use of a calibrating technique is important for diagnosing distal obstructing lesions which might endanger healing of a strictureplasty or anastomotic suture lines.
- It has been our practice to resect extensively diseased segments of bowel in addition to performing strictureplasty. An optimal surgical procedure requires salvage

Table I. Maintenance Drug Therapy

Drug	No. of patients	
	Preop	Postop
Prednisone	9	1
Salazopyrine	2	0
Pentasa	3	5
Metronidazole	9	1
Azathioprine	0	3

Table II. Serum Albumin Levels and Total Lymphocyte Counts Before and After Operation (± SEM)

Measurement	Preop	Postop
Serum albumin, g/L	37.8 ± 5.8	44.3 ± 4.9
Total lymphocytes, $\times 10^9$/L	1.134 ± 0.493	1.106 ± 0.454

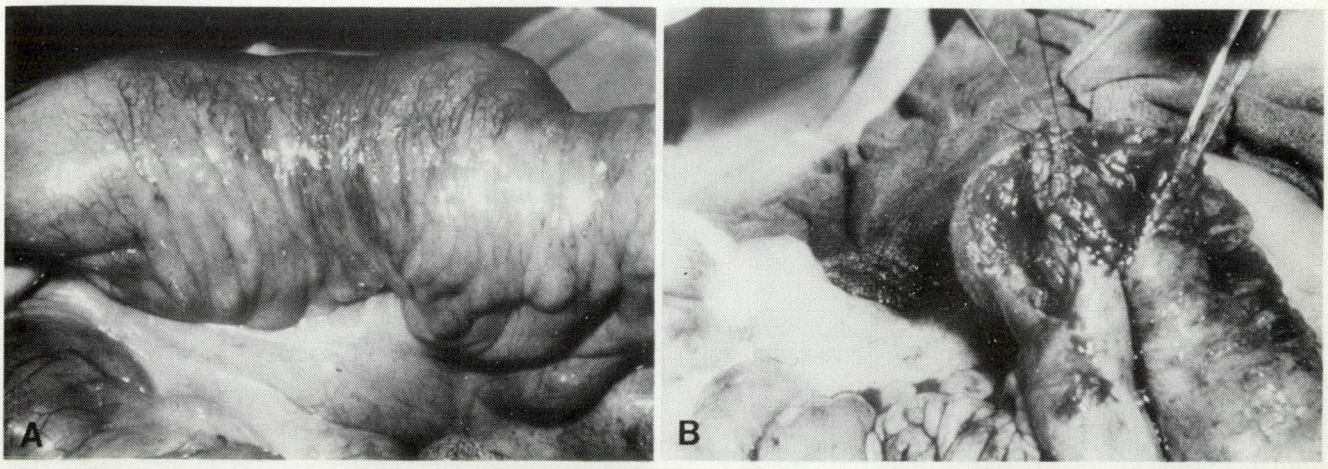

FIG. 2. Longer strictures are opened longitudinally and folded into two limbs. Back wall is closed with interrupted sutures (B), followed by closure of anterior wall.

of as much bowel as possible while removing areas not amenable to strictureplasty but which may compromise the safety and outcome of the procedure.

Symptomatic recurrence occurred in four (28%) of our patients and appeared to be due to progression of disease in three. Based on the experience of others,[10,11] a high recurrence rate can be expected in patients with extensive disease, and it remains to be seen how many of our patients will require repeated operative procedures, including strictureplasty, during long-term follow-up.

Strictureplasty in our experience has proven to be a safe method of relieving obstructive symptoms in patients with widespread small-bowel Crohn's disease. Major improvement in symptoms associated with reversal of weight loss is the usual result. An acceptable early rate of symptomatic recurrence, usually due to progression of disease, has been seen associated with a 14% reoperation rate.

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Identification and Importance of Lymphocyte Subpopulations in the Regional Lymph Nodes of Breast Cancer Patients

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To determine whether the presence of metastatic cancer cells in lymph nodes is accompanied by changes in lymphocyte subpopulations identified in tissue sections, the authors studied metastatic and nonmetastatic lymph nodes from eight patients with breast cancer and lymph nodes of three control patients. In all metastatic lymph nodes, T cells were seen in close contact with infiltrating cancer cells; B cells tended to accumulate focally, apart from cancer cell nests. In both metastatic and nonmetastatic lymph nodes from breast cancer patients, the fractional areas occupied by the T_4 (helper) and T_8 (suppressor/cytotoxic) lymphocytes were comparable. The B-cell fractional area was significantly ($p < 0.01$) greater in nonmetastatic than in metastatic nodes. The fractional area occupied by the T_8 lymphocytes in the breast cancer patients was significantly ($p < 0.01$) greater than in the normal lymph nodes, but no difference was noted in the fractional area occupied by the T_4 cells. These findings indicate that all lymph nodes in breast cancer patients are characteristically increased in suppressor/cytotoxic lymphocytes, and the presence of metastatic cancer cells in the nodes is manifested by a depletion of B lymphocytes.

Les auteurs ont étudié des ganglions métastasiés et non métastasiés provenant de huit patientes souffrant de cancer du sein, ainsi que les ganglions de trois patientes témoins, afin de déterminer si la présence de cellules cancéreuses métastatiques dans les ganglions s'accompagne de modifications des sous-populations lymphocytaires identifiées dans les coupes histologiques. Dans tous les ganglions métastasiés, des lymphocytes T ont été vus en contact étroit avec les cellules tumorales infiltrantes; les lymphocytes B avaient tendance à s'accumuler en foyers, à l'écart des nids de cellules cancéreuses. Dans les ganglions métastasiés et non métastasiés, les surfaces occupées par les lymphocytes T_4 (helper) et T_8 (suppresseurs/cytotoxiques) étaient comparables. La surface des lymphocytes B était significativement plus importante ($p < 0.01$) dans les ganglions non métastasiés que dans les ganglions métastasiés. Chez les patientes cancéreuses, la surface occupée par les lymphocytes T_8 était significativement plus grande ($p < 0.01$) que dans les ganglions normaux, mais aucune différence significative n'a été observée en ce qui a trait à la surface prise par les lymphocytes T_4. Ces résultats indiquent qu'il y a une augmentation caractéristique des lymphocytes suppresseurs/cytotoxiques dans tous les ganglions des patientes atteintes de cancer du sein et que la présence de cellules tumorales métastatiques dans les ganglions se manifeste par une déplétion des lymphocytes B.

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Accepted for publication Sept. 20, 1988

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There is circumstantial evidence of a relationship between immunocompetence and the prognosis of malignant disease.[1,2] The discovery of monoclonal antibodies, which are useful in identifying different subsets of lymphocytes,[3,4] has made it possible to investigate some of the complex aspects of the immune mechanism as it relates to locoregional immunity.

One of the early clinical applications of monoclonal antibodies was determining lymphocyte subsets in normal human lymphoid tissues,[5] and subsequent studies[6] shed light on the nature of lymphocytes in solid tumour tissue. The pattern and subtypes of these infiltrating cells at the host–tumour interface and the types of lymphocytes present in malignant and benign tissues were identified.

No one has yet accurately identified the lymphocytes in regional lymph nodes or the difference, if any, in the amount of T-cell subsets in metastatic and nonmetastatic lymph nodes and estimated their relative distribution. In this study we attempt to identify the distribution of T and B cells in lymph nodes of patients with breast cancer, using the indirect immunoperoxidase technique with specific antihuman T- and B-cell monoclonal antibodies. We also try to determine if there is a difference in the T-cell subsets in metastatic and nonmetastatic lymph nodes.

Patients and Methods

Eight patients operated on for stage I or II breast cancer at the Royal Victoria Hospital, Montreal, between 1984 and 1985, served as the study population. Six lymph nodes from three patients who underwent surgery for non-neoplastic or noninflammatory disease were used as controls to quantitate the surface area of different lymphocyte subsets in normal lymphoid tissue. For breast cancer patients, the number of lymph nodes with or without metastases was determined by routine histopathologic methods.

Tissue

Tissue blocks of 12 lymph nodes from eight breast cancer patients were studied as follows. After excision, the lymph nodes were serially sectioned and fixed in formalin for histopathologic assessment. Adjacent sections were snap-frozen in liquid nitrogen and stored at −80°C until immunostaining of the lymphocyte subpopulations was done. Thick cryostat sections (5 μm thick) were prepared and air dried for 1 hour.

The functional characteristics of the lymphocyte subpopulations defined by monoclonal antibodies is listed in Table I (OKT from Ortho Diagnostic Systems Inc., Raritan, NJ; B_1 from Coulter Electronics Inc., Hialeah, Fla.)

Immunoperoxidase Staining

Six sections (5 μm thick) were cut from each lymph node. Four sections served for identification of lymphocyte subsets, one as a negative control and one for routine staining with hematoxylin and eosin. The negative control section included omission of the first layer of monoclonal antibodies which was replaced by normal mouse serum. The staining procedure was performed at room temperature, as previously described.[7] Briefly, the sections are handled as follows: placed in pH 7.4, 0.01M TRIS (tromethamine) buffer for 10 minutes; incubated with saturating concentrations of monoclonal antibod-

Table I. Functional Characteristics of Lymphocyte Subsets as Defined by Monoclonal Antibodies

Lymphocyte subset	CD Classification*	Specificity
Antibody OKT_{11}	CD 2	Pan T lymphocytes
OKT_8	CD 8	Suppressor/cytotoxic T lymphocytes
OKT_4	CD 4	Helper/inducer T lymphocytes
B_1	CD 20	B lymphocytes

*International classification of clusters of differentiation (CD).

Table II. Fractional Areas Occupied by Lymphocyte Subsets in Normal Lymph Nodes*

Control no.	Lymphocyte subsets			
	T_{11}	T_8	T_4	B_1
1	33 (1)	11.4 (1)	25 (1)	17.5 (2)
2	22 ± 1.4 (2)	11.8 (1)	23.5 ± 0.7 (2)	14 (2)
3	23 ± 2.8 (2)	11.6 (1)	19.5 ± 4.9 (2)	17.7 (2)
Mean	26 ± 6.0	11.6 ± 8.4	22.6 ± 2.8	16.3

*Numbers represent % fractional areas, expressed as ± 1 standard deviation, occupied by lymphocyte subsets in total area of microscope fields. Numbers in parentheses refer to number of lymph nodes examined.

Table III. Lymphocyte Subsets in Lymph Nodes of Breast Cancer Patients

Cancer no.	No. of nodes resected	No. of nodes examined	Lymphocyte subsets*				
			T_{11}	T_4	T_8	T_4/T_8	B_1
1	2 1 +	1 +	ND	28	24	1.16	5.5
	1 −	1 −	ND	24	30.2	0.8	15.6
2	11 1 +	1 +	28	32	28	1.14	ND
	10 −	3 −	29.3	39.5	24.8	1.46	19.4
3	10 1 +	0 +					
	9 −	1 −	ND	43	30	1.43	ND
4	18 0 +	0 +					
	18 −	1 −	ND	37	26	1.42	ND
5	17 0 +	0 +					
	17 −	1 −	ND	27	21	1.29	24
6	4 0 +	0 +					
	4 −	1 −	ND	50	48	1.25	ND
7	19 0 +	0 +					
	19 −	1 −	ND	54	32	1.69	ND
8	10 1 +	1 +	ND	ND	ND	ND	4.2
	9 −	0 −					

*% of fractional areas occupied by different lymphocyte subsets in metastatic and nonmetastatic lymph nodes. + = metastatic, − = nonmetastatic, ND = not determined.

ies at 37°C for 1 hour; washed in TRIS buffer; incubated with peroxidase-conjugated rabbit antimouse immunoglobulin (Dakopatts, A/S, Glostrup, Denmark) for 20 minutes; washed in TRIS buffer; incubated with peroxidase-conjugated swine antirabbit immunoglobulin (Dakopatts) for 20 minutes; rinsed with TRIS buffer; the peroxidase reaction product developed with the dimethylaminobenzidine chromogen, washed with tap water; counter stained with hematoxylin; washed, dehydrated and mounted.

For each lymph node, photomicrographs of immunostained sections representing different lymphocyte subsets were analysed by quantitative morphometry, using a microcomputer and the Bioquant program (R and M Biometrics Inc., Nashville, Tenn.). The surface area of one lymphocyte subset in each section was calculated and related to the surface area of the total microscopic field. The lymphocytes corresponding to the various subsets were found to be clustered in discrete areas within the lymph nodes, as previously documented by studies of normal lymph nodes.[8] The fractional area of each subset was calculated as the ratio of its surface area relative to the total microscopic field. The mean fractional area of different lymphocyte subsets was calculated as the mean of at least six photomicrographs. The calculated mean for all patients in a given group was analysed using Student's *t*-test for unpaired data.

Results

Individual values of the nodes in the control patients are shown in Table II and results on the 12 lymph nodes from the eight cancer patients in Table III. The mean value for each lymphocyte subset in control, nonmetastatic and metastatic lymph nodes is presented in Table IV. Fractional areas occupied by lymphocyte subsets in nonmetastatic lymph nodes from stage I and stage II patients are summarized in Table V.

When the different lymphocyte subsets in nonmetastatic lymph nodes of breast cancer patients were quantitated and compared with those of lymph nodes from normal controls, the proportion of T_4 cells and B cells in the nodes of cancer patients was found to be slightly, but not significantly, larger. However, the mean of T_8 lymphocytes was 2.6-fold greater ($p < 0.01$) in nonmetastatic nodes from breast cancer patients than in the controls.

When the proportion of different lymphocyte subsets in both nonmetastatic and metastatic lymph nodes was compared, there was no significant difference in the mean areas of T_8 and T_4 cells. However, there were four times fewer B cells in the metastatic than the nonmetastatic lymph nodes.

When the different lymphocyte subsets in metastatic nodes were compared with the control nodes, the mean areas occupied by T_4 cells were not significantly different. However, there was a marked depletion of B lymphocytes in the metastatic nodes and the proportion of T_8 cells was significantly ($p < 0.01$) greater.

Comparison of different lymphocyte subsets in nonmetastatic lymph nodes from stage I and stage II patients showed no significant difference in the mean areas of T_8 and T_4 cells.

This study also revealed that the majority of lymphocytes infiltrating cancer tissue were T cells, which were often seen in intimate contact with infiltrating cancer cells; however, there was no predominant pattern of the type of T-cell lymphocyte subpopulation infiltrating these cancers. Apart from cancer cell nests, B cells tended to accumulate focally.

Table IV. Fractional Areas Occupied by Lymphocyte Subsets*

	Lymphocyte subsets			
Origin of node	T_{11}	T_8	T_4	B_1
Control	26	11.6	22.6	16
Nonmetastatic	29.3	30.1†	40.8	19.6
Metastatic	28.0	26.0†	30.0	4.8‡

*Numbers represent % area occupied by lymphocyte subsets in total area of microscope fields.
†Statistically significant ($p < 0.01$) compared with control nodes.
‡Statistically significant ($p < 0.01$) compared with nonmetastatic and control nodes.

Table V. Fractional Areas of Lymphocyte Subsets T_4 and T_8 in Nonmetastatic Lymph Nodes in Stage I and Stage II Patients

	Lymphocyte subsets	
Stage	T_4	T_8
I	42.2 (5)	31.4 (5)
II	31.75 (2)	27.5 (2)

Numbers represent % fractional areas occupied by lymphocyte subsets in total area of microscopic field. Numbers in parentheses refer to number of patients.

Discussion

The importance of T and B cell infiltrates in primary malignant tumour tissue has been examined in both clinical and experimental models. A discrepancy in the density of T and B cell infiltrates in cancerous and noncancerous breast tissue has

been noted. Shimokawara and colleagues[9] reported that B cells were predominant and T cells scanty in noncancerous breast lesions, while T cells predominated in cancerous breast tissue. They also showed a significant inverse correlation between the intensity of the T-cell infiltrate and the clinical stage. The infiltrates were dense in breast cancer without lymph-node metastases but were scanty in advanced clinical stages, suggesting that the infiltrating T cells in cancerous tissue represent host resistance. Berg[10] also reported fewer metastases and a higher cure rate in breast cancer with dense lymphocytic infiltrates. Black and colleagues[11] suggested that patient survival is superior in breast cancer with marked lymphocytic infiltration. In contrast, Schoorl and colleagues,[12] reporting on T and B cells in human breast cancer, indicated that T cells predominated in benign breast tissue. Giorno[6] examined the microanatomic distribution of different lymphocyte subsets in benign and malignant human breast tissue and found that in malignant tissue most of the T cells were of the T_8 subset, organized in single cells in the tumour stroma or invading tumour nests, while T_4 cells predominated in the lymphoid aggregates associated with benign tissue. Rowe and Beverley[13] reported that T lymphocytes existed in similar proportion in benign and malignant breast tissue.

Our study demonstrated that the lymph nodes of breast cancer patients displayed marked changes in their B and suppressor/cytotoxic T cells. B-cell depletion was associated with the presence of metastasis in the lymph nodes. The increase in suppressor/cytotoxic T cells was associated with concomitant breast cancer whether or not it had metastasized to the lymph nodes. No marked difference was seen in nodes from stage I and stage II patients, but the number in each group did not allow a reliable statistical evaluation of possible changes in lymphocyte subset populations.

The study also showed that the amount of T lymphocytes and their different subsets were present in similar proportions in metastatic and nonmetastatic lymph nodes of breast cancer. However, B cells were denser in nonmetastatic than metastatic lymph nodes, suggesting that an effector humoral response might be depleted when metastasis occurs. We also found that metastatic and nonmetastatic lymph nodes of breast cancer patients contained more T_8 (suppressor-/cytotoxic) lymphocytes than did normal lymph nodes from control patients. It remains to be established whether the generation of these suppressor/cytotoxic lymphocytes is directly involved in the host's immune surveillance against breast cancer.

It would appear that breast cancer cells metastasizing to regional lymph nodes cause an increase in the number of T-cell subsets as well as B cells.

In conclusion, breast cancer is accompanied by marked changes in lymphocyte subpopulations of associated axillary lymph nodes. Most remarkably, the recruitment of suppressor/cytotoxic cells, even before metastasis occurs, is consistent with the notion that breast cancer mounts an early cellular immune response as a result of unidentified factors associated with tumour growth.

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Clinical Significance and Measurement of the Length of the Right Main Bronchus

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It is important for surgeons, pathologists, anesthetists and anatomists to know the length of the right main bronchus. It extends from the carina of the trachea to the origin of the right upper lobe bronchus, but an exact method for measuring it has never been described.

Using bronchography, the authors measured the length of the right main bronchus in 24 patients. The posteroanterior projection taken at a standard distance (1.8 m) from the patient was used to minimize distortion due to the technique; if present, the distortion would not be more than 5% and would be an increase rather than a decrease in length.

The mean length of the right main bronchus was found to be 1.09 cm (range from 0 to 2.9 cm).

The clinical importance of this measurement is discussed. The authors conclude that many anatomy textbooks err in describing the length of the right main bronchus as 2.0 to 5.0 cm, but are correct in describing the left main bronchus as being about 5 cm long.

Il est important que les chirurgiens, pathologistes et anesthésistes connaissent bien la longueur du tronc bronchique droit. Il s'étend de l'éperon trachéal jusqu'à l'origine de la bronche lobaire supérieure droite. Toutefois, on n'a jamais décrit de méthode exacte de le mesurer.

A l'aide de la bronchographie, les auteurs ont mesuré la longueur du tronc bronchique droit de 24 patients. La projection postéro-antérieure prise à distance standard (1.8 m) du patient fut utilisée dans le but de minimiser la distorsion due à la technique. Si elle était présente, cette distorsion ne pourrait pas dépasser 5%, et elle aurait tendance à surévaluer la longueur plutôt qu'à la minimiser.

La longueur moyenne mesurée du tronc bronchique droit a été de 1.09 cm (avec un écart de 0 à 2.9 cm).

On commente l'importance clinique de cette mesure. Les auteurs concluent que plusieurs ouvrages d'anatomie sont dans l'erreur quand ils décrivent la longueur du tronc bronchique droit comme pouvant varier de 2.0 à 5.0 cm, mais qu'ils sont exacts quand ils donnent environ 5 cm comme longueur du tronc bronchique gauche.

The right main bronchus — from the carina of the trachea to the origin of the right upper lobe bronchus — is easily seen during bronchoscopy and at surgery, but is often inaccurately described.

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Accepted for publication Sept. 14, 1988

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The length of the right main bronchus is of great importance to pathologists, surgeons and anesthetists during resection of the right lung or the upper lobe, or the upper lobe with the "sleeve" of the right main bronchus, for example. There is minimal clearance proximally so it is of practical importance to know the length of the main bronchus.

The established rule for resection of bowel cancer is to take at least 5 cm of macroscopically healthy bowel on either side of the malignant lesion. The necessary clearance with respect to the lung or a lobe is usually given as 1.5 to 2.0 cm.

For endobronchial anesthesia, a double-lumen tube or an endobronchial balloon on the right side might cause encroachment on the right upper lobe bronchus.

The surgical pathologist must carefully examine the proximal resection lines of right-sided bronchial specimens, even more so than those from other areas.

The purpose of this study was to re-examine the tracheobronchial tree in order to identify accurately the take-off point of the right upper lobe bronchus.

Methods and Results

The literature does not describe a standard technique for consistently and accurately measuring distances in the tracheobronchial tree. In this study, to determine the length of the right main bronchus, the carina

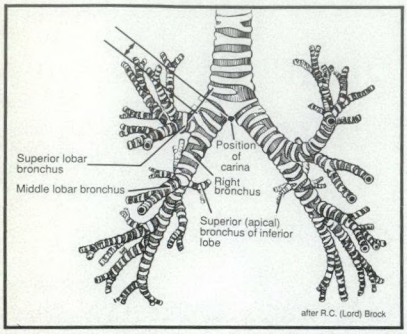

FIG. 1. Method of measuring right main bronchus (vertical distance from carina to origin of right upper lobe bronchus), which was done from life-size bronchograms (adapted from cast of bronchial tree by R.C. [Lord] Brock depicted in *Gray's Anatomy*[1]).

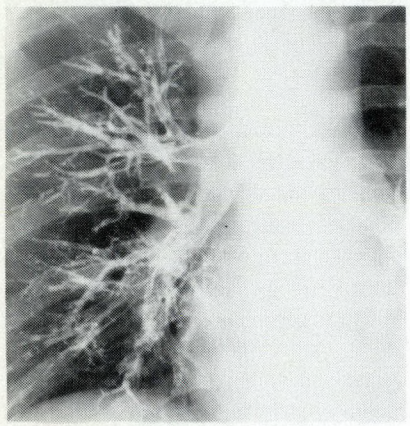

FIG. 2. Anteroposterior bronchogram.

Table I. Distance of the Right Upper Lobe Bronchus from Carina in 24 Patients

Distance, cm	No. of patients
0 – 0.5	6
0.6 – 1.0	6
1.1 – 1.5	7
1.6 – 2.0	3
2.1 – 2.5	1
2.6 – 3.0	1

was identified and the vertical distance between it and the upper border of the right upper lobe bronchus measured (Fig. 1).

Such measurements were made from the bronchograms of 24 patients, in whom "good filling" was obtained. Bronchography was done in the posteroanterior projection at a standard distance (1.8 m) from the patient to minimize distortion which, if present, was not more than 5% and was an increase rather than a decrease in length (Fig. 2).

The results are tabulated in Table I. The take-off point ranged from 0 to 2.9 cm below the carina (mean 1.09 cm, median 1.10 cm).

Discussion

Many anatomy books, including Gray's and Cunningham's[1-3] describe the right main bronchus and give its length as about 2.5 cm (Table II[1-10]). *Grant's Method of Anatomy*[4] states that the right upper lobe bronchus arises 2 to 5 cm from the tracheal bifurcation. However, Boyden,[8] in an excellent work on the segmental anatomy of the lung, states that the right upper lobe bronchus arises almost at the bifurcation of the trachea, that is, opposite the carina. He remarked: "Unfortunately, it has not been possible to provide bronchograms, but this has been partially compensated for by lateral views of a pair of lungs that have been injected with vinyl acetate and then dissected."

In another text[9] the main bronchus appeared to have been taken from the measurement of one cast only of an injected bronchial tree.

The relationship between the right upper lobe bronchus and the carina can be assessed in a variety of ways — during surgery or endoscopy, by radiologic or imaging techniques, in the cadaver by direct inspection or from a cast of the bronchial tree. No one method is ideal, but bronchography gives quite accurate reproductions, is easily performed and avoids the distortion of postmortem changes. Moreover, the bronchogram gives almost life-size definition. Using this method, we found the mean length of the right main bronchus in our 24 patients to be 1.09 cm, somewhat shorter than the length noted in most textbooks.

Table II. Length of Right Main Bronchus Reported by Various Authors

Authors	Length, cm
Williams and Warwick (Gray), 1980[1]	About 2.5
Romanes (Cunningham), 1981[2]	About 2.5
Hollinshead and Rosse, 1985[3]	About 2.5
Basmajian (Grant), 1980[4]	2.0 – 5.0
Basmajian, 1981[5]	No more than 5.0
Gardner and associates, 1969[6]	About 3.0
Hamilton, 1976[7]	No given measurement
Boyden, 1955[8]	No distance. Right upper lobe opposite carina
Last, 1972[9]	4.0
Ellis and Feldman, 1983[10]	2.5

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Acute Scrotal Pain in Children: Prospective Study of Diagnosis and Management

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Forty-eight boys were assessed for an acutely painful scrotum. Thirty-six (75%) of them underwent radionuclide scanning of the scrotum; the average age of this group was 11 years. The scan revealed epididymitis in 19 cases, spermatic cord torsion in 9, appendix testis torsion in 7 and acute hernia-hydrocele in 1. The diagnosis was confirmed at operation in all nine cases of spermatic cord torsion. Boys who had epididymitis received antibiotics only; all were available for short-term follow-up, and 16 were also assessed at a mean of 6 months after infection. Only one boy had testicular atrophy; he had undergone repair of an inguinal hernia, which could not be ruled out as a cause. Bacteriuric epididymitis occurred in three boys; two had known predisposing genitourinary anomalies, the third had no abnormalities. Boys who had nonbacteriuric epididymitis were investigated by renal and pelvic ultrasonography or voiding cystourethrography; no important abnormalities were detected. This prospective study indicates that radionuclide scanning can reliably differentiate spermatic cord torsion from other acute scrotal disease.

Quarante-huit garçons souffrant d'une douleur aiguë au scrotum ont fait l'objet de cette évaluation. Trente-six (75%) d'entre-eux ont subi une scintigraphie isotopique du scrotum; l'âge moyen chez ce groupe était de 11 ans. La scintigraphie a révélé une épididymite dans 19 cas, une torsion du cordon spermatique dans 9, une torsion de l'appendice testiculaire dans 7 et une hernie hydrocèle aiguë dans 1. Le diagnostique été confirmé lors de l'opération dans les neuf cas de la torsion du cordon spermatique. Les garçons souffrant d'épididymite ont reçu des antibiotiques seulement; tous ont pu être revu à court terme pour des examens de contrôle et 16 ont aussi été évalué 6 mois, en moyenne, après l'infection. Un seule garçon a présenté une atrophie testiculaire. Il avait subi la réparation d'une hernie inguinale, intervention qui ne peut pas être mise hors de cause. Trois garçons ont eu une épididymite avec bactériurie; deux avaient des anomalies génito-urinaires prédisposantes connues, alors que le troisième en était exempt. Les garçons ayant eu une épididymite sans bactériurie ont fait l'objet d'examens par échographie rénale et pelvienne ou par cysto-urétrographie permictionnelle; aucune anomalie importante ne fut décelée. Cette étude prospective montre que la scintigraphie isotopique peut différencier avec certitude les torsions du cordon spermatique des autres lésions aiguës du scrotum.

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Presented at the annual meeting of the Canadian Urological Association, Banff, Alta., June 21–25, 1987

Accepted for publication June 16, 1988

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An acutely painful scrotum in a child is of concern to parents and physicians, not only because of the discomfort it causes, but also because of possible impairment of fertility. Numerous studies[1–4] have shown that in torsion of the spermatic cord the time between onset of symptoms and surgical correction is inversely related to the subsequent viability of the testicle. Since the problem was traditionally believed to account for most cases of acutely painful scrotum in children, immediate surgical exploration was advocated.[2,4–6] However, recent studies,[1,7,8] including one carried out at our institution,[7] have indicated that nonsurgical conditions such as acute epididymitis are much more common in boys than was previously thought. Moreover, new imaging techniques provide a more accurate diagnosis so that, in many cases, surgery can be avoided.[9] With the advent of radionuclide scanning of the scrotum, we decided to institute a prospective study to determine the reliability of this investigation in diagnosing acute scrotal conditions in boys.

Because epididymitis in boys is considered bacterial in origin and secondary to underlying genitourinary anomalies, standard management has been antibiotic therapy followed by appropriate investigations for conditions that result in obstruction of the lower urinary tract or involve abnormal connec-

tions between the reproductive and urinary tracts. However, several studies[10,11] have indicated that most episodes of epididymitis occur in boys with normal genitourinary tracts and are not associated with bacteriuria. In this study we attempted to answer three questions.

- Is radionuclide scanning a reliable means of differentiating epididymitis from spermatic cord torsion?
- What is the frequency of bacteriuric epididymitis in boys?
- What is the incidence of underlying genitourinary anomalies in boys with epididymitis?

Patients and Methods

All 48 boys less than 16 years old who presented to the emergency department of the Izaak Walton Killam Hospital for Children in Halifax between September 1985 and September 1987, suffering from an acutely painful scrotum were entered into the study. Those suffering trauma to the genitalia were excluded, as were neonates, who were cared for at another institution. In addition to a routine analysis, the urine specimen was subjected to culture and sensitivity examination. Whenever the clinical diagnosis was in doubt, radionuclide scanning of the scrotum was performed. We intended to operate without the delay of scanning if testicular torsion was the most likely diagnosis. However, in practice, there was no case in which scanning did delay surgery; therefore, all boys who had an equivocal diagnosis underwent radionuclide scanning.

The scanning procedure usually took less than 15 minutes. A bolus of technetium-99m pertechnetate was injected intravenously, then serial images of the scrotum were obtained.[12] Patients with a diagnosis of epididymitis were not treated surgically but were given a course of antibiotics effective against most enteric pathogens. Repeat physical examinations were carried out several days after presentation and following convalescence, at which time the boys were investigated for underlying genitourinary anomalies.

Results

Epididymitis

Epididymitis was diagnosed in 19 boys (Table I), who ranged in age from 4 months to 15 years (mean 10.7 years). All underwent radionuclide scanning (Fig. 1). They were not explored surgically but were given a course of antibiotics effective against most enteric pathogens. Because they did not have surgical confirmation of the diagnosis, they were followed up closely by clinical examination within 2 weeks of the onset of their symptoms. If a diagnosis of torsion was missed, the child would be expected to have severe pain over several days, unresponsive to antibiotic therapy, and subsequently testicular atrophy would develop. However, at 2-week follow-up all the children in this group were convalescing without problems. Three boys were then lost to follow-up.

The remaining 16 boys underwent another clinical examination at a mean of 6 months after the acute episode (range from 1 to 20 months). Testicular size and symmetry were judged to be normal for age in all but one boy in whom the testis on the side previously involved by epididymitis was half the size of the contralateral testis. He had had an inguinal hernia repaired 2 years before and no postoperative record was available to indicate if the atrophy was secondary to his surgery.

Urinalysis was performed for 16 boys in this group. In 13 the findings were normal. The other three had pyuria; *Staphylococcus pyogenes* was cultured from one specimen, that of a 9-year-old boy who had undergone repair for hypospadias and was known to have a penile urethral fistula; *Pseudomonas aeruginosa* was cultured from another specimen, that of an 11-year-old boy whose history included numerous urinary tract infections secondary to imperforate anus, sacral agenesis and a neurogenic bladder; the third culture was sterile. Culture of the urine from one boy whose urinalysis was normal grew *Escherichia coli*. Voiding cystourethrography and renal ultrasonography in this 4-month-old child did not reveal any anomalies. All other cultures were sterile. Two 15-year-old boys gave a history of sexual activity, but urine cultures showed no growth of *Chlamydia*.

Two boys who had normal urinalyses and negative cultures received no antibiotics; both recovered promptly. The others received 7-day courses of appropriate antibiotics, most commonly co-trimoxazole orally, followed by amoxicillin and

Table I. Diagnosis and Radionuclide Scan in 48 Boys

Diagnosis	Total no. (%)	Scan	No scan
Acute epididymitis	19 (40)	19	0
Torsion spermatic cord	11 (23)	9	2
Torsion appendages	13 (27)	7	6
Hernia/hydrocele	3 (6)	1	2
Idiopathic scrotal edema	1 (2)	0	1
Tumour	1 (2)	0	1
Totals, no. (%)	48 (100)	36 (75)	12 (25)

tetracycline in dosages appropriate for size and age. Two boys who had fevers were treated parenterally with gentamicin.

Nine of the 13 boys with negative urine cultures were investigated to rule out predisposing factors for epididymitis. Radiologic investigations were omitted in four boys (in two at the parents' request and in the two who had possible sexual exposure). Voiding cystourethrography and renal ultrasonography were carried out in five cases, pelvic and renal ultrasonography in three and voiding cystourethrography and intravenous urography in one. None of these studies indicated any abnormalities.

Torsion of the Spermatic Cord

In 11 boys a diagnosis of spermatic cord torsion was made. These boys ranged in age from 7 to 16 years (mean 12.5 years). Nine underwent radionuclide scanning (Fig. 2) and all underwent surgery to confirm the diagnosis. Four boys who delayed seeking medical attention for more than 24 hours had infarcted testes which were removed. In no instance did scanning delay operation or lead to misdiagnosis.

Torsion of the Appendix Testis

Appendix testis torsion was diagnosed in 13 boys, who ranged in age from 3 to 14 years (mean 10.1 years). Seven underwent radionuclide scanning. In one of these the scan was equivocal; spermatic cord torsion could not be ruled out until operation was performed. In the other cases, the radiologist could confidently rule out spermatic cord torsion but could not always make the diagnosis of appendix testis torsion. However, clinical examination (the "blue dot sign" or point tenderness at the appendix) was usually diagnostic.

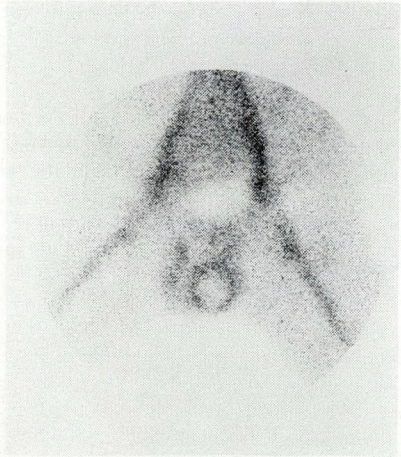

FIG. 1. Technetium-99m pertechnetate scrotal scan from 15-year-old boy with 24-hour history of right scrotal pain and swelling. There was recent sexual exposure. Urinalysis was normal and subsequent routine culture and culture for *Chlamydia* were negative. Scan shows increased activity of right hemiscrotum and along cord, in keeping with epididymitis. Three days after initiating course of tetracycline, swelling and pain had markedly decreased.

FIG. 2. Technetium-99m pertechnetate scrotal scan from 15-year-old boy with 24-hour history of left scrotal pain and swelling. Urinalysis was normal. Scan shows ring of increased activity surrounding photopenic defect in middle of left hemiscrotum. Diagnosis of spermatic cord torsion was made and confirmed at surgery. Testicle was not viable and orchiectomy and contralateral orchiopexy were carried out.

Eight boys in this group underwent excision of the infarcted appendage to relieve the pain, the other four were managed conservatively.

Discussion

Previous studies have indicated that spermatic cord torsion is the most common cause of an acutely painful scrotum in boys.[2,4,5] However, other reviews[1,8] have noted the increasing frequency of nonsurgical conditions, especially epididymitis. Only 23% of boys in this study had spermatic cord torsion compared with 40% who had epididymitis and 27% who had torsion of the appendix testis. The age distribution was of little diagnostic value. Other studies[4,7] have also noted this fact and the considerable overlap of clinical findings in these conditions. Since spermatic cord torsion is often difficult to rule out clinically, many authors[2,4-6] have advocated immediate surgical exploration. However, since epididymitis is no longer considered a rare cause of acute scrotal pain, this policy may lead to unnecessary operation. The development of radionuclide scrotal scanning, therefore, has been a major advance in the diagnosis of these often clinically confusing conditions.

Because none of the boys with epididymitis in this study was surgically explored, follow-up examination was essential to rule out the possibility of spermatic cord torsion being misdiagnosed as epididymitis. We reviewed all patients with epididymitis within 2 weeks of their acute episodes and none had findings suggestive of a missed torsion. At repeat examination, a mean of 6 months later, all but one boy had a palpably normal testis. The technetium-99m pertechnetate scrotal scan is a sensitive and selective

diagnostic tool in evaluating the acutely painful scrotum and at our institution has obviated the need for surgical exploration in many cases. Other studies[1,9] have reported similar encouraging results, so it is likely that this imaging technique will become common in assessing acute scrotal pain in children. However, when the scan cannot be obtained without delaying patient management or if the scan is equivocal, emergency scrotal exploration remains the diagnostic procedure of choice.

We found that most boys with epididymitis had normal urinalysis and sterile urine. This "nonspecific epididymitis" is reported[10,11] to be the most common type in boys, and our inability to identify any underlying genitourinary anomalies is in agreement with these studies. It has been postulated that these infections are of viral origin or are sterile inflammation secondary to reflux of urine into the genital tract, but neither theory has been proven. It is important to note that boys with epididymitis and sterile urine do not have underlying anomalies and therefore do not require extensive genitourinary investigations. Although most of these boys are treated with antibiotics, their recovery may be just as successful with rest and analgesics, as in two of our cases.

Conversely, of the three boys with positive urine cultures, two had known genitourinary abnormalities, so a positive urine culture does appear to warrant a diligent search for underlying anomalies.

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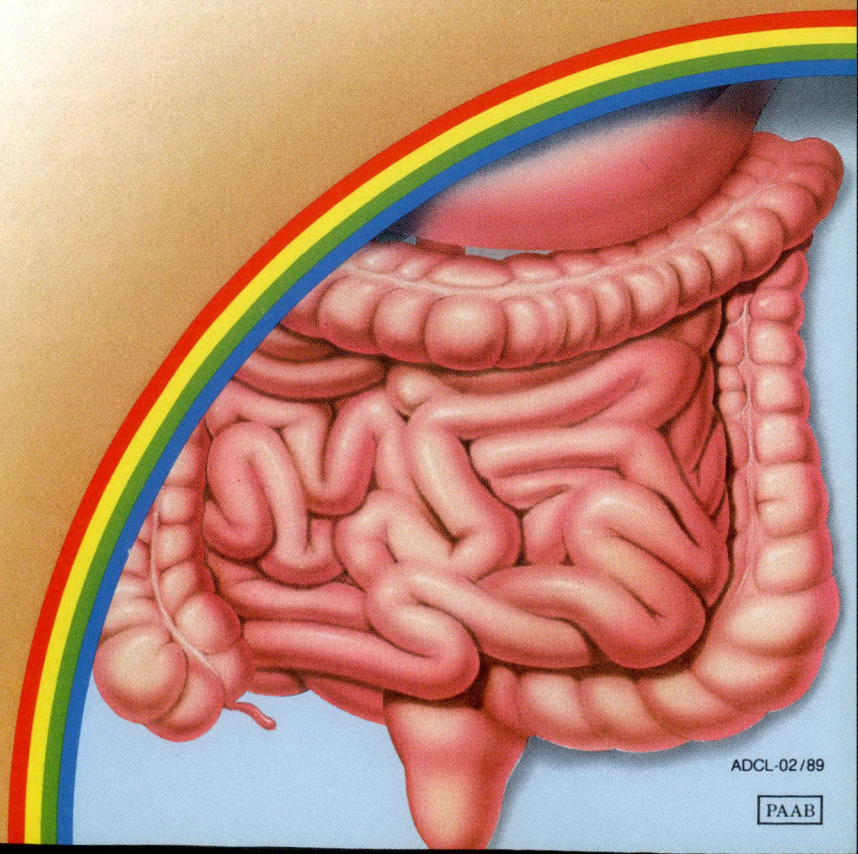

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Indications and Clinical Uses

Treatment : CLAFORAN (cefotaxime sodium) may be indicated for the treatment of infections caused by susceptible strains of the designated micro-organisms in the diseases listed below.

Lower respiratory tract infections : pneumonia and lung abscess caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*), other streptococci (excluding enterocci, e.g. *S. faecalis*), *Straphylococcus aureus* (penicillinase and non-penicillinase producing), *Escherichia coli*, *Hemophilus influenzae*, (including ampicillin resistant strains) and unspecified *Klebsiella* species.

Urinary tract infections : caused by *Escherichia coli*, unspecified *Klebsiella* species (including *K. pneumoniae*), *Proteus mirabilis*, indole positive *Proteus*, *Serratia marcescens* and *Staphylococcus epidermidis*. Also, uncomplicated gonorrhea caused by *N. gonorrhoeae* including penicillin resistant strains.

Bacteremia / Septicemia : caused by *Escherichia coli*, unspecified *Klebsiella* strains and *Serratia marcescens*.

Skin infections : caused by *Staphylococcus aureus* (penicillinase and non-penicillinase producing, *S. epidermidis*, Group A streptococci, *Escherichia coli*, *Proteus mirabilis* and indole positive *Proteus*.

Intra-abdominal infections : caused by *Escherichia coli*, and unspecified *Klebsiella* species.

Gynecological infections : including pelvic inflammatory disease, endometritis and pelvic cellulitis caused by *E. coli*, Group A streptococci and *Staphylococcus epidermidis*; anaerobic bacteria including unspecified *Peptococcus* and *Peptostreptococcus* strains and some strains of *Bacteroides fragilis*. In several cases, although clinical cures were achieved, bacteriological follow-up was not available.

Clinical experience with CLAFORAN in anaerobic infections is limited. CLAFORAN has been used with some success in wound and intra-abdominal infections against some strains of unidentified *Bacteroides* and anaerobic cocci.

CLAFORAN has been shown to be active against some strains of *Pseudomonas*. In the treatment of infections encountered in immunosuppressed and granulocytopenic patients, results of therapy with CLAFORAN have not been impressive.

CLAFORAN should not be considered in the treatment of enterococcal infections, i.e. *Streptococcus faecalis*.

Specimens for bacteriologic culture should be obtained prior to therapy in order to isolate and identify the causative organisms and to determine their susceptibilities to CLAFORAN. Therapy may be instituted before results of susceptibility studies are known; antibiotic treatment should be re-evaluated once these results become available.

Prophylactic Use : The administration of CLAFORAN perioperatively (preoperatively, intraoperatively and postoperatively) may reduce the incidence of certain infections in patients undergoing elective surgical procedures (e.g. abdominal or vaginal hysterectomy, gastrointestinal and genitourinary tract surgery) that may be classified as contaminated or potentially contaminated.

In patients undergoing caesarian section who are considered to be at increased risk of infection, intraoperative (after clamping the umbilical cord) and postoperative use of CLAFORAN may also reduce the incidence of certain postoperative infections. Effective use for elective surgery depends on the time of administration (see Dosage and Administration).

For patients undergoing gastrointestinal surgery, preoperative bowel preparation by mechanical cleansing as well as with a non-absorbable antibiotic (e.g. neomycin) is recommended.

If there are signs of infection, specimens for culture should be obtained for identification of the causative organism so that appropriate therapy may be instituted.

Contraindications

CLAFORAN is contraindicated in patients who have shown hypersensitivity to cefotaxime sodium, the cephalosporin or the penicillin groups of antibiotics.

Warnings

Before therapy with CLAFORAN is instituted, it must be carefully determined whether the patient has had previous hypersensitivity reactions to cefotaxime, cephalosporins, penicillins or other drugs. CLAFORAN should be given with caution to patients with Type 1 hypersensitivity reactions to penicillin. Antibiotics, including CLAFORAN should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to CLAFORAN occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. epinephrine, antihistamine, pressor-amines or corticosteroids).

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea during the administration of CLAFORAN. This colitis can range from mild to life-threatening in severity.

Treatment with broad spectrum antibiotics, such as CLAFORAN, alters the normal flora of the colon and may permit overgrowth of *Clostridium difficile* or other clostridia. It has been established that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of colitis may respond to discontinuation of CLAFORAN and replacement with a suitable specific antibiotic. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated. When the colitis is not relieved by discontinuance of CLAFORAN administration or when it is severe, an antibiotic specifically effective in antibiotic-associated pseudomembranous colitis (e.g. vancomycin) or other suitable therapy may be indicated. Other possible causes of colitis should also be considered (see Adverse Reactions).

Precautions

CLAFORAN (cefotaxime sodium) should be prescribed with caution in individuals with a history of lower gastrointestinal disease, particularly colitis.

The safety of CLAFORAN in pregnancy has not been established. Consequently, use of the drug in pregnant women requires that the likely benefit from the drug be weighed against the possible risk to the mother and fetus.

Use of CLAFORAN in women of child-bearing potential requires that the anticipated benefits be weighed against the possible risks.

Cefotaxime is excreted in human milk in low concentrations. Caution should be exercised when the drug is administered to nursing mothers.

Prolonged use of CLAFORAN may result in the overgrowth of nonsusceptible organisms. Constant evaluation of the patient's condition is essential. If superinfection occurs, therapy should be discontinued and appropriate measures taken.

Although CLAFORAN rarely produces alterations in kidney function, evaluation of renal status is recommended, especially in severely ill patients receiving high doses.

Patients with markedly impaired renal function should be placed on the special dosage schedule recommended under Dosage and Administration, because normal dosage in these individuals is likely to produce excessive and prolonged serum antibiotic concentrations.

Positive direct Coomb's test is known to develop in individuals during treatment with the cephalosporin group of antibiotics, including cefotaxime sodium.

In laboratory tests a false positive reaction to glucose may occur with reducing substances but not with the use of specific glucose oxidase methods.

Adverse Reactions

The most frequent adverse reactions with their frequency of occurrence are : Hypersensitivity (1.8%) : Rash, pruritus, fever. Local (5%) : Injection site inflammation with intravenous administration. Pain, induration and tenderness after intramuscular injection. Gastrointestinal (1.7%) : Colitis, diarrhea, nausea and vomiting. Symptoms of pseudomembranous colitis can appear during or after CLAFORAN treatment. Hemic and Lymphatic System (< 1%) : Mild, reversible leukopenia, granulocytopenia and thrombocytopenia have been reported. Some patients developed positive direct Coomb's test during treatment with CLAFORAN. Genitourinary System (< 1%) : Moniliasis, vaginitis. Liver (< 1%) : Transient elevations in SGOT, SGPT, serum LDH and serum alkaline phosphatase levels have been reported. Kidney (< 1%) : Increased serum creatinine and BUN have occasionally been observed. Central Nervous System (0.2%) : Headache.

Symptoms and Treatment of Overdosage

Since no case of overdosage has been reported to date with CLAFORAN, no specific information on symptoms or treatment is available. Treatment of overdosage should be symptomatic.

Dosage and Administration

CLAFORAN (cefotaxime sodium) may be administered intramuscularly or intravenously after reconstitution (see Table with recommended mode of reconstitution according to route of administration).

Dosage

Adults

The dosage of CLAFORAN should be determined by susceptibility of the causative organisms, severity of the infection and condition of the patient.

Guidelines for Dosage of CLAFORAN (cefotaxime sodium)

Type of Infection	Daily Dose (g)	Frequency and Route
Uncomplicated Gonorrhea	1	1 g IM (single dose)
Uncomplicated infections	2	1 g every 12 hours IM or IV
Moderately severe to severe infections	3-6	1-2 g every 8 hours IM or IV
Very severe infections (e.g. septicemia)	6-8	2 g every 6-8 hours IV
Life-threatening infections	up to 12	2 g every 4 hours IV

To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are as follows.

(a) 1 g IM or IV administered ½ to 1½ hours prior to the initial surgical incision to ensure that adequate antibiotic levels are present in the serum and tissues at the start of surgery

(b) 1 g IM or IV administered 1½ to 2 hours following the first dose; for lengthy operative procedures, additional intraoperative doses may be administered, if necessary, at appropriate intervals (1½ to 2 hours) during surgery

(c) 1 g IM or IV administered within 2 hours following completion of surgery

The total cumulative prophylactic dose should not exceed 6 g in a 12 hour period.

Caesarian Section Patients

The first dose of 1 g is administered IV as soon as the umbilical cord is clamped. The second and third doses should be given as 1 g IM or IV at 6 and 12 hours after the first dose.

Neonates, Infants, and Children

The following dosage schedule is recommended :

Neonates :	0-1 week of age	50 mg / kg IV q 12 h
	1-4 weeks of age	50 mg / kg IV q 8 h

Infants and children (1 month to 12 years) : For body weights less than 50 kg, the recommended daily dose is 50 to 100 mg / kg IM or IV of body weight divided into 4 to 6 equal doses, or up to 180 mg / kg / day for severe infections.

For body weights 50 kg or more, the usual adult dosage should be used.

The maximum daily dosage should not exceed 12 grams.

Administration of CLAFORAN should be continued for a minimum of 48 to 72 hours after the patient defervesces or after evidence of bacterial eradication has been obtained; a minimum of 10 days of treatment is recommended for infections caused by Group A beta-hemolytic streptococci in order to guard against the risk of rheumatic fever or glomerulonephritis; frequent bacteriologic and clinical appraisal is necessary during therapy of chronic urinary tract infections and may be required for several months after therapy has been completed; persistent infections may require prolonged treatment. Doses less than those recommended should not be employed.

Dosage for Patients with Impaired Renal Function

In patients with estimated creatinine clearance of less than 20 mL / min / 1.73m² the dose of CLAFORAN should be halved (see Precautions).

If serum creatinine values alone are available, the following formula (based on sex, weight, and age of the patient) may be used to convert these values into creatinine clearance.

$$\text{Males : } \frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine}} \quad \text{Females : } 0.85 \times \text{above value}$$

Administration

Intramuscular : CLAFORAN should be injected well within the body of a relatively large muscle such as the upper outer quadrant of the buttock (i.e. gluteus maximus); aspiration is necessary to avoid inadvertent injection into a blood vessel.

Intravenous : The intravenous route is preferable for patients with bacteremia, bacterial septicemia, or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

For bolus administration a solution containing 1 or 2 g of CLAFORAN can be injected over a period of 3 to 5 minutes. Using an infusion system, it may also be given over a longer period of time through the tubing system by which the patient may be receiving other intravenous solutions. Butterfly* or scalp vein type needles are preferred for this type of infusion. However, during infusion of the solution containing CLAFORAN, it is advisable to discontinue temporarily the administration of other solutions at the same site.

Reg'd TM of Abbott Laboratories.

Reconstitution

For Intramuscular Use : CLAFORAN should be reconstituted with Sterile Water for Injection or Bacteriostatic Water for Injection in accordance with the volumes recommended in the following table.

Reconstitution Table

Intramuscular	Volume to be Added to Vial (mL)*	Approximate Available Vol. (mL)	Approx. Average Concentration (mg/mL)
500 mg vial	2	2.2	230
1 g vial	3	3.4	300
2 g vial	5	6.0	330

*shake to dissolve.

For direct intravenous injection (bolus) and / or continuous intravenous infusion : 500 mg, 1 and 2 g vials should be reconstituted with at least 10 mL of Sterile Water for Injection. Reconstituted solution may be further diluted with 50 to 1000 mL of the fluids recommended for IV infusion.

Reconstitution Table

Intravenous	Volume to be Added to Vial (mL)*	Approximate Available Vol. (mL)	Approx. Average Concentration (mg/mL)
500 mg vial10	10.2	50	
1 g vial	10	10.4	95
2 g vial	10	11.0	180

*shake to dissolve.

Solutions for IV Infusion : CLAFORAN is compatible with the following infusion fluids :

- Sterile Water for Injection
- 0.9% NaCl injection
- 5% dextrose injection
- 0.9% NaCl and 5% dextrose injection
- 0.45% NaCl and 5% dextrose injection
- 0.2% NaCl and 5% dextrose injection
- Sodium Lactate injection
- 5% dextrose and 0.15% KCl injection
- Plasma-Lyte 56 Electrolyte Solution in 5% dextrose injection
- Ringer's injection
- Lactated Ringer's solution
- Lactated Ringer's with 5% dextrose injection

CLAFORAN is also compatible with lignocaine 1%.

A solution of 1 g of CLAFORAN in 14 mL of Sterile Water for Injection is isotonic.

Stability of Solution

Storage : Solutions of CLAFORAN range from light yellow to amber, depending on concentration and the diluent used. The solutions tend to darken depending on storage conditions and should be protected from elevated temperatures and excessive light.

**Reg'd TM of Baxter-Travenol Laboratories.

CLAFORAN reconstituted in the original vial as described under Reconstitution maintains satisfactory potency for 24 hours at room temperature (25°C) and for 48 hours under refrigeration (0-5°C). Only freshly prepared reconstituted solutions may be further diluted with 50 to 1000 mL of the recommended infusion fluids in Viaflex** intravenous bags. Such solutions maintain satisfactory potency for 24 hours at room temperature (25°C) and for 72 hours under refrigeration (0-5°C). Any unused solutions should be discarded.

CLAFORAN reconstituted with 1% lignocaine maintains satisfactory potency for up to 24 hours at room temperature and 48 hours under refrigeration (reference to lignocaine restrictions is advisable).

CLAFORAN solutions exhibit maximum stability in the pH 5-7 range.

Special Instructions : Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Solutions of CLAFORAN range from light yellow to amber, depending on concentration and diluent used. The dry powder as well as solutions tend to darken, depending on storage conditions.

Incompatibilities : Solutions of CLAFORAN must not be admixed with aminoglycoside solutions. If CLAFORAN and aminoglycosides are to be administered to the same patient, they must be administered separately and not as a mixed injection.

Solutions of CLAFORAN should not be prepared with diluents having a pH above 7.5 such as Sodium Bicarbonate Injection.

Availability

Claforan (cefotaxime sodium) is supplied as a sterile, white to pale yellow powder, in vials containing 500 mg, 1.0 and 2.0 g of cefotaxime sodium (expressed as acid on a dry basis).

Storage : CLAFORAN in the dry state should be stored at room temperature, protected from light and heat.

Product monograph available on request

Reference

Jones R.N. et al. : Antibiotic Prophylaxis of 1036 Patients Undergoing Elective Surgical Procedures. The American Journal of Surgery, 1987; 153 : 341-346.

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Diurnal Variation in Admission to Hospital of Women in Labour

William D. Fraser, MD;*‡ Frances H. McLean, BScN;† Robert H. Usher, MD†

In women having spontaneous labour or premature rupture of the membranes there is a marked diurnal variation in times of admission to hospital.

Analysis of 4755 nulliparous women with single pregnancies in cephalic presentation at term, indicated that they presented in labour or with premature rupture of the membranes nearly twice as frequently during the night as during the evening. The peak hours for delivery were late morning and afternoon.

The authors discuss previously published reports of similar findings and of a diurnal variation in maternal hormone levels in humans and experimental animals. The potential clinical importance of this phenomenon is considered.

On constate une variation diurne importante quant au moment d'admission à l'hôpital pour les femmes qui entrent en travail spontanément ou pour celles qui subissent une rupture prématurée des membranes.

L'analyse de 4755 nullipares ayant eu une grossesse simple avec présentation céphalique à terme, révèle qu'elles arrivèrent en travail ou après rupture prématurée des membranes près de deux fois plus souvent durant la nuit que durant la veillée. Les périodes de pointe sur l'accouchement furent la fin de la matinée et l'après-midi.

Les auteurs commentent les publications antérieures signalant des résultats similaires ainsi que les rapports d'une variation diurne des taux d'hormones maternelles chez l'humain et chez l'animal d'expérience. Ils considèrent l'importance clinique que pourrait avoir ce phénomène.

In this study we review a serendipitous observation made during investigation of the variation in labour outcomes by time of day among nulliparous patients.[1] A marked diurnal variation was noted in the times of admission to hospital of nulliparous women at term who had diagnoses of either spontaneous labour or spontaneous rupture of membranes. The tendency for labour to begin at certain times of day has been described previously,[2] but, as with the regulation of labour onset in general, it is not well understood. The purpose of this report is to emphasize the importance of this clinical finding.

Population and Methods

This study was conducted at the Royal Victoria Hospital, Montreal. A computerized database was used to record data from all pregnant women.[3] The time of admission, the time of delivery, the duration of rupture of membranes, the duration of labour, parity and method of delivery were among the variables entered on the computer.

Between January 1978 and March 1984, 4228 pregnant women admitted in labour (group 1) and 527 admitted with ruptured membranes but not in labour (group 2) were included in the study. The following criteria were necessary: nulliparity, gestation period of 37 or more weeks, singleton pregnancy, cephalic presentation, labour not induced. The time of admission to hospital was analysed for both groups and time of delivery for group 1. Rates of admission by time of day were compared using the χ^2 goodness of fit test (Ryan BF, Jouer BL, Ryan TA: Minitab, Duxbury Press, Boston, Mass., 1985).

Findings

The number of admissions during the night (24:00 to 08:00 hours) was significantly greater ($p < 0.001$) in group 1 than that during the day (08:00 to 16:00 hours) or evening (16:00 to 24:00 hours) (Table I, Fig. 1). The mean interval from admission to delivery did not vary by time of admission. Delivery rates peaked in the late morning and afternoon.

The same pattern of admissions was evident in group 2 women as in group 1. The actual time of labour onset or membrane rupture was less accurate because these events oc-

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‡Sponsored by the Alberta Heritage Foundation for Medical Research

Accepted for publication June 2, 1988

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curred at home and the timing was noted from the patient's recollection. Women admitted in labour stated it had started, on average, 3.6 hours before. The others claimed the membranes ruptured, on average, 2.4 hours before admission. If these intervals are taken into account, the peak period for onset of labour or rupture of membranes at home would be between 20:00 and 02:00 hours.

Discussion

Standard obstetric texts, in discussing the initiation of parturition, make no mention of a circadian pattern to labour onset.[4–6] Malek,[7] in a series of 70 000 women, demonstrated that labour began more frequently between 22:00 and 04:00 hours; Shettles,[2] in a series of more than 4000 patients, also reported that labour onset was more common at night. Glattre and Bjerkedal[8] reviewed all births in Norway over a 10-year period and found a cyclicity in the timing of delivery. As was observed in our study, nulliparous patients with spontaneous onset of labour more commonly delivered during daytime hours. They concluded that diurnal variation in rate of delivery is probably mediated by factors that regulate the time of labour onset.

How is the rhythmicity of labour onset controlled? Ducsay and associates[9] have described a circadian pattern in uterine activity near term in the rhesus monkey, a species also known to initiate labour at night. Peak uterine activity occurs between 22:00 and 02:00 hours. Further study[10] confirmed this cyclic uterine activity and demonstrated a circadian pattern to fetal plasma progesterone and dehydroepiandrosterone sulfate levels, with peak steroid concentrations corresponding to periods of peak uterine activity. This suggests that fetal adrenal glands control the diurnal rhythm in uterine contractility.

In the human, maternal plasma steroid concentrations have been monitored in the third trimester.[11,12] Both progesterone and estriol demonstrate a circadian pattern before term. However, estriol loses its circadian pattern as term approaches.[11] While the interactions between

Table I. Number of Admissions

Hour of onset or rupture	In labour	Ruptured membranes, not in labour
Night	(1938)	(254)
24:00	221	37
01:00	229	30
02:00	256	36
03:00	252	32
04:00	282	27
05:00	250	33
06:00	255	37
07:00	193	22
Day	(1288)	(143)
08:00	211	12
09:00	218	19
10:00	180	25
11:00	156	27
12:00	160	22
13:00	135	15
14:00	116	15
15:00	112	8
Evening	(1002)	(130)
16:00	115	14
17:00	93	14
18:00	103	18
19:00	116	18
20:00	148	11
21:00	133	13
22:00	134	17
23:00	160	25
Totals	4228	527
	$\chi^2 = 326.5$ $p < 0.001$	$\chi^2 = 52.9$ $p < 0.001$

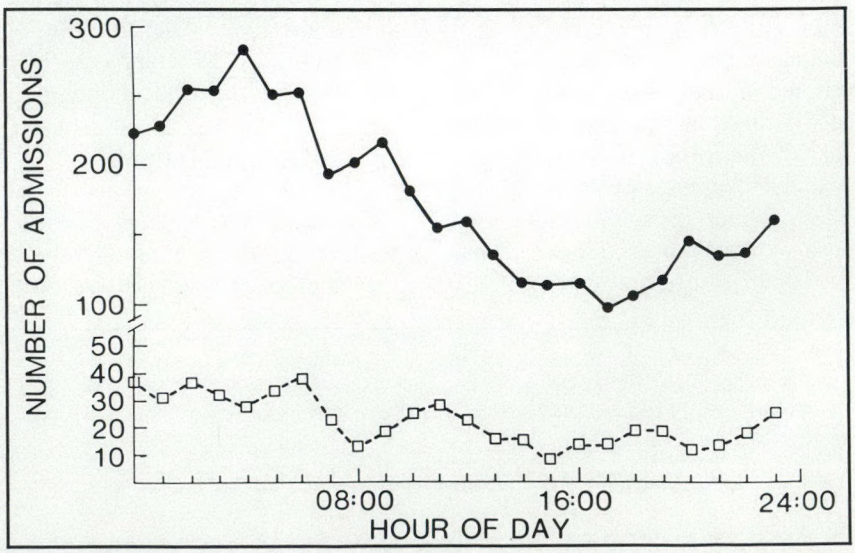

FIG. 1. Time of admission of term, primiparous patients in spontaneous labour (circles) or with premature rupture of membranes (squares).

fetal and maternal steroid rhythms and their role in regulating labour onset remain to be defined, they may provide the basis for an explanation of its rhythmicity.

Further studies are needed to determine whether the same diurnal variation in labour onset or premature rupture of membranes exists before term. The following questions need clarification: Should infusion rates for tocolytic agents be increased during late evening and night hours? Would induction of labour be more successful if initiated in the evening? Does the identical diurnal variation in onset of labour and premature rupture of the membranes imply that the latter is also the result of increased uterine activity, albeit imperceptible?

Fundamental knowledge regarding the onset of labour, as well as practical clinical considerations, provides incentives to increase our understanding of the significance of nature's choice as to when labour begins.

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Surgical Treatment of Post-traumatic Kyphosis: a Report of 16 Cases

Alain Jodoin, MD, FRCSC;* Philippe Gillet, MD;† Pierre R. Dupuis, MD, FRCSC;‡ Gilles Maurais, MD, FRCSC§

Thoracic and lumbar spine fractures may lead to symptomatic progressive kyphosis for which surgery remains a controversial treatment. Sixteen patients with kyphosis were treated surgically at the Sacré-Coeur Hospital in Montreal between 1979 and 1985. The mean follow-up was 38 months.

Initially, treatment of the fractures varied. On average the post-traumatic kyphosis was surgically corrected 34 months later.

The corrective procedure consisted of staged anterior and posterior fusion with instrumentation (six patients), posterior fusion with instrumentation (five), staged anterior fusion, posterior osteotomy and fusion with instrumentation (four), posterior osteotomy and fusion with Harrington instrumentation (one). Anterior decompression was also performed in 5 of the 10 patients who had anterior fusion. There was no major perioperative complication.

Pain was relieved in 13 patients and 9 of 11 had substantial neurologic improvement. Two patients had nonunion of posterior grafts, but these united after revision. The mean loss of correction in the early postoperative period was 3.5°.

The authors conclude that surgical treatment of post-traumatic symptomatic progressive kyphosis is effective and safe.

Les fractures des colonnes thoracique et lombaire peuvent mener à une cyphose évolutive symptomatique pour laquelle le traitement chirurgical demeure discutable. Entre 1979 et 1985, 16 patients souffrant de cyphose ont été opérés à l'Hôpital du Sacré-Coeur de Montréal. Le suivi s'étend en moyenne sur 38 mois.

Initialement, le traitement des fractures a varié. En moyenne, les cyphoses post-traumatiques furent corrigées chirurgicalement au bout de 34 mois.

Les techniques correctives employées furent les suivantes: fusions antérieure et postérieure en deux temps avec instruments (six patients), fusion postérieure avec instruments (cinq), fusion antérieure en deux temps, ostéotomie postérieure et fusion avec instruments (quatre), ostéotomie postérieure et fusion avec instrument de Harrington (un). Une décompression antérieure a aussi été pratiquée chez 5 des 10 patients qui eurent une fusion antérieure. Aucune complication peropératoire importante n'a été enregistrée.

La douleur fut soulagée chez 13 patients et une amélioration neurologique importante fut obtenue chez 9 patients sur 11. Dans deux cas, il y eut absence de soudure d'une greffe postérieure, mais la fusion fut obtenue après révision. Pendant la période postopératoire immédiate, la perte de correction moyenne était de 3.5°.

Les auteurs concluent que le traitement chirurgical des cyphoses post-traumatiques évolutives symptomatiques est efficace et sûr.

Fractures of the thoracic and lumbar spines can lead to progressive symptomatic kyphosis,[1-8] which frequently is a result of inadequate initial management.[2,3,7-12] Although there is controversy over whether the initial treatment of a fractured spine should be conservative or surgical, there is no doubt that failure to correct and stabilize acute post-traumatic kyphosis increases the likelihood that the deformity will progress.[1-3,5,8-10,13] Post-injury laminectomy is especially deleterious.[2,3,8,14-22]

Post-traumatic kyphosis can cause disabling pain or progressive neurologic impairment, due to tenting of the cord over the apex of the curve or by direct compression by a bony fragment in the neural canal.[2,3,8,10,11,14-24]

This condition has recently been treated surgically by an anterior, posterior or even combined approach.[3,7,11,18,22,25,26] Our study was undertaken to establish the indica-

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Presented at the annual meeting of the Canadian Orthopaedic Association, Hamilton, Ont., June 2–6, 1985

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Accepted for publication June 2, 1988

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tions, results and complications of this type of surgery.

Patients and Methods

We reviewed the charts of 16 patients (12 men, 4 women) who had progressive, symptomatic, post-traumatic kyphosis and were treated at Sacré-Coeur Hospital in Montreal between 1979 and 1985. Medical records, preoperative, immediate postoperative and follow-up x-ray films were reviewed. All patients were examined personally, except one who was assessed by questionnaire and had x-ray films taken elsewhere.

Initial management of the fractures was carefully correlated with the patient's clinical status at corrective surgery, the indications for and techniques of which were reviewed. The last follow-up considered pain, curve correction, neurologic deficit and complications.

Findings

The mean age of the 16 patients was 33 years (range from 17 to 56 years).

Fractures involved the thoracic spine in five patients, the thoracolumbar junction in eight and the lumbar spine in three. Patients were treated initially as shown in Table I. Eleven received their initial treatment in other medical centres.

Table I. Initial Treatment of 16 Patients

Procedure	No. of patients
Bed rest + body cast or bracing	9
Posterior Harrington rods + fusion	3
Laminectomy + bed rest	1
+ Harrington rods	1
Anterior decompression + rib strut grafting	1
Roy–Camille plates + posterior fusion	1

Results of Initial Management

All nine patients treated by bed rest or orthosis subsequently had back pain, six (nos. 1, 6, 7, 8, 10, 16 in Table II) suffered neurologic irritation or deficit; patient 1 had anesthesia at T4 with motor loss in the left leg. Eight patients (nos. 1, 6, 7, 8, 9, 10, 12, 16) had increasing deformity. In four (nos. 1, 6, 7, 16), an incomplete myelographic block and a central spinal stenosis were demonstrated on lateral tomography. Computed tomography demonstrated a central spinal stenosis in patients 9 and 15; the latter suffered transient paraplegia.

Of the patients managed by posterior instrumentation and fusion, patient 2 had an ataxic gait and a pyramidal tract irritation syndrome, thought to be caused by dislodgement of the Harrington rods. Patient 3 had pain and increasing kyphosis as did patient 13 who also had spasticity; both these patients had dislodgement of their Harrington rods.

Patient 15, managed by Roy–Camille plates and posterior fusion had a decreased lumbar lordosis. Because of the resulting anterior projection of the trunk, this patient needed crutches to stand and walk, even with bilateral long leg orthosis. Patient 16 had anterior impingement of the spinal canal by the posterior aspect of L4, documented by computed tomography.

Delayed posterior fusion in patient 14 did not prevent increasing kyphosis or improve his paraparesis.

Patient 5, who underwent anterior decompression and rib strut grafting, had neurologic improvement initially, but 5 months later he experienced a loss of correction with recurrence of his neurologic deficit.

The mean time between the initial injury and surgical correction of the kyphosis was 34 months (range from 5 months to 14 years). Indications for corrective surgery were back pain, neurologic impairment or progression of the curve, or a combination of these.

Surgical Procedures Used to Treat the Kyphosis (Table II)

The surgical technique used depended on the initial treatment, the radiologic findings in patients with neurologic symptoms and configuration of the deformity.

Posterior Harrington instrumentation and fusion were required in five patients; three (nos. 3, 5 and 8) required compression Harrington rods and two (nos. 9 and 11) distraction rods.

Posterior osteotomy, Harrington instrumentation and fusion were required for patient 2.

Staged anterior and posterior fusion with instrumentation, with or without anterior decompression were carried out in six patients (nos. 1, 4, 6, 7, 12 and 16). Patient 6 required anterior release and fibular strut and intersomatic grafting followed by posterior instrumentation with Harrington distraction rods and fusion. In patient 7, an anterior release, fibular and rib strut grafting were followed by Harrington instrumentation and fusion; patient 12 required multilevel release with intersomatic grafting. In patient 4, posterior distraction instrumentation and fusion resulted in posterior nonunion, so 2 years later anterior fusion and instrumentation were necessary.

Finally, staged anterior decompression, fibular strut grafting or iliac strut grafting and anterior Harrington instrumentation, followed by posterior osteotomy with instrumentation and fusion were carried out on patients 10, 13, 14 and 15. In patient 15 the Roy–Camille

plates, initially applied, were removed.

Postoperatively, each patient was nursed on a Stryker frame. On postoperative day 7 a Cotrel brace or cast was applied until solid fusion was demonstrated radiologically, usually after 6 months.

Complications

Five patients had problems postoperatively. In patient 2 the Harrington rods became dislodged after 6 months, but he resumed full work, even though the correction achieved by the rods was lost.

Patient 4 had a serious urinary tract infection. Her posterior fusion did not unite and she required an anterior fusion 2 years later. Patient 12 had a pressure sore under a Cotrel cast; the sore resolved after 10 days of bed rest on a Stryker frame and another cast was applied

Table II. Data on 16 Patients With Post-Traumatic Kyphosis

No.	Sex	Age, yr	Fracture level	Initial treatment	Time from injury to correction, mo	Preop status	Surgical technique	Postop curve, °	Postop status at last follow-up	Follow-up, mo
1	M	31	T4	Harris–Taylor brace	10	30° curve Back pain Muscle weakness Spasticity Hypoesthesia Bladder impairment	1. Ant. decompression T3, T4 Iliac strut graft 2. HD rods Post. fusion	32	30° curve Brown–Sequard syndrome Spastic paraparesis of T4 Walks with 1 cane Myelographic block Incomplete decompression?	48
2	M	34	L1	HD rods and post. fusion	5	30° curve Rod loosening Back pain Spasticity Ataxic gait	Post. osteotomy HD rods Post. fusion	17	34° curve Morning stiffness No neurologic deficit Resumed work (fireman)	36
3	M	17	T9	HD rods and post. fusion 15°	6	25° curve Rod loosening Increased pain	Compression rods Post. fusion	26	27° curve No pain	21
4	F	42	L2	Bed rest Laminectomy L2, L3	144	25° curve Pain Limp Postop nonunion Increased pain	HD rods Post. fusion Ant. fusion with ant. Dwyer compression instrumentation	20	20° curve Pain at scar site	60
5	M	53	T12	Ant. decompression and rib strut graft	7	30° curve Muscle weakness and hypoesthesia after initial recovery	HC rods Post. fusion	25	25° curve Walks with 1 cane No pain	42
6	F	32	T12	Brace	36	52° curve Back pain Paresthesia Impaired voiding	1. Ant. strut graft 2. HD rods Post. fusion	45 22	30° curve No pain Bladder normal Resumed work	32
7	F	23	T12	Cast	12	34° curve Back pain Hypoesthesia Myelogram + Tomogram +	1. Ant. strut graft 2. HD rods Post. fusion	17 8	15° curve No pain Resumed work	72
8	M	22	L3	Cast	15	10° curve Back pain Radicular pain, Lasègue sign +	HC rods Post. fusion	7	11° curve No pain Resumed work	60
9	M	28	L1	Brace	18	15° curve Back pain Spinal stenosis	HD rods Post. fusion	13	15° curve No pain Resumed work and sports	46

HD = Harrington distraction, HC = Harrington compression, ant. = anterior, post. = posterior, + = positive.

until solid fusion occurred without further problems. Posterior fusion also failed in patient 13 who needed revision with Harrington instrumentation 2 years later; successful union resulted. Patient 14 had a voiding problem early postoperatively and required catheterization.

Clinical Outcome

The mean follow-up was 38 months (range from 19 to 72 months). Pain improved or disappeared in 10 patients, 3 showed slight improvement but 1 did not show any improvement (Table II).

In patients with kyphosis of the thoracic spine, the curve was reduced from a mean of 38° to 27° (range from 20° to 35°). In the thoracolumbar spine, the improvement was from a mean of 39° to 27° (range from 8° to 34°). In the lumbar spine, the reduction was

Table II (Continued). Data on 16 Patients With Post-Traumatic Kyphosis

No.	Sex	Age, yr	Fracture level	Initial treatment	Time from injury to correction, mo	Preop status	Surgical technique	Postop curve, °	Postop status at last follow-up	Follow-up, mo
10	M	31	T8-9 10-11	Brace	10	40° curve Spastic paraparesis Hypoesthesia Ataxic gait Bladder and bowel problems Myelogram +	1. Ant. decompression Fibular strut graft 2. Post. osteotomy HC rods and fusion	25	25° curve Still increased reflexes Resumed work and sports	36
11	M	56	T7	Brace	22	20° curve Back pain	HD rods Post. fusion	20	20° curve Solid fusion but pain	19
12	M	18	T6-7	Brace	15	75° curve Back pain Unable to work or run	1. Ant. release and graft 2. HC rods Post. fusion	35	35° curve Pain at upper hooks Resumed work	33
13	M	24	T12	HD rods Post. fusion	22	40° curve Paresthesia Back pain Bladder impairment Spasticity	1. Ant. decompression T12 Fibular strut graft T11–L1 2. Post. osteotomy HC rods and fusion	15	32° curve Light pain	30
14	M	18	L1	1. Laminectomy and 1 HD rod without fusion 2. Post. fusion	52	45° curve Paresis for 3 mo (needed crutches) Sphincter hypotonia Anesthesia of heels Back pain	1. Ant. decompression L1 Iliac strut graft T12–L2 Ant. Harrington instrumentation 2. Post. osteotomy HC rods and fusion	34	34° curve No pain Muscle improvement by 4 mo Sensibility improved Sphincter tone unchanged Removed orthosis 2 mo postop without permission	24
15	M	17	L4	Post. fusion and instrumentation by Roy–Camille plates without correction of kyphosis	22	Loss of lumbar lordosis with ant. projection of trunk and instability without crutches Muscle weakness below L3 Sphincter hypotonia Need for orthosis of both legs Low back pain	1. Ant. decompression L4 Iliac strut graft L3–L5 2. Removal of plates and screws Post. osteotomy HC rods and fusion	−10	Restoration of normal lordosis with ability to stand without crutches and improved gait	25
16	F	30	L1	Bed rest and orthosis	14	40° curve (5° in 1 yr) Back pain Hypoesthesia ant. aspects of thighs No muscle weakness Slight stenosis	1. Ant. release and iliac strut graft T12–L2 Ant. Harrington rods 2. Posterior Harrington–Luque instrumentation with fusion	8	Pain improved Back to normal activities	24

HD = Harrington distraction, HC = Harrington compression, ant. = anterior, post. = posterior, + = positive.

from a mean of 12° to 7° (range from −10° to 20°).

Postoperatively, there was an average loss of correction of 3.5° (range from 0° to 17°).

In patient 15, lumbar lordosis was restored which greatly improved his trunk balance.

Neurologically, the paresthesia and hypoesthesia disappeared or was greatly diminished soon after the operation in the seven patients noted to have these problems. Radicular pain and a positive Lasègue sign disappeared in patient 8. Pyramidal syndrome disappeared in patient 2 and was markedly improved in patients 10 and 13, but it remained unchanged in patient 1.

Muscle strength returned to normal in patient 10 and improved in three others; it was unchanged in patient 1. Ataxic gait resolved in patients 2 and 10. Sphincter function returned to normal in two patients (6 and 10) but was unchanged in patients 1, 13, 14 and 15.

Eight patients returned to work. Patient 11, who complained of pain, would not return to work even though he had a solid fusion, normal spinal curve and no neurologic symptoms. As a result, his eligibility for sought-after compensation has been difficult to assess.

Four patients were still too disabled to resume physical activities and were not expected to improve. Two patients (nos. 4 and 13) resumed light work.

Case Report

The following case report is a representative example of our 16 patients who suffered post-traumatic kyphosis.

A 30-year-old woman (patient 16) sustained a fracture of L1 in a car accident. The fracture was first treated by bed rest and application of a body jacket. Fourteen months later she was referred to our institution. She complained of back pain and hypoesthesia over the anterior aspect of both thighs. Preoperative assessment revealed a sharp 40° kyphosis from T12 to L2 (Fig. 1). This deformity had increased 5° over the previous year. Myelography (Fig. 2) demonstrated only slight stenosis at the fracture level. An anterior release and iliac strut grafting from T12 to L2 with anterior Kostuik–Harrington instrumentation was carried out. The kyphosis was reduced to 8° (Fig. 3), and no late loss of correction was observed at follow-up 24 months later.

Discussion

Three main factors contribute to the progression of post-traumatic kyphosis:[27] failure of the anterior elements under compressive loading, failure of the posterior elements under tensile loading and increased physiological load after "healing" because of increased moment arm proportional to the magnitude of the kyphosis.

These factors make burst fractures particularly prone to a progressive kyphotic deformity,[9] especially if the initial angulation is more than 30°;[2] multiple-level fractures are even more susceptible.[2,7]

Laminectomy, done initially in patients 4 and 14, further destabil-

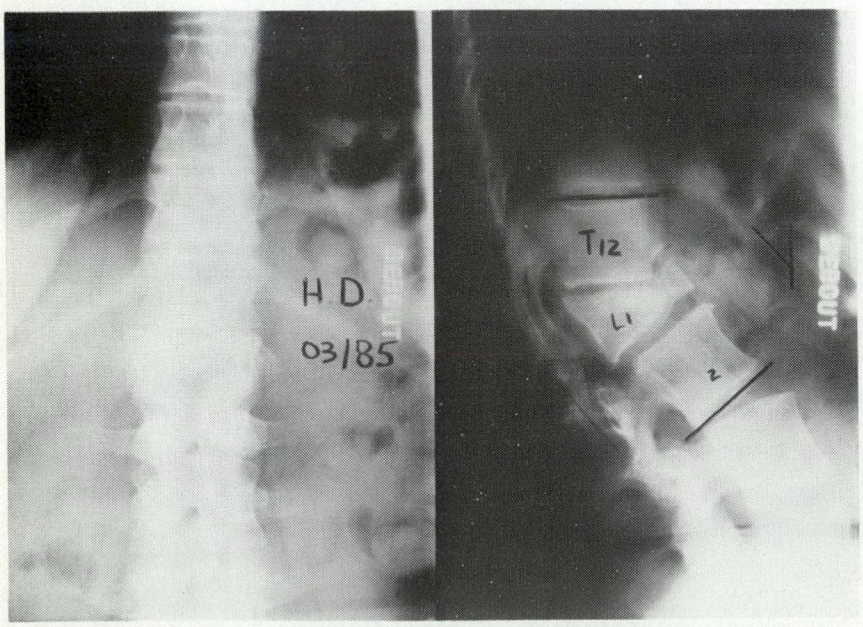

FIG. 1. Anteroposterior and lateral views showing kyphosis of 40° from T12–L2.

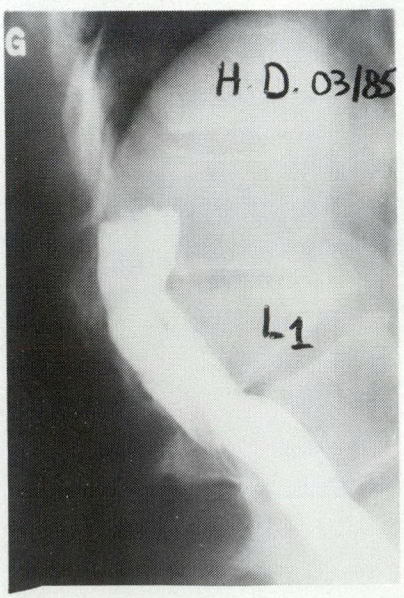

FIG. 2. Myelogram demonstrates slight stenosis at L1.

izes the spine and is ineffective in decompressing neural elements, except in rare instances when the fractured laminae have moved anteriorly, compressing the neural elements.[2-4,6,8,10,12,14,15,17-19,21-24]

Posterior instrumentation and fusion to stabilize the curve is sometimes the only procedure required; when pain is the sole complaint and the curve is slight, it has proven effective.[3]

We believe that a solid fusion should be the ultimate aim in most cases of post-traumatic kyphosis. For example, in case 2 correction was entirely lost when the upper hooks dislodged 4 months after surgery. However, this patient had complete neurologic recovery and was able to resume work when fusion was finally achieved 2 months later. This phenomenon has been attributed to correction of microinstability.[1]

To demonstrate spinal canal encroachment and the need for decompression it is important to obtain a laminagram,[3] myelogram[2,3] and computed tomogram.[2,10,17] Compression is anterior, due to a bony fragment at the apex of the curve, so decompression must be anterior.[2,3,8,10,11,14,15,17,18,21-24,28] Milder deformities can be corrected with posterior instrumentation and fusion.[10,16] In patients previously operated on, who have severe deformity, a posterior osteotomy is helpful.

In patients not previously operated on, distraction rods using the three-pressure-point method are effective.[2] Distraction must be minimal to prevent overstretching the cord[2,8] and the rods should be contoured; square-ended rods are used in the lumbar area.[10] Compressive devices are more effective but carry the risk of pushing bony elements into the spinal canal; these devices should be used only if an anterior decompression was performed initially.

Anterior grafting is essential in severe kyphosis for biomechanical reasons.[8,9,17-20,22,25,27,28] A rib strut graft is mechanically weak, hence fibular or iliac strut grafting with anterior instrumentation is suggested.

The anterior approach provides the best exposure for decompression[2,3,14,19,21,23,24] and anterior strut grafting. The posterolateral approach is inadequate.[11,21]

Solid fusion is imperative. For example, our patient 5 was treated initially by anterior decompression and rib strut grafting. Because the fusion was not solid, the correction obtained at surgery was lost and the original neurologic deficit reappeared. Subsequent use of Harrington compression rods and posterior fusion resulted in partial neurologic recovery.

We agree with the recommendation of others[2,3,18,24] that a posterior fusion be performed in all cases, including those who have an anterior fusion.

In the future, anterior decompression and fusion may be safe enough and strong enough to preclude the use of the posterior method in the treatment of post-traumatic kyphosis, but at present this is not the case.

When neurologic improvement is not achieved by anterior decompression, myelography or computed tomography, or both, should be repeated.

No major surgically related complication occurred in this series and most patients returned to their previous employment. Even some of the very disabled with ataxic gait, muscle weakness and spasticity, returned to full work and sports 1 year after the procedure.

Effective correction of symptomatic post-traumatic kyphosis is possible, even when a neurologic deficit has been present for several months.[2,3,11,14,19,23,24,28] Corrective surgery should be considered when a deformity progresses after a spinal fracture, whatever the initial treatment. This is especially true if there is concomitant progressive neurologic deficit.

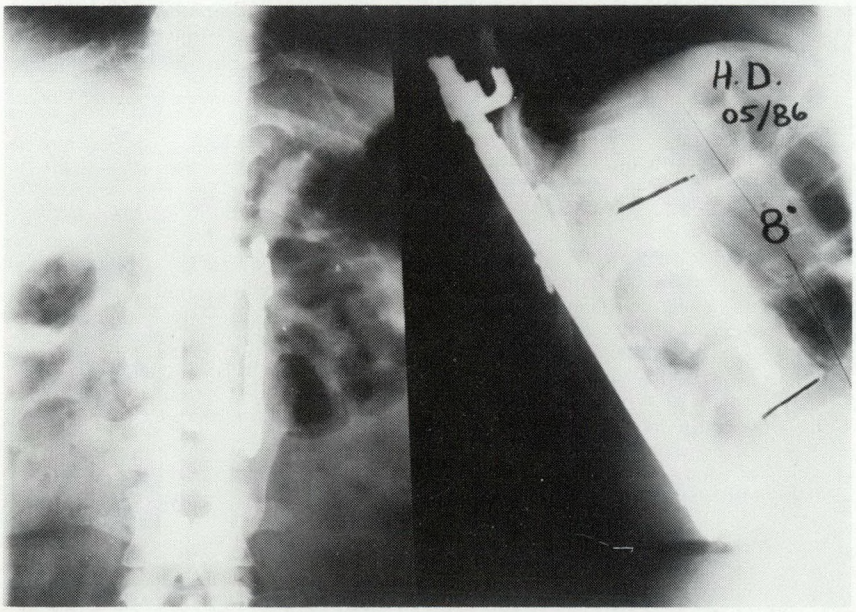

FIG. 3. Anteroposterior and lateral views show kyphosis reduced to 8° with anterior and posterior instrumentation and posterior fusion.

We thank Doctor Guy Paiement for his help in reviewing this paper.

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BOOKS RECEIVED

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

Kidney Transplantation. Edited by Luis H. Toledo-Pereyra. 397 pp. Illust. F.A. Davis Company, Philadelphia, 1988. $73.00 (US). ISBN 0-8036-8504-1.

Outpatient Surgery. 3rd edition. Edited by George J. Hill. 729 pp. Illust. W.B. Saunders Company, Philadelphia; W.B. Saunders Company Canada Limited, Toronto, Ont., 1988. $86.50. ISBN 0-7216-2104-X.

Principles of Organ Transplantation. Edited by M. Wayne Flye. 687 pp. Illust. W.B. Saunders Company, Philadelphia; W.B. Saunders Company Canada Limited, Toronto, Ont., 1989. $180.00. ISBN 0-7216-1323-3.

Sabiston's Essentials of Surgery. Edited by D.C. Sabiston, Jr. 1249 pp. Illust. W.B. Saunders Company, Philadelphia; W.B. Saunders Company Canada Limited, Toronto, Ont., 1987. $55.95. ISBN 0-7216-7874-2.

Techniques of Percutaneous Gastrostomy. Edited by Jeffrey L. Ponsky. 127 pp. Illust. Igaku-Shoin Medical Publishers, Inc., New York; W.B. Saunders Company Canada Limited, Toronto, Ont., 1988. $71.50. ISBN 0-89640-139-1.

Vascular Birthmarks. Hemangiomas and Malformations. Edited by John B. Mulliken and Anthony E. Young. 483 pp. Illust. W.B. Saunders Company, Philadelphia; W.B. Saunders Company Canada Limited, Toronto, Ont., 1988. $216.00. ISBN 0-7216-6601-9.

continued on page 50

Perioperative Chemotherapy for Primary Sarcoma of Bone

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Preoperative chemotherapy for primary osteosarcoma has usually been accompanied by a prolonged delay between withdrawal before operation and resumption after. This is because animal studies showed impaired wound healing associated with perioperative chemotherapy. Clinical studies, however, have not shown this to be the case. The authors describe their experience in eight patients who had osteosarcoma and Ewing's sarcoma of the extremities and received one to three cycles of chemotherapy preoperatively. Chemotherapy consisted of Adriamycin, cis-platinum and vincristine. Definitive surgery on the primary tumour was done 1 to 4 days after the last dose. Amputation was performed on seven patients and tumour resection for limb salvage on one. No wound healing or infectious complications were encountered. The ensuing course of chemotherapy was not delayed by the surgical procedure. The authors conclude that it is feasible to combine neoadjuvant chemotherapy and early surgery in the management of high-grade primary bone sarcoma.

La chimiothérapie préopératoire des ostéosarcomes primitifs est habituellement accompagnée d'un délai prolongé entre l'interruption médicamenteuse avant l'opération et la reprise du traitement après. Ceci découle d'études animales qui ont montré une altération du mécanisme de cicatrisation de plaie reliée à la chimiothérapie préopératoire. Toutefois, les études cliniques n'ont rien révélé de similaire. Les auteurs décrivent le traitement de huit patients souffrant d'ostéosarcome ou de sarcome d'Ewing des extrémités, qui reçurent de un à trois cycles de chimiothérapie préopératoire. Le traitement était composé d'Adriamycine, de cis-platine et de vincristine. L'opération définitive eut lieu de 1 à 4 jours après la dernière dose. Une amputation fut pratiquée chez sept patients, alors que le dernier subissait une résection tumorale visant à sauvegarder le membre. Aucune complication infectieuse ou de cicatrisation ne fut observée. La poursuite du traitement de chimiothérapie ne fut pas retardée par l'intervention chirurgicale. Les auteurs concluent que, dans le traitement des ostéosarcomes primitifs au stade avancé, il est possible d'associer chimiothérapie "néoadjuvante" et chirurgie précoce.

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Supported in part by a grant from the Hanson Foundation

Accepted for publication Aug. 30, 1988

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Chemotherapy before definitive treatment of a primary malignant tumour has become popular in the past decade. The advantages of this "neoadjuvant" approach include early eradication of systemic micrometastases and in-vivo sensitivity testing of tumour cells to specific antineoplastic agents, thus allowing early modification of chemotherapy regimens.[1] This approach has been used successfully to treat osteosarcoma and has been proposed for the management of operable Ewing's sarcoma.[2,3] Surgery on the primary tumour usually is performed 3 to 4 weeks from the last course of chemotherapy to allow recovery from its side effects. Chemotherapy is seldom resumed for another 2 to 3 weeks, until the surgical wound has healed completely. The patient, therefore, may not receive systemic therapy for 6 or more weeks during the early, critical period of antineoplastic therapy. This delay was considered inevitable because animal experiments[4,5] showed that perioperative chemotherapy significantly impaired wound healing. On the other hand, most clinical studies[6,7] have shown little effect of adjuvant chemotherapy on postsurgical recovery. In this report we describe our experience in carrying out surgery on primary bone tumours immediately after chemotherapy without deleterious effect on wound healing.

Patients and Materials

Between May 1985 and August 1987, eight patients with primary bone sarcoma of the extremities were given chemotherapy before definitive surgery (Table I). Chemotherapy was administered over 2 days. One to three courses were given and surgery was scheduled within 1 to 4 days of the last dose of cytotoxic therapy. The choice of surgical procedure was not affected by perioperative chemotherapy. Postoperative chemotherapy was scheduled to resume 3 weeks from the start of the last course before surgery, provided blood counts had returned to a satisfactory level (absolute neutrophil count of 1.0×10^9/L and platelets of 100×10^9/L) and the surgical wound appeared healed. All patients were followed up regularly to assess complications at the surgical sites.

Findings

The median age of patients at the time of diagnosis was 16.5 years and all were male. Five patients with osteosarcoma received one to three cycles of cis-platinum–Adriamycin preoperatively. Two boys (nos. 4 and 5) received one cycle of high-dose methotrexate a week earlier, followed by cis-platinum–Adriamycin. The man with Ewing's sarcoma received vincristine and Adriamycin immediately before tumour resection and insertion of a prosthesis. He had received one course each of vincristine–Adriamycin and vincristine–cyclophosphamide previously. The median time to surgery from the last dose of chemotherapy was 2.2 days. No immediate postoperative complication was encountered. No wound infection, fever or hematoma was noted. All patients were discharged 5 to 10 days (median 7 days) after surgery. Moderate neutropenia (absolute neutrophil count between 0.2 and 0.5×10^9/L) was encountered in all patients, but thrombocytopenia of less than 100×10^9/L was found in only one. Chemotherapy was resumed 3 weeks from the last treatment in all patients except no. 3, whose treatment was delayed for 1 week because of neutropenia. No wound dehiscence or impairment of healing was found and the mean follow-up was 28 months (range from 5 to 45 months).

Discussion

The effects of antineoplastic agents on wound healing have been investigated extensively. Controversy exists as to the importance of findings in animal experiments and their applicability to clinical practice. Devereux and colleagues[4,5] administered Adriamycin 6.0 mg/kg intravenously to rats at various times before and after surgery. Serious impairment of wound tensile strength resulted because of defective collagen synthesis. The most deleterious effect was observed when treatment was given preoperatively or intraoperatively, and the addition of local radiotherapy potentiated the impairment.[8] Lawrence and associates[9] reported a similar finding and postulated that Adriamycin-induced myelosuppression resulted in a decreased amount of local chemotactic and growth factors normally derived from granulocytes and platelets. This in turn led to decreased wound cellularity and collagen accumulation. In contrast, an earlier study[10] showed that Adriamycin up to a dose of 10 mg/kg had no adverse effect on wound healing regardless of the time of treatment in relation to the time of injury. Cis-platinum, when given at 5.0 mg/kg, impaired wound healing,[11] but studies[12,13] using one-third to one-half of this dosage showed no noticeable effect on healing of skin wounds or intestinal anastomoses in animals.

The clinical effects of adjuvant chemotherapy on wound healing were more acceptable. Patients with advanced breast cancer received several courses of Adriamycin and cyclophosphamide before mastecto-

Table I. Clinical Characteristics of Patients

Patient no.	Age, yr	Tumour type*	Location	Perioperative chemotherapy†	Interval to surgery, d	Surgical procedure
1	16	OS	Fibula	CA	1	Above-knee amputation
2	21	OS	Femur	CA	3	High thigh amputation
3	17	OS	Tibia	CA	4	Above-knee amputation
4	13	OS	Femur	M/CA	2	Above-knee amputation
5	8	OS	Femur	M/CA	3	Above-knee amputation
6	13	ES	Humerus	VA/VC/VA	2	Limb salvage
7	23	OS	Tibia	CA X 3	2	Above-knee amputation
8	23	OS	Tibia	CA X 3	1	Above-knee amputation

*OS = osteosarcoma, ES = Ewing's sarcoma.
†CA = cis-platinum, 100 mg/m^2, d 1, Adriamycin, 35.0 mg/m^2, d 1 and 2; M = methotrexate 8.0 g/m^2, d 1 with folinic acid rescue; VA = vincristine, 1.5 mg/m^2, d 1, Adriamycin, 75 mg/m^2, d 2; VC = vincristine, 1.5 mg/m^2, d 1, cyclophosphamide 1.4 g/m^2, d 2.

my and had no increase in wound complications.[6] However, surgery was not usually performed until 3 or more weeks after the end of chemotherapy. Nissen-Meyer and associates[7] administered a single course of cyclophosphamide (5.0 mg/kg daily for 6 days) within several days of mastectomy and found no increase in the wound complication rate compared with control patients who underwent surgery only. The effect of preoperative chemotherapy on wound healing in skeletal tumours has been reported. Bertermann and colleagues[14] summarized the experience of the T4, T7 and T10 protocols from New York's Memorial Hospital, where high-dose methotrexate and Adriamycin were given to osteosarcoma patients, the last dose being given 1 to 2 weeks before limb-salvage surgery. No increase in wound complications was seen, but 6% of the patients required amputation because of wound infection.

The addition of radiotherapy to preoperative chemotherapy seems to increase the risk of wound complications. Denton and associates[15] administered Adriamycin intra-arterially and local radiotherapy preoperatively to 30 patients with bone and soft-tissue sarcoma. Poor wound healing necessitated amputation in two patients. Two others had wound necrosis requiring débridement and skin grafting. A randomized trial of perioperative brachytherapy showed a substantial increase in wound complication rate compared with control patients. The addition of Adriamycin at 60.0 mg/m^2 did not increase the wound problems, but most patients received chemotherapy more than 2 weeks after surgery.[16] Similarly, preoperative cis-platinum therapy and radiotherapy in patients with head and neck tumours led to a 25% increase in hospital stay because of slow wound healing, but only 1 of the 28 patients suffered wound dehiscence.[17]

The present study showed no deleterious effect on wound healing when Adriamycin, cis-platinum and vincristine were administered in standard doses several days before surgery. It is, therefore, possible to continue neoadjuvant chemotherapy without interruption to treat micrometastases and also to include surgery for local disease control. This is especially important in the case of highly proliferative tumours; Goldie and Coldman[18] illustrated a steep quantitative relation between tumour size and the likelihood of cure. We used a similar approach to treat one child with a large malignant sacrococcygeal teratoma obstructing the rectum. The child received cis-platinum 120 mg/m^2, VP-16 (etoposide) 360 mg/m^2, vincristine 2.0 mg/m^2 and bleomycin 50 mg/m^2 2 days before tumour resection and no complications developed. Similarly, if the primary tumour has progressed during preoperative chemotherapy with other cytotoxic agents (such as high-dose methotrexate for osteosarcoma), alternative treatment with Adriamycin and cis-platinum may be given immediately without awaiting recovery from surgery. Another advantage of administering chemotherapy before surgery is the avoidance of treatment in the early postoperative period, when complications such as atelectasis and malnutrition are frequently present and drains and catheters are in place.[19]

However, one must be careful in extrapolating the results of this small series to other chemotherapeutic agents and surgical procedures used in the treatment of different neoplastic diseases. The problem of wound healing with perioperative chemotherapy may be more frequent when complicated surgical procedures are performed. Our patients were healthy without other adverse factors such as sepsis, steroid use and local irradiation during chemotherapy and surgery. Further clinical observations and comparative trials are necessary to evaluate the effect of perioperative chemotherapy in other malignant tumours.

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reported that continuing administration of any antibiotic beyond 24 hours following surgery increases the possibility of adverse reactions but, in the majority of surgical procedures, does not reduce the incidence of subsequent infection.

If signs of postsurgical infection should appear, specimens for culture should be obtained for identification of the causative organism(s) so that appropriate therapy may be instituted.

CONTRAINDICATIONS

MEFOXIN® is contraindicated in persons who have shown hypersensitivity to cefoxitin or to the cephalosporin group of antibiotics.

WARNINGS

Before therapy with MEFOXIN® is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to MEFOXIN®, cephalosporins, penicillins or other drugs. MEFOXIN® should be given with caution to penicillin-sensitive patients.

There is some clinical and laboratory evidence of partial cross-allergenicity between cephamycins and the other beta-lactam antibiotics, penicillins and cephalosporins. Severe reactions (including anaphylaxis) have been reported with most beta-lactam antibiotics.

Pseudomembranous colitis has been reported with virtually all antibiotics. This colitis can range from mild to life threatening in severity. Antibiotics should therefore be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. It is important to consider a diagnosis of pseudomembranous colitis in patients who develop diarrhea in association with antibiotic use. While studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis, other causes should also be considered.

Any patient who has demonstrated some form of allergy, particularly to drugs, should receive antibiotics including MEFOXIN® with caution.

If an allergic reaction to MEFOXIN® occurs, administration of the drug should be discontinued. Serious hypersensitivity reactions may require treatment with epinephrine and other emergency measures.

PRECAUTIONS

The total daily dosage should be reduced when MEFOXIN® is administered to patients with transient or persistent reduction of urinary output due to renal insufficiency (see DOSAGE AND ADMINISTRATION) because high and prolonged serum antibiotic concentrations can occur from usual doses.

In patients treated with MEFOXIN® a false-positive reaction to glucose in the urine may occur with Benedict's or Fehling's solutions but not with the use of specific glucose oxidase methods.

Using the Jaffe Method, falsely high creatinine values in serum may occur if serum concentrations of cefoxitin exceed 100 μg/mL. Serum samples from patients treated with MEFOXIN® should not be analyzed for creatinine if withdrawn within two hours of drug administration.

Increased nephrotoxicity has been reported following concomitant administration of cephalosporins and aminoglycoside antibiotics.

The safety of MEFOXIN® in the treatment of infections during pregnancy has not been established. If the administration of MEFOXIN® to pregnant patients is considered necessary, its use requires that the anticipated benefits be weighed against possible hazards to the fetus. Reproductive and teratogenic studies have been performed in mice and rats and have revealed no evidence of impaired fertility or harm to the fetus due to MEFOXIN®.

Cefoxitin has been observed in the milk of nursing mothers receiving the drug.

Prolonged use of MEFOXIN® may result in the overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential and if superinfection occurs during therapy, appropriate measures should be taken. Should an organism become resistant during antibiotic therapy, another antibiotic should be substituted.

In children 3 months of age or older, higher doses of MEFOXIN® (100 mg/kg/day and above) have been associated with an increased incidence of eosinophilia and elevated SGOT.

ADVERSE REACTIONS

MEFOXIN® is generally well tolerated. Adverse reactions rarely required cessation of treatment and usually have been mild and transient.

Local Reactions
Thrombophlebitis has occurred with intravenous administration. Some degree of pain and tenderness is usually experienced after intramuscular injections using water. Induration has occasionally been reported.

Allergic
Maculopapular rash, urticaria, pruritus, eosinophilia, fever and other allergic reactions have been noted.

Gastrointestinal
Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Blood
Transient eosinophilia, leukopenia, neutropenia, hemolytic anemia, and thrombocytopenia have been reported. Some individuals, particularly those with azotemia, may develop positive direct Coombs tests during therapy with MEFOXIN®.

Liver Function
Transient elevations in SGOT, SGPT, serum LDH, and serum alkaline phosphatase have been reported.

Kidney
Elevations in serum creatinine and/or blood urea nitrogen levels have been observed. As with the cephalosporins, acute renal failure has been reported rarely. The role of MEFOXIN® in changes in renal function tests is difficult to assess, since factors predisposing to prerenal azotemia or to impaired renal function have often been present.

TREATMENT OF OVERDOSE

Other than general supportive treatment, no specific antidote is known. MEFOXIN® can be eliminated by dialysis in patients with renal insufficiency.

DOSAGE AND ADMINISTRATION

MEFOXIN® may be administered intravenously or intramuscularly when required. (See complete monograph on ADMINISTRATION and RECONSTITUTION.)

TREATMENT DOSAGE

Adults

The usual adult dosage is 1 g or 2 g of MEFOXIN® every 6 to 8 hours. Dosage and route of administration should be determined by severity of infection, susceptibility of the causative organisms, and condition of the patient. The usual adult dosages are shown in the Table below.

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 g	1 g every 6-8 h I.V. or I.M.
Moderately severe or severe infections	6-8 g	1 g every 4 h or 2 g every 6-8 h I.V.
Infections commonly needing antibiotics in higher dosage (e.g. gas gangrene)	12 g	2 g every 4 h or 3 g every 6 h I.V.

*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.

Adults 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 h
Moderate impairment	29-10	1-2 g	every 12-24 h
Severe impairment	9-5	0.5-1 g	every 12-24 h
Essentially no function	<5	0.5-1 g	every 24-48 h

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.

Neonates (Including Premature Infants), Infants and Children (See WARNINGS for Neonates under ADMINISTRATION in the complete monograph.)

Premature Infants with Body Weights Above 1500 g	20-40 mg/kg every 12 h I.V.
Neonates	
0-1 week of age	20-40 mg/kg every 12 h I.V.
1-4 weeks of age	20-40 mg/kg every 8 h I.V.
Infants	
1 month to 2 years of age	20-40 mg/kg every 6 h or every 8 h I.M. or I.V.
Children	20-40 mg/kg every 6 h or every 8 h I.M. or I.V.

In severe infections, the total daily dosage in infants and children may be increased to 200 mg/kg, but not to exceed 12 g per day.

MEFOXIN® is not recommended for the therapy of meningitis. If meningitis is suspected, an appropriate antibiotic should be used.

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 or abdominal 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.

AVAILABILITY

MEFOXIN® is supplied as sterile powder in boxes of 10 vials:

3356 Ca - 1 g cefoxitin as sodium salt
3357 Ca - 2 g cefoxitin as sodium salt

Storage
MEFOXIN® in the dry state should be stored below 30° C.

PRODUCT MONOGRAPH AVAILABLE ON REQUEST

(425-a,6,87x)

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Above-Knee Femoropopliteal Reconstruction With Polytetrafluoroethylene: a Good Alternative to Saphenous Vein Bypass

F. Laurendeau, MD, FRCSC;* J. Lassonde, MD, FRCSC†

Over 6½ years, 64 femoropopliteal bypasses were done on 55 patients, using polytetrafluoroethylene (PTFE). The PTFE was chosen because previous surgery or small diameter prohibited the use of saphenous vein. The distal anastomoses were always placed above the knee. Patency rates were 92% at 1 month, 76% at 1 year, 72% at 2 years and 59% at 3 years, and then reached a plateau of 55% at 4 years. When autogenous vein is not available, PTFE is the material of choice for femoropopliteal reconstruction. The results compare favourably with those using saphenous vein in an above-knee situation.

Sur une période de 6½ ans, 64 dérivations fémoro-poplitées ont été pratiquées chez 55 patients à l'aide de tubulures de polytétrafluoroéthylène (PTFE). Le PTFE était choisi quand une chirurgie antérieure ou le petit calibre des vaisseaux interdisait l'emploi d'une veine saphène. Les anastomoses distales ont toujours été faites au-dessus du genou. Les taux de perméabilité ont été de 92% à 1 mois, de 76% à 1 an, de 72% à 2 ans et de 59% à 3 ans, pour ensuite atteindre un plateau de 55% après 4 ans. Quand il est impossible d'utiliser une veine autogène, le PTFE est le matériau de premier choix pour la reconstruction fémoro-poplitée. Les résultats se comparent favorablement à ceux des saphènes dans les oblitérations au-dessus du genou.

It is generally agreed that autologous saphenous vein is the best material to use for reconstruction in femoropopliteal disease, especially when the distal anastomosis is below the knee joint. However, in a number of patients, the vein is either absent, due to previous surgery, or of inferior quality. In this context, it is suggested that polytetrafluoroethylene (PTFE) may function as well as the saphenous vein in above-knee reconstruction. We report our experience with PTFE over a 78-month period.

Patients and Methods

The records of patients who underwent femoropopliteal bypass grafting for arterial occlusive disease at the Hôpital Maisonneuve-Rosemont between Jan. 1, 1979 and July 1, 1985 were reviewed. Sixty-four above-knee PTFE grafts were placed in 55 patients (48 men and 7 women) who ranged in age from 45 to 86 years (mean age 62 years) (Fig. 1). In all patients, the

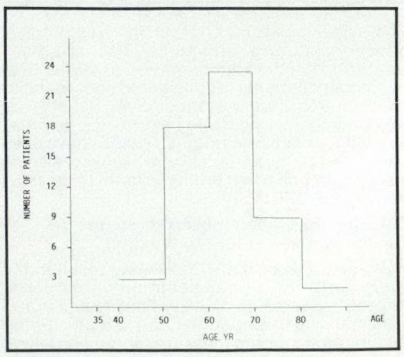

FIG. 1. Age distribution.

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Accepted for publication July 5, 1988

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saphenous vein was either absent or of insufficient diameter (less than 4 mm). The operations were performed for ischemic problems with rest pain or trophic changes, or both (34), and for claudication alone (30). This inordinately high frequency of patients operated on for claudication alone was due to a more liberal use of the procedure in the early part of the study. We are more conservative now. Preoperatively, all patients underwent aortofemoral angiography and noninvasive hemodynamic assessment with segmental pressure and pulse volume recordings. Follow-up, complete for all but two patients, ranged from 12 to 84 months. Graft occlusion was determined by clinical, noninvasive or angiographic methods.

Fifteen patients were diabetic, but only 5 were insulin dependent. A previous vascular procedure had been performed on 17 patients, 10 of whom had a thrombosed venous femoropopliteal graft (Table I).

The PTFE grafts measured 6 mm in diameter in 27 patients, 8 mm in 32 and 10 mm in 5. Use of the 10-mm graft has been discontinued.

Results

By life-table analysis the cumulative patency rates were 92% at 30 days, 76% at 1 year, 72% at 2 years and 59% at 3 years; they reached a plateau of 55% at 4 years. There was no statistical difference whether the bypass was performed for claudication or ischemic rest pain.

Table I. Previous Vascular Procedures

Procedure	No. of patients
Failed venous femoropopliteal bypass	10
Aorto–bifemoral bypass	4
Aorto–bi-iliac bypass	1
Aortic endarterectomy	1
Common femoral endarterectomy	1

There were five early thromboses (within 30 days). In all of these cases, the surgery was performed for ischemic rest pain and with an outflow tract of poor quality, that is with only one patent vessel distally. Three of the distal anastomoses had been placed on an isolated popliteal artery. Only one of these graft failures was followed by amputation.

There were three late thromboses, at 2, 5 and 24 months respectively; they were successfully thrombectomized, and the grafts remained patent thereafter. Three other late thromboses, at 4, 7 and 60 months were followed by a major amputation.

There were no operative deaths. Eight patients died between 2 months and 6 years postoperatively, five of myocardial infarction and three of lung carcinoma. Late mortality was 15%.

One patient presented with a graft infection and was found to have a false aneurysm which prompted removal of the graft without loss of the limb.

Discussion

The PTFE graft was first used in 1974,[1] and other reports detailed early and intermediate patency rates.[2,3] Aneurysmal dilatation was noted early in the initial series[4] and corrected by an additional layer around the graft. Since then, the material has been used extensively. However, application of the findings from previous reports has been hindered by differences in patient selection and reporting methodology. It is generally agreed that the ideal conduit for leg revascularization should have an adequate diameter, compliance characteristics similar to the recipient arteries, a permanent nonthrombogenic surface and resistance to biodegradation by atherosclerosis.[5]

There is clear evidence that the saphenous vein provides the best results when used in infrapopliteal anastomoses.[6] Recently, there has been a resurgence of reports showing excellent results with the nonreversed in-situ saphenous vein.[7] However, some investigators[8] have noted the unsuitability of the saphenous vein in 3% to 21% of patients. Szilagyi and colleagues[9] have demonstrated that the quality of the vein, determined by its diameter, presence of varices, fibrotic valves and diffuse sclerosis, has correlated well with long-term patency. In many patients, the saphenous vein is absent due to previous surgery.

Reports[10,11] show that a PTFE graft may function as well as the saphenous vein when the distal anastomosis lies above the knee.

Christenson and colleagues[12] found a significantly higher cumulative patency rate when the distal anastomosis of a PTFE graft was placed above the knee than below. Their findings corresponded with earlier reports by Kidson and associates[13] and Raithel and Groitl.[14]

Some[15] have recommended the use of PTFE in preference to the autologous vein graft in the above-the-knee situation, arguing that this preserves the saphenous vein for treatment of distal occlusive disease which might subsequently develop. Since the requirements for autologous saphenous vein assume greater importance as smaller calibre vessels are reached, the argument for its preservation for use in bypassing to the level of the tibial vessels seems rational, but we are not yet ready to adopt this policy.

In our series, indications for using the PTFE graft were absence of the saphenous vein or insufficient diameter of the vein. Moreover, the distal anastomosis was always performed above the knee.

Our data confirm the observation of other investigators that PTFE may safely be used for above-knee femoropopliteal bypass with the expectation of results equivalent to those achieved with saphenous vein. Although experience with the synthetic graft has increased, both early thrombosis and late graft occlusion continue to pose serious problems. Anastomotic neointimal hyperplasia and progression of the disease are mainly responsible for late failure. There is increasing evidence that antiplatelet treatment can lessen the thrombogenicity of the graft.[16] It is also well known that PTFE bypasses are unique in that thrombectomy alone can sometimes restore long-term patency after early thrombosis.[17]

Only longer follow-up and randomized patient selection will determine whether PTFE is superior to autogenous saphenous vein for lower extremity bypass.[18] In cases of severe ischemia and in the rarer cases of disabling claudication, when the distal anastomosis can be performed above the knee, saphenous vein should be the first choice. However, if the vein is not available, PTFE seems to be a durable and dependable long-term alternative.

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Adrenal Myelolipomatous Nodules Mimicking Adrenal Neoplasms: Report of Three Cases

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The authors describe three cases of adrenal myelolipoma. In the first two, unilateral adrenal masses, assumed to represent adrenal neoplasms, were found during urologic examination; the correct diagnosis was made by frozen-section examination during operation. The third case involved bilateral adrenal lesions diagnosed at autopsy in a patient suspected to have metastatic cancer. Histologic, immunohistochemical and electron microscopic studies revealed polyclonal lesions composed of hematopoietic cells and fat cells. Radiologic recognition and fine-needle biopsy of these lesions are important to avoid unnecessary surgery in asymptomatic cases. Since the lesions cannot be regarded as true neoplasms, the authors suggest that the name myelolipoma should be replaced by the term myelolipomatous nodule.

Les auteurs décrivent trois cas de myélolipomes surrénaliens. Dans les deux premiers cas, une masse surrénalienne unilatérale prise pour un cancer de la surrénale fut découverte à l'examen urologique; le diagnostic exact fut posé à l'examen des coupes en congélation. Le troisième cas comprenait des lésions surrénaliennes bilatérales qui furent diagnostiquées à l'autopsie chez un patient soupçonné d'être atteint d'un cancer métastatique. Les examens histologiques, immunohistochimiques, ainsi que la microscopie électronique, révélèrent des lésions polyclonales composées d'éléments hématopoïétiques et de cellules adipeuses. L'identification radiologique et la ponction-biopsie à l'aiguille fine de ces lésions sont de première importance si l'on veut éviter une chirurgie inutile dans les cas asymptomatiques. Puisque ces lésions ne peuvent pas être considérées comme de véritables néoplasies, les auteurs suggèrent de remplacer le vocable de myélolipome par celui de nodule myélolipomateux.

Adrenal myelolipomas, rare lesions unassociated with hormone production, are composed of hematopoietic cells and fat cells resembling bone marrow. They were first described by Gierke in 1905[1] and were named "myelolipomas" by Oberling in 1929.[2]

These lesions are usually found incidentally or at autopsy in 0.08%[3] to 0.2%[4] of cases. The first case of surgically removed myelolipoma was reported by Dyckman and Freedman[5] in 1957. Subsequently, several other cases of myelolipomas have been described.[6-8] Ultrasonography and, especially, computed tomography are helpful in identifying a fat-containing mass, suggesting the diagnosis, but are not pathognomonic of myelolipoma.[9]

We present two patients who had myelolipomas removed surgically and in whom the preoperative diagnosis was adrenal neoplasm; in a third patient, bilateral adrenal myelolipomas suspected to be metastatic cancer were found at autopsy.

Case Reports

Case 1

A 55-year-old obese woman was admitted for investigation of a left suprarenal mass, discovered during evaluation of recurrent urinary tract infection. She complained of decreased energy and a weight gain of 4.5 kg over the past 3 months. Symptoms of feeling hot and sweaty, suggesting a pheochromocytoma, were attributed to menopause. In the past she had been involved in a motor vehicle accident and had sustained vertebral fractures and hepatic and splenic lacerations necessitating splenectomy. She was being treated for long-standing hypertension and hy-

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Accepted for publication Aug. 12, 1988

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pothyroidism. On examination she was in no distress, her blood pressure was 130/90 mm Hg and optic fundi showed grade II hypertensive changes.

Blood cell count, electrolyte values, renal and liver function test results and serum calcium and phosphorus levels were all normal. Thyroid function tests on thyroxine supplementation gave normal results. Intravenous pyelography revealed a large left intra- or suprarenal lesion, which was shown on ultrasonography to be a solid adrenal mass measuring 5 × 6 cm. This was confirmed by computed tomography. Angiography showed the mass to be avascular. An adrenal pheochromocytoma was suspected, although catecholamine and vanillylmandelic acid values in a 24-hour urine specimen were normal. Elective left adrenalectomy was performed and examination of a frozen-section led to the diagnosis of myelolipoma.

Case 2

A 58-year-old moderately obese man was admitted for investigation of a right adrenal mass discovered by ultrasonography during examination for long-standing hypertension. He was asymptomatic and his blood pressure was 170/100 mm Hg. No abnormality was found on physical examination.

Blood cell count, electrolyte values, renal and liver function test results and serum calcium and magnesium levels were normal. Catecholamine and vanillylmandelic acid levels in a 24-hour urine specimen were normal. Levels of testosterone, androstenedione, dehydroepiandrosterone sulfate, adrenocorticotropic hormone (ACTH), cortisol and 17-ketosteroids were within the normal range. A chest x-ray film showed a moderately enlarged heart and the electrocardiographic findings were consistent with an old anterior myocardial infarction. Ultrasonography revealed an echogenic right suprarenal mass measuring 6.5 × 7.2 cm, which was shown by computed tomography (Fig. 1) to be attached to the adrenal gland. It had a low CT number of −60 to −70, suggestive of a fat-containing lesion. There was also suggestion of a mass of similar attenuation 1.5 cm in diameter associated with the left adrenal gland. A nonfunctioning adrenocortical adenoma was suspected. Elective resection of the mass and right adrenal gland was performed and the diagnosis of myelolipoma was made by frozen-section examination.

Case 3

A 56-year-old man was admitted with pneumonia due to *Haemophilus* sp. Relevant history included alcohol abuse complicated by pancreatitis, liver disease, a perforated ulcer 21 years previously requiring gastrectomy and vagotomy, hypertension and, more recently, open reduction and internal fixation for a fractured humerus, complicated by osteomyelitis. On physical examination he was afebrile and had a blood pressure of 120/80 mm Hg. Findings on chest examination were consistent with the diagnosis of pneumonia.

Laboratory investigation revealed leukocytosis (leukocyte count 29.6 × 10^9/L), hyponatremia (114 mmol/L), hypocalcemia (1.74 mmol/L), normal serum amylase (75 U/L), hypoproteinemia (total protein 40 g/L) and hypoalbuminemia (albumin 19 g/L). Ultrasonography was technically poor and revealed no abnormality. A chest x-ray film demonstrated bilateral pleural effusions, consolidation of the left lung and a normal-sized heart. A computed tomogram revealed bilateral pleural effusions, a mass suggestive of a pancreatic pseudocyst, enlargement of both adrenal glands to about 3.5 cm with attenuation values suggestive of soft-tissue and retroperitoneal lymphadenopathy. These findings suggested metastatic carcinoma, with lung or pancreas as possible primary sites.

The patient's respiratory failure progressed and he died. At autopsy, bilateral adrenal myelolipomas were found. Death was attributed to a pancreatic pseudocyst, extending to the thoracic cavity with serofibrinous pericarditis and massive bilateral pleural effusions causing the respiratory failure.

Examination of the Specimens

For light microscopy, tissue samples were fixed in 10% formalin and embedded in paraffin. Sections 4 to 6 μm thick were stained with hematoxylin and eosin, Gordon–Sweet silver and Giemsa methods. For immunohistochemical analysis, the avidin-biotin-peroxidase complex (ABC) technique[10,11] was used. Sections were stained for Factor VIII, lysozyme, leukocyte common antigen, immunoglobulins and light chains. For electron microscopy, small pieces of tissue were fixed in 2.5% glutaraldehyde, osmicated, dehydrated in graded alcohol, processed through propylene oxide and embedded in an Epon-Araldite mix-

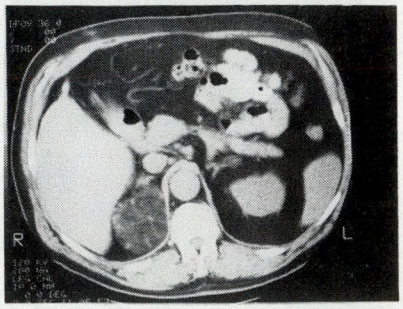

FIG. 1. Computed tomogram of abdomen, showing fat-containing lesion attached to right adrenal gland.

ture. Semithin sections were stained with toluidine blue, and appropriate areas were selected for ultrastructural study. Ultrathin sections were stained with uranyl acetate and lead citrate and investigated with a Philips-410 LS electron microscope.

Gross Findings

The specimen from case 1 consisted of an adrenal gland and attached fat weighing 97.5 g and measuring 7 × 7 × 4 cm. The cut surface was hemorrhagic, firm and brown with areas of yellow, fatty tissue.

In case 2 the specimen consisted of an adrenal gland with an attached, encapsulated, soft mass weighing 103 g and measuring 8.5 × 5.5 × 4 cm. The attached mass was round, red-yellow and measured 7 × 4.5 × 4 cm. The cut surface was dark red with yellow, fatty areas. Incorporated in the capsule were foci of attenuated adrenal cortex.

The right adrenal gland in case 3 weighed 8.5 g. Attached to the lower pole was an encapsulated, soft mass measuring 2.5 × 5.5 × 7.5 cm. The left adrenal gland weighed 12.5 g and also had an encapsulated, soft mass, measuring 4 × 3 × 1.5 cm, attached to its lower pole (Fig. 2). The cut surfaces were hemorrhagic and red-brown.

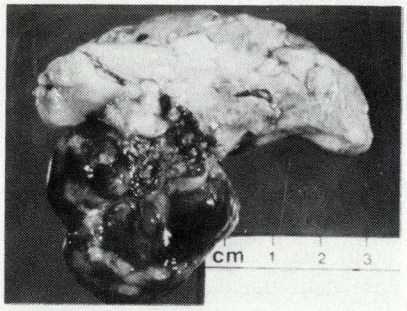

FIG. 2. Encapsulated soft mass (4 × 3 × 1.5 cm) attached to lower pole of left adrenal gland.

Histologic Findings

Each lesion consisted of hematopoietic cells and fat cells in variable amounts (Fig. 3). Areas of residual zona fasciculata and zona glomerulosa cells were seen under the adrenal capsule. Scattered foci of zona fasciculata and zona reticularis cells were noted throughout the lesions.

In case 1, the lesion was located within the cortex, expanding it. Adipose tissue was predominant. In case 2, the lesion was a discrete, encapsulated mass which was slightly more cellular than in case 1. Both lesions in case 3 were discrete, encapsulated masses and were more cellular than the lesions in the other two patients. They showed extensive hemorrhage and hemosiderin deposit.

The composition of the hematopoietic cells was identical in all three cases. Megakaryocytes were prominent. Scattered collections of lymphocytes and cells of the erythroid series were seen. Myeloid elements in which the Giemsa stain demonstrated cytoplasmic granules were present in various phases of development. The Gordon–Sweet silver stain revealed a delicate reticulin framework and occasional small vascular channels. No calcification was present.

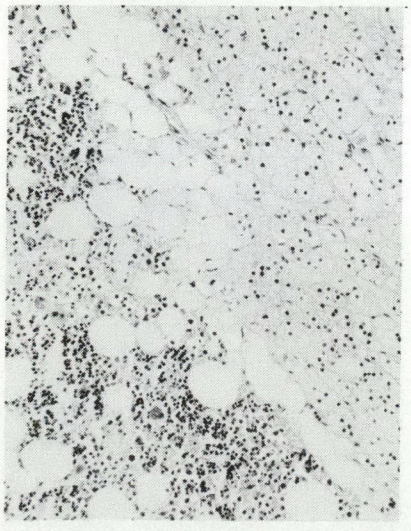

FIG. 3. Hematopoietic and fat cells with adjacent residual adrenal cortex (hematoxylin and eosin, original magnification × 100).

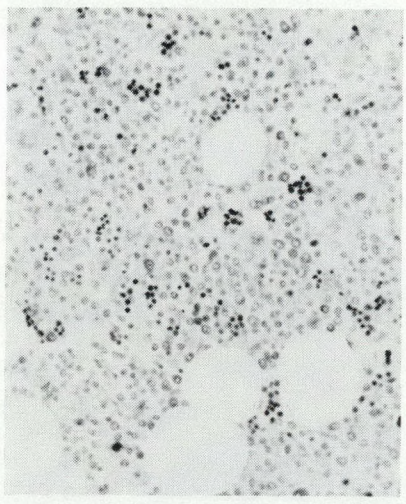

FIG. 4. Immunohistochemical stain for lysozyme showing immunoreactivity in monocytes, neutrophils and their precursors (ABC stain, original magnification × 250).

Immunohistochemical Findings

Staining for Factor VIII was positive in megakaryocytes and endothelial cells lining vascular channels. Immunoreactivity for lysozyme was seen in monocytes, neutrophils and their precursors (Fig. 4). Immunostaining was especially strong in patients 1 and 3. Staining for leukocyte common antigen was diffusely positive in all cases. Staining for immunoglobulins IgG, IgA and IgM and light chains showed focal positivity in the lesions, indicating the presence of plasma cells.

Electron Microscopic Findings

Case 3 was not studied because of postmortem autolysis. The adrenal cortical cells in case 2 showed typical ultrastructural features of steroid-producing cells with abundant cytoplasm containing numerous lipid droplets, smooth endoplasmic reticulum membranes, parallel

arrays of rough endoplasmic reticulum, many mitochondria exhibiting characteristic cristae and occasional electron-dense granules.

Electron microscopy of the lesions gave findings consistent with those of light microscopy (Figs. 5 and 6). Cells representing all three hematopoietic lines were observed. Irregularly shaped erythrocytes were seen within vascular channels as well as within cellular areas which also contained megakaryocytes, lymphocytes and granulocytes in various stages of maturation. Megakaryocytes with large, multilobed nuclei and abundant cytoplasm were identified. Lymphocytes were recognized by small, round nuclei with indented chromatin, microvilli and sparse organelles. Neutrophils, basophils and eosinophils were identified by their characteristic nuclei and cytoplasmic granules. Endothelial cells, fat cells, fibroblasts and interspersed collagen bundles were also seen.

Discussion

Adrenal myelolipomas are endocrinologically nonfunctioning. Our light microscopic, immunohistochemical and electron microscopic studies showed that they are composed of hematopoietic cells and fat cells resembling bone marrow.

The size of myelolipomas varies from microscopic to 8 cm diameter, and giant myelolipomas have been reported.[12-14] The clinical presentation and morphologic features have previously been described by Del Gaudio and Solidoro.[6] As in our three patients, most of the previously described lesions were discovered incidentally during gastrointestinal or urologic examination. Most patients were middle-aged; the youngest reported was a 12-year-old girl with bilateral adrenocortical hyperplasia and hypertension.[15] Many clinical associations have been noted, including obesity, hypertension, chronic systemic disease (e.g., malignant disease, cardiovascular disease, osteomyelitis, pyelonephritis), serious burns and endocrinopathies.[16]

The pathogenesis of myelolipomas is unclear. Most[3,12] agree that they are derived from undifferentiated stromal cells within the adrenal cortex which undergo myeloid metaplasia and proliferate to form a tumour-like mass. Alternatively, myeloid metaplasia may develop within pre-existing adrenocortical nodules. Collections of myeloid cells and fat cells have been described in the adrenal gland, in nonfunctioning adrenal nodules and in association with adrenocortical nodular hyperplasia, such as in Cushing's disease.[8,17] Boudreaux and colleagues[12] reported a sequential proliferative process resulting in the formation of a myelolipoma in a hyperplastic adrenal cortex. As with myelolipomas, these accumulations are associated with increasing age and have also been seen in patients with elevated blood ACTH levels and those under stress. They are rare in children and have not been noted in healthy young patients who have died suddenly. Their polyclonal character, emphasized by our immunohistochemical and electron microscopic studies, indicates that myelolipoma is a misnomer since this implies a neoplasm. We suggest that the term myelolipoma be replaced with that of myelolipomatous nodule, which is more consistent with the nature of the lesion.

The stimulus causing proliferation of hematopoietic and fat cells remains enigmatic. The hypothesis of Olsson and colleagues[3] that tissue necrosis is the basic stimulus, is supported by the finding of myelolipomatous change in adrenal glands of patients dying from severe burns. Tumour necrosis and fat necrosis in obese patients, especially those with hypertension, may also stimulate cell proliferation. A review of 10 patients by Ayyat and associates[18] showed associations with tissue necrosis. Two cases, one of a myelolipoma associated with 17-hydroxylase deficiency[19] and another with Cushing's disease,[20] suggest that hormonal dysfunction may play an etiologic role in the development of

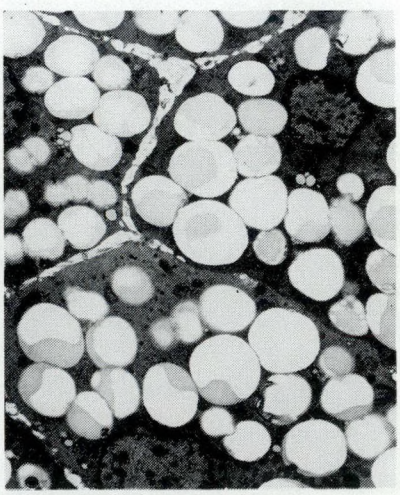

FIG. 5. Ultrastructure of adrenal cortical cells showing abundant cytoplasm and lipid droplets (uranyl acetate and lead citrate stain, original magnification × 2400).

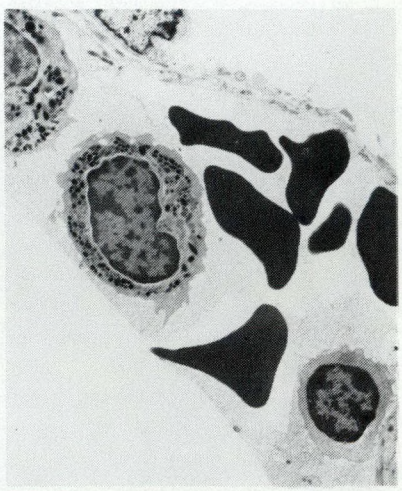

FIG. 6. Ultrastructure of lesions showing endothelial cell, erythrocytes, two granulocyte precursors and small lymphocyte (uranyl acetate and lead citrate stain, original magnification × 2400).

the lesion. Selye and Stone[21] produced myelolipomatous changes in adrenal cortices of rats injected with necrotic tumour extracts, testosterone and thyroxine, and proposed that tissue necrosis in the presence of ACTH is important in the pathogenesis of this disease. Boudreaux and colleagues[12] emphasized the etiologic role of humoral agents released during tissue necrosis, increased ACTH secretion and androgenic stimulation.

In this series, patients 1 and 2 were middle-aged, obese and suffered from hypertension. Our first patient had a history of hypothyroidism and was receiving thyroxine. She also had a history of trauma to the same side as the adrenal lesion. Endocrinologic investigations were normal in this case and in case 2, and the involved adrenal gland in each case contained no other lesions. Case 3 was a middle-aged man with chronic pancreatitis and a history of hypertension and osteomyelitis.

Local tissue necrosis combined with thyroxine may have been responsible for the development of the myelolipoma in case 1. In case 3, extensive tissue necrosis associated with stress-induced elevated ACTH levels may have contributed to the development of bilateral lesions. Fat necrosis associated with obesity and hypertension, as described previously,[3] may have played a role in case 2; however, no endocrinologic disturbance was demonstrated. The common factor appears to be tissue necrosis; the role of hormones may be to augment or modify the effect of the necrosis. Selye and Stone[21] produced myeloid tissue in the adrenal glands of rats injected with crude anterior pituitary extracts rich in ACTH. With the addition of testosterone, myeloid and adipose tissue developed. Thyroxine had a synergistic effect.

As with previously reported cases,[6] adrenal neoplasms were suspected and surgical excision was performed to establish the diagnosis. Radiologic investigations may reveal a radiolucent mass with displacement of the kidney and there may be associated areas of calcification.[6,22] When fatty components predominate, ultrasonography typically shows an echogenic mass;[6] similarly, computed tomography will demonstrate a fat-containing tumour.[23] These appearances vary depending on the proportion of fat to myelogenous components. If nonfatty components predominate, heterogeneous atypical images will result.[6] Angiography reveals an avascular lesion. Radiologic recognition is important since surgical excision is not necessary for small, asymptomatic lesions.[6] These patients must be followed radiologically. Fine-needle aspiration guided by computed tomography may be used to diagnose this lesion[6,20,23] when the differentiation from malignant disease is difficult.

We thank Debbie Lietz, May Wong and the Medical Photography Department of St. Michael's Hospital for their assistance.

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The Risk of Occult Invasive Breast Cancer After Excisional Biopsy Showing In-Situ Ductal Carcinoma of Comedo Pattern

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Between Jan. 1, 1985 and Aug. 31, 1987, 62 in-situ ductal carcinomas with a predominantly comedo pattern were identified in 61 patients in British Columbia from excisional biopsy of a palpable or mammographically demonstrable lesion of a breast. The biopsies were intended to remove the lesion completely. Fifty-seven (92%) of the 61 patients required wide re-excision or total mastectomy, usually within a month of the initial biopsy. Occult invasive disease was demonstrated in 14 of the re-excision specimens (24.5%) and residual in-situ carcinoma was present in a further 24 (42.1%), giving an overall rate of residual disease of 66.6%.

Axillary lymph nodes were sampled in 54 cases. Metastases were found in two cases (3.7%) and each was associated with occult infiltrating ductal carcinoma in the breast. This suggests that in-situ ductal carcinoma having a predominant comedo pattern may be more widespread and associated with a higher incidence of invasive ductal carcinoma than is generally believed.

En Colombie-Britannique, du 1er janvier 1985 au 31 août 1987, 62 cas de cancer in situ des canaux galactophores de type comédon ont été identifiés chez 61 patientes à partir de la biopsie-exérèse d'une tumeur mammaire palpable et visible à la mammographie. Les biopsies visaient à éliminer les tumeurs complètement. Cinquante-sept (92%) des 61 patientes ont nécessité une ré-excision plus large ou une mastectomie totale, habituellement moins d'un mois après la biopsie initiale. Un cancer invasif occulte fut démontré dans 14 prélèvements de ré-excision (24.5%) et un carcinome in situ résiduel était présent chez 24 autres (42.1%), pour un taux global de cancer résiduel de 66.6%.

Des prélèvements de ganglions axillaires furent pris dans 54 cas. Dans deux cas, des métastases étaient présentes et, chaque fois, elles étaient reliées à un cancer invasif occulte des canaux galactophores. Ces données indiquent que les carcinomes in situ des canaux galactophores de type comédon sont possiblement plus répandus et associés à une incidence plus élevée de cancers invasifs qu'on l'imagine généralement.

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Accepted for publication Apr. 29, 1988

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Screening programs designed to identify carcinoma of the breast at an early stage will result in the diagnosis of more preinvasive ductal carcinomas. When intraductal carcinoma has been identified by biopsy, management decisions must be based upon the likelihood of occult invasive carcinoma being present and on the future risk of invasive disease in the same breast.

Intraductal carcinoma can be classified morphologically into cribriform, comedo, papillary, solid and clinging forms,[1] the cribriform and comedo groups being the most common. It has been stated[2] that there is little value in distinguishing between these variants. The incidence of occult invasive ductal carcinoma following repeat biopsy or total mastectomy has been reported to range from 6% to 21%.[3–6] Furthermore, it is known that approximately 1% of patients with intraductal carcinoma and no evidence of infiltration on microscopy have ipsilateral axillary lymph-node metastases.[7]

Thymidine-labelling studies have suggested that the morphologic subgroups of intraductal carcinoma have significantly different cell kinetics.[8] It is interesting that comedocarcinoma has a relatively high rate of proliferation and apparently a greater malignant potential than

cribriform-papillary intraductal carcinoma.

At the Cancer Control Agency of British Columbia, patients with comedocarcinoma are believed to be at higher risk of harbouring occult invasive disease than those with other forms of intraductal carcinoma. To demonstrate conclusively a real difference in the incidence of occult invasion between the morphologic subgroups of in-situ carcinoma would require the simultaneous comparison by a small group of tumour pathologists of all subgroups of in-situ carcinoma seen in a given period. Before embarking upon such a study we considered it necessary to examine the incidence of occult invasive ductal carcinoma found in a subsequent wider excision specimen after the initial biopsy diagnosis of in-situ ductal carcinoma of predominant comedo pattern. We considered a comparative study of all variants justified only if the incidence of occult invasive carcinoma for in-situ comedocarcinoma was higher than generally accepted. In this paper we describe our experience.

Patients and Methods

Available records in the cancer registry showed that in British Columbia between Jan. 1, 1985 and Aug. 31, 1987, 4476 patients were found to have invasive or preinvasive breast cancer. Of this number, 3137 (70%) were referred to the Cancer Control Agency of British Columbia from hospitals throughout the province. At this institution all available histopathology sections are reviewed by a small number of reference tumour pathologists whenever a new patient is seen. During the study period, 55 patients were referred to the agency having a diagnosis of in-situ ductal carcinoma of the breast of predominant comedo pattern (50% or more of the observed disease) following excisional biopsy. Patients with metastases or Paget's disease of the nipple were excluded.

Six patients with in-situ comedocarcinoma, not referred to the agency, were identified from the cancer registry. For each, histopathology sections were available and were reviewed. They met our criteria and were included in the study.

Thus, 61 patients with in-situ comedocarcinoma of the breast were eligible for further study. In all, the biopsy was undertaken to remove all disease present. If a mammographically detected lesion was removed using fine-wire localizing techniques, a postoperative mammogram was obtained to confirm that all detectable disease had been removed. One patient underwent simultaneous biopsy of each breast and was found to have bilateral comedocarcinoma. This patient was considered as two separate cases, giving a total of 62 biopsies (cases); this represents 1.4% of all cases of invasive and preinvasive breast cancer known to have occurred in British Columbia during the study period.

From a review of the clinical records, the following information was extracted: age at diagnosis, mode of presentation, palpability of the lesion and mammographic findings.

The initial biopsy specimens were re-examined before entering the patients into the study. A diagnosis of in-situ ductal carcinoma of predominant comedo pattern was confirmed if 50% or more of the in-situ carcinoma was associated with central necrosis. Specimens with evidence of stromal invasion were excluded. Completeness of excision was based on resection margins; the extent of observed disease was not quantified.

If it was thought that the diseased tissue was not completely excised, the patient underwent either wide local re-excision or total mastectomy. Irrespective of the initial surgical procedure, low-level axillary node dissection was performed. Any subsequent excision specimens were reviewed and the following features recorded: evidence of invasive disease, the presence of residual disease (disease in the same quadrant as the excisional biopsy), the presence of multifocal disease (disease in a different quadrant), an assessment of the excision margins, evidence of axillary node metastases and the number of axillary nodes harvested.

Findings

The mean age of the 61 patients at presentation was 53.6 years (range from 28 to 80 years). The presenting features were a breast lump in 31 cases (50%), mammographic abnormalities in 25 (40%) and nipple discharge in 6 (10%).

Treatment Method

Because of doubt concerning the adequacy of the original excision, 41 total mastectomies and 16 wide local re-excisions were performed. Infiltrating carcinoma was found in four of the latter necessitating total mastectomy in three; the fourth had radical radiotherapy to the breast. The definitive surgical procedures performed, therefore, were 44 total mastectomies and 13 wide local re-excisions. The five remaining cases for which the patient did not undergo further surgical treatment after the initial biopsy were excluded from the remainder of the study. In 55 (89%) cases sampling of the axillary lymph nodes provided tissue suitable for staging. Of the 57 carcinomas for which the patient required re-excision or total mastec-

tomy, the surgery was performed within 1 month of the initial excisional biopsy in 47 (82%). In seven (12%) cases the second operation was performed within 2 months and in three (5%) more than 2 months from the time of the original biopsy.

One patient underwent further surgery only when recurrent disease at the original biopsy site and in the ipsilateral axilla became clinically apparent 11 months after the incisional biopsy. The re-excision revealed infiltrating carcinoma in the breast and axillary lymph nodes. It is impossible to determine whether occult invasive disease was present at the time of the original biopsy, but it was considered likely so the patient was classified accordingly.

Pathological Features of the Biopsy Specimen

All the excisional biopsy specimens were confirmed as showing in-situ comedocarcinoma, without evidence of stromal invasion. The excision margins could not be evaluated in 34 cases. In 21 specimens the in-situ ductal carcinoma involved the excision margin so the lesions were deemed to have been incompletely excised. Seven specimens had excision margins clear of disease.

Pathological Features of the Wide Excision or Mastectomy Specimen

In the 44 total mastectomy and 13 wide excision specimens, no residual or multifocal in-situ ductal carcinoma was evident in 19 (33.3%) cases. Residual in-situ ductal carcinoma was found in the same quadrant as the biopsy site in 24 (42.1%), and in 14 other cases (24.5%) infiltrating ductal carcinoma was found at the biopsy site together with in-situ ductal carcinoma. There was, therefore, residual ductal carcinoma within the breast after the original biopsy in 38 cases (66.6%).

The histologic findings in these specimens were compared with the clinical presenting features (Table I). Patients presenting with nipple discharge appeared at highest risk for subsequent residual (33%) or infiltrating (50%) carcinoma.

Multifocal in-situ ductal carcinoma was observed in 12 (27%) of the 44 total mastectomy specimens. All cases of multifocal in-situ ductal carcinoma in the initial biopsy specimen were associated with residual in-situ or infiltrating ductal carcinoma in the wider excision specimen also.

Axillary Lymph-Node Involvement

The number of nodes harvested was specified in 47 of the 55 cases; a mean of 9.2 nodes were obtained from each patient (range from 1 to 30). Excluding the patient in whom re-excision and axillary node dissection were delayed until she presented with recurrent disease, there were two cases of axillary node metastases in the 54 patients who underwent axillary node dissection within 1 month of excisional biopsy. All cases of axillary node metastases were associated with occult invasive carcinoma in the re-excision specimen.

Table I – Histologic Findings of Mastectomy or Re-excision Specimen Compared With Clinical Presentation

	Presenting features, no. (%)		
Histologic findings	**Lump**	**Mammographic abnormalities**	**Nipple discharge**
No. residual carcinoma, n = 19	10 (34)	8 (36)	1 (16)
Residual in-situ carcinoma, n = 24	13 (45)	9 (41)	2 (33)
Infiltrating carcinoma, n = 14	6 (21)	5 (23)	3 (50)
Totals	29	22	6

Discussion

We believe that this is the first report on the incidence of occult invasive breast cancer after an initial diagnosis of in-situ ductal carcinoma of predominant comedo pattern. Residual in-situ carcinoma was present in 42.1% of the re-excision specimens and infiltrating carcinoma was present in a further 24.5% of the study population, for a total incidence of residual disease of 66.6%. When no attempt is made to stratify the disease into morphologic subgroups, the incidence of occult invasive carcinoma is higher than the generally quoted range of 6% to 21%.

There was no demonstrable difference in the pathological findings, whether the patient presented with a palpable breast lump or with a mammographic abnormality. The association between nipple discharge and infiltrating carcinoma is probably due to random variation in a small subgroup. Otherwise, clinical presentation was of no value in predicting the subsequent need for mastectomy or re-excision.

Rosen and colleagues[3] reported a series of 129 excisional biopsies from 121 patients having a frozen- or paraffin-section diagnosis of non-invasive breast cancer. Of this group, 103 required total mastectomy, and occult invasive cancer was subsequently diagnosed in 6%.

Carter and Smith[4] reported a series of 38 patients shown to have intraductal carcinoma on biopsy; 7 (18%) had invasive carcinoma in the

subsequent mastectomy specimen. Thirty-six patients underwent definitive surgery within 1 month of the biopsy, but the remaining two had a treatment interval of 20 months and 63 months, raising the possibility that the invasive disease developed after the original biopsy.

Lagios and associates[5] reported a series of 80 breast biopsies, the specimens of which were found to contain in-situ ductal carcinoma; in 53 cases the breast was subsequently resected. Occult invasive cancer was seen in 21% of the resected breasts and multicentric disease in 32%. One lymph-node metastasis (2%) was found. This report suggests that the size of the original lesion was an important predictive factor for the presence of both occult invasion and multicentric foci of disease in the resected breast.

Fentiman and associates[6] examined 82 mastectomy specimens, which were previously shown to contain in-situ ductal carcinoma. Overall, 13 breasts (16%) contained invasive disease and no case of axillary node metastasis was observed. It is of interest that the results were tabulated with specific reference to the morphologic subgroup of in-situ disease. The data clearly showed that in-situ disease of comedo pattern made up 25% of the original biopsy specimens and yet accounted for 46% of the occult invasive cancers. This result is not statistically significant but does suggest that in-situ comedocarcinoma is associated with a higher incidence of occult infiltrating carcinoma.

Until recently, total mastectomy was accepted as the treatment of choice for in-situ ductal carcinoma because most patients treated in this way were cured of their disease. However, in the case of small infiltrating breast cancers, local excision and radical radiotherapy have produced results comparable to those of the various forms of radical mastectomy.[9,10] This has led to the paradox that women with infiltrating carcinoma may be treated by breast-conserving techniques, but those who present with in-situ ductal carcinoma undergo total mastectomy. It has been suggested[9,11–16] that conservative breast techniques be evaluated in the management of in-situ ductal carcinoma. Clearly, each case should be judged on its suitability for breast conservation. The criteria that are usually used are familiar, from application in the management of infiltrating ductal carcinoma (i.e., breasts are easy to examine, follow-up must be reliable and resection margins clear of disease). However, in this series, 66.6% of patients with in-situ comedocarcinoma had residual disease in the re-excision specimen and 24.5% of them had occult infiltrating carcinoma. In all cases, the surgeon performing the excisional biopsy attempted to remove all diseased tissue, yet in two-thirds of patients the diseased tissue was only partially excised. We suggest that in-situ comedocarcinoma may be a morphologic variant of in-situ carcinoma in which the disease is sufficiently widespread and likely to be associated with occult invasive carcinoma that either a very wide local excision or total mastectomy is necessary. If wide local excision is to be considered as a treatment option, it is recommended that all excised specimens be carefully marked to facilitate pathological assessment of the excision margins and that if the lesion was detected mammographically, the findings on a postoperative mammogram should be within normal limits. Ideally, this should be performed about 1 month postoperatively when the reactive changes secondary to surgery have subsided. Any patient treated conservatively should be followed up closely with regular physical examination and screening mammography.

Conclusions

There is no evidence to suggest that in-situ comedocarcinoma carries a worse prognosis than other forms of in-situ ductal carcinoma. However, it appears to be more widespread and associated with a higher incidence of occult invasive carcinoma than has previously been accepted. This observation is consistent with the hypothesis that in-situ comedocarcinoma is a more kinetically active variant of intraductal disease and may progress to invasive disease over a shorter time.

When considering conservative procedures for this type of breast cancer, the surgeon should bear in mind that residual in-situ or invasive ductal carcinoma in close proximity to the excision biopsy cavity was found in 66.6% of breasts requiring re-excision in this series. The pathologist should take great care when assessing the excision margins before concluding that conservative breast surgery is adequate. If the adequacy of excision of an in-situ ductal carcinoma of predominant comedo pattern is in doubt, then further surgery, either wide local excision or total mastectomy combined with low-level node dissection is advised.

We thank Colleen Mackie for clerical assistance and Patricia Thomas for help preparing the manuscript.

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BOOK REVIEWS

THE CLINICAL MANAGEMENT OF THE RENAL TRANSPLANT RECIPIENT WITH CYCLOSPORINE. Edited by Ronald M. Ferguson and Bruce G. Sommer. Grune & Stratton, Orlando, Fla.; W.B. Saunders Company Canada Limited, Toronto, 1986. $88.25. ISBN 0-8089-1823-0.

This monograph is an interesting and comprehensive review of the many aspects of renal transplantation associated with cyclosporine therapy. Every conceivable treatment of the kidney transplant is covered in this book and it provides convincing evidence that cyclosporine has been a major advance in the management of transplant rejection. However, the criteria used for monitoring a patient being treated with cyclosporine, the best time to start the drug and the duration of treatment are still controversial. The field is advancing so rapidly that with the advent of the monoclonal antibody immunoassay technique the methods for measuring cyclosporine levels are probably outdated. Therefore, many of the figures and levels quoted in this monograph will probably no longer apply. In spite of this, this book conveys the importance of careful monitoring of cyclosporine levels in the first few months after transplantation and that a critical decision must be made regarding the maintenance level of cyclosporine required to prevent rejection but avoid nephrotoxicity.

After reading this monograph I was not quite sure which regimen is preferred initially to prevent kidney rejection — ALG and prednisone followed by cyclosporine, or cyclosporine both preoperatively and intraoperatively. Excellent results can be obtained from the use of both regimens. No doubt better assay techniques will help answer this question.

Although the use of cyclosporine represents a major advance in the prevention of rejection, important factors such as the technical skill of the surgeon, short ischemic times of the donor kidneys and good matches between donor and recipient are still of great importance in the success of transplantation programs.

This book makes excellent reading for physicians associated with renal transplantation. At the same time it will be of interest to other physicians who use cyclosporine.

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HAIR TRANSPLANTATION. 2nd edition. Edited by Walter P. Unger and Rolf E.A. Nordström. 768 pp. Illust. Marcel Dekker, Inc., New York, 1988. $125.00 (US). ISBN 0-8247-7724-7.

Drs. Unger and Nordström have provided an excellent reference work to state of the art hair transplantation. This greatly expanded second edition involves many authors, each an expert in his field. In addition, most authors include the contributions of other transplant surgeons. This, along with thoughtful editorial comments, gives the text excellent balance.

The major strength of this book is

continued on page 64

Management of Gallstone Ileus

Roderick G. Syme, MD, FRCSC

A recent case of recurrent gallstone ileus prompted a retrospective review of 14 cases of the disease seen at St. Joseph's Hospital, Hamilton, between 1970 and 1986. The condition is uncommon and usually occurs in elderly women who have a history of gallbladder disease and concomitant medical illness. Twelve patients underwent surgery; 1 who had a "one-stage" enterolithotomy, cholecystectomy and repair of fistula died postoperatively. Nine patients who had enterolithotomy alone experienced notable morbidity; they included three who had recurrent biliary tract problems, all of which were managed successfully. The author concludes that enterolithotomy alone should be the standard procedure for gallstone ileus. Cholecystectomy and repair of cholecyst–enteric fistula should be done later only if there are continuing or recurrent symptoms.

A l'occasion de la récidive d'un iléus causé par des calculs biliaires, on a procédé à l'étude rétrospective de 14 cas similaires qui ont été vus entre 1970 et 1986 à l'hôpital St-Joseph de Hamilton. Cette affection est peu fréquente et survient habituellement chez des femmes âgées qui ont des antécédents de calculs biliaires et une maladie coexistante. Douze malades furent opérés; 1 patiente qui subit une intervention "en un temps" comprenant entérolithotomie, cholécystectomie et réparation de fistule, mourut après l'opération. Neuf patientes qui avaient subi une entérolithotomie seule, présentèrent une morbidité marquée dont trois cas de récidive des problèmes biliaires, complications qui purent toutes être réglées. L'auteur conclut que l'entérolithotomie seule doit être considérée comme l'intervention standard dans les cas d'iléus calculeux. La cholécystectomie et la réparation des fistules cholécysto–entériques doivent être différées et pratiquées seulement s'il y a persistance ou récidive des symptômes.

Gallstone ileus (mechanical obstruction of the gastrointestinal tract by one or more gallstones in the bowel lumen) was first described by Bartholini in 1654.[1] In 1890, Courvoisier[2] reported 131 cases of gallstone ileus, with a death rate of 44% from the 125 related operations. Although the condition is rare, causing only 1% to 3% of all intestinal obstructions,[3-5] gallstone ileus is reported to be the cause of nonstrangulating obstruction in 24% of patients over 65 years of age.[6-9] Despite improvements in surgical technique and postoperative care, both morbidity and mortality from the disease remain high.[8] Reports of recurrent gallstone ileus, cholangitis, carcinoma of the gallbladder and other postenterolithotomy biliary tract problems[10-16] have prompted some[8,17-22] to recommend "one-stage" enterolithotomy, cholecystectomy and repair of cholecyst–enteric fistula. A recent case of recurrent gallstone ileus after enterolithotomy prompted a review of our 17-year experience with gallstone ileus.

Case Report

A 75-year-old obese woman complained of vomiting, crampy upper abdominal pain and distension and no bowel movement for 72 hours. Her medical history included appendectomy, inguinal herniorrhaphy, hypertension and arthritis. On examination, she was afebrile, nonicteric and in mild distress. Bowel sounds were present and there was minimal tenderness with guarding in the left lower quadrant of the abdomen. Plain abdominal x-ray films (Fig. 1) demonstrated air in the biliary tree and dilated loops of bowel containing a gallstone.

At laparotomy, a gallstone 2.5 cm in diameter was removed from the terminal ileum. No other stones were palpated, and an inflammatory mass in the right upper quadrant was not interfered with. The patient did well and was discharged home 2 weeks later on a full diet.

Six days after discharge, she returned to hospital with a 12-hour history of vomiting and abdominal pain. Repeat plain abdominal x-ray films (Fig. 2) demonstrated dilated loops of bowel containing another gallstone. Careful review of her previous abdominal films (Fig. 1) re-

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Accepted for publication June 13, 1988

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vealed the outline of a stone in the gallbladder.

At repeat laparotomy, a gallstone 4.5 cm in diameter was removed from the upper jejunum and the nonresolving inflammatory mass in the right upper quadrant was not disturbed. When the two stones were placed together (Fig. 3), they formed a cast of the gallbladder, a picture similar to that published by Raiford[17] 25 years ago. The patient had a minor wound infection after the second operation but was well at follow-up 18 months later.

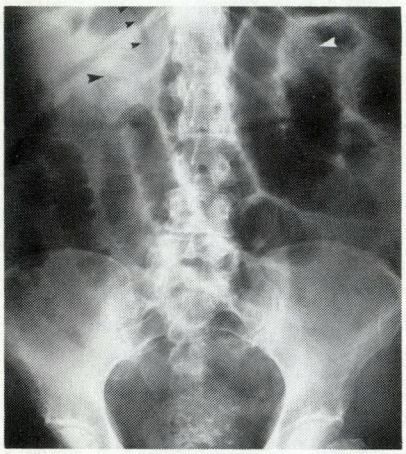

FIG. 1. Abdominal film, first admission, showing obstructed loops of bowel, air in biliary tree (small black arrows), gallstone causing obstruction (white arrow) and second gallstone in gallbladder (large black arrow).

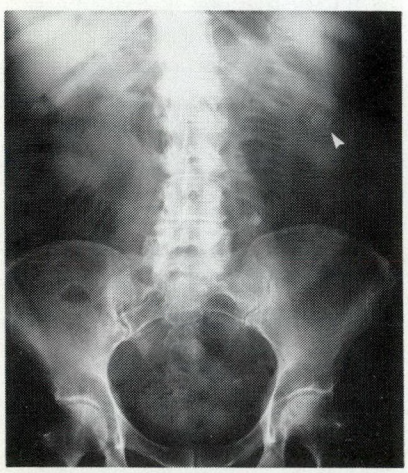

FIG. 2. Abdominal film, second admission shows bowel obstruction with second gallstone (arrow).

Our Experience

The medical records of 14 patients (13 women, 1 man) who had a diagnosis of gallstone ileus and were seen at St. Joseph's Hospital, Hamilton, between January 1970 and December 1986 were reviewed. Demographic characteristics, clinical presentation, laboratory and radiology reports as well as operative findings, procedure and outcome were abstracted for analysis.

The patients ranged in age from 58 to 97 years (mean 75.7 years). Six (42.8%) had a history of gallbladder disease and seven had concomitant medical disease (diabetes mellitus five, hypertension three, heart disease two, airway disease one). Although all patients had pain and vomiting and in over 70% there was abdominal tenderness, the history and physical findings were nonspecific. The commonest biochemical abnormality, leukocytosis, was evident in only eight cases. Delay in presentation was common; it ranged from 0.5 to 7.0 days (mean 4.2 days) from the onset of symptoms.

Plain x-ray films of the abdomen were obtained and records were assessed in all cases for the presence of Rigler's[23] four signs of gallstone ileus (Table I). A correct radiologic diagnosis was made preoperatively in 64.2% of patients.

Two patients did not undergo surgery. A 97-year-old woman who was moribund on admission, declined surgery and died within 48 hours; the second had severe respiratory disease and the obstruction resolved with the passage of a stone per rectum. Of the 12 patients who underwent surgery, 9 had enterolithotomy alone and 1 had an enterolithotomy, cholecystectomy and repair of the fistula ("one-stage" procedure). The two remaining patients had clinical and radiologic findings of gallstone ileus, but at laparotomy, no stone was evident. In one, the gallbladder was removed and the fistula repaired; in the other the fistula was not taken down.

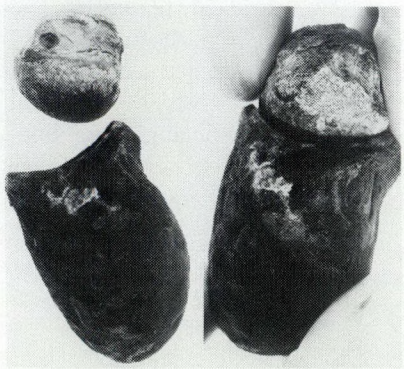

FIG. 3. Two gallstones together forming cast of gallbladder.

Stones were found in the terminal ileum in six patients and in the jejunum in four. Their diameter ranged from 2.5 to 7.0 cm (mean 4.2 cm). Two patients had more than one stone and 11 had an inflammatory mass in the right upper quadrant at laparotomy.

There were two deaths (14.2%); the 97-year-old woman already mentioned and the patient who underwent the "one-stage" procedure. The latter, a 79-year-old woman, had intra-abdominal sepsis requiring repeat laparotomy for drainage of abscesses. Despite aggressive treatment including zipper installation for peritoneal toilet, she acquired the adult respiratory distress syndrome followed by multisystem organ failure and died 1 month postoperatively.

The most common complication was wound infection, which occurred in six patients, only one of whom had received antibiotics pre-

Table I. Rigler's Radiologic Signs of Gallstone Ileus

Sign	No. of patients (%)
Air in the biliary tree	9 (64.3)
Bowel obstruction	14 (100)
Stone visualized	3 (21.4)
Change in position of a previously observed stone	2 (14.3)

operatively. Of the nine patients who underwent enterolithotomy alone, only two were problem-free postoperatively. Five had wound infections, which led in one case to dehiscence and in another to late incisional hernia. Three of this group had recurrent biliary tract problems: one had a common-bile-duct stone managed successfully by endoscopic retrograde cholangiopancreatography and sphincterotomy; one had recurrent biliary colic managed by cholecystectomy, exploration of the common bile duct and repair of the cholecyst–enteric fistula 3 months after enterolithotomy; and one (our case report) had recurrent gallstone ileus managed with repeat enterolithotomy.

Discussion

This study, consistent with other published series,[24-29] shows that gallstone ileus is an uncommon disease of elderly women, approximately half of whom have a history of gallbladder disease. There is often a delay of several days in seeking medical attention and they frequently have concomitant medical conditions complicating management. Unfortunately, history, physical findings and laboratory data are of little help in diagnosis. Radiologic criteria, as put forward by Rigler,[23] allowed us to make a correct preoperative diagnosis of gallstone ileus in 64.2% of patients, which compares favourably with the less than 50% reported in most other series.[22,25,27]

Most gallstones entering the intestine are small enough to be passed uneventfully. As in other series,[24-29] we found no stone smaller than 2.5 cm in diameter causing obstruction of the bowel. In over 90% of our patients operated on (11 of 12), an inflammatory mass was noted in the right upper quadrant, raising the controversial issue of appropriate management: enterolithotomy alone or enterolithotomy in combination with cholecystectomy and closure of the fistula ("one-stage" procedure). In our small series, the one patient who underwent the latter procedure died and another (in whom the stone appeared to have passed) underwent cholecystectomy and repair of fistula without enterolithotomy and survived. The nine patients who underwent enterolithotomy alone all survived but not without morbidity, which included recurrent biliary tract problems in three. Nevertheless, all complications in the enterolithotomy group were successfully managed using standard approaches, including endoscopy and open surgery. Although this series is too small to be of statistical significance, we, as surgeons, are often forced to make decisions based on such reports when dealing with conditions as uncommon as gallstone ileus.

The "one-stage" procedure of enterolithotomy, cholecystectomy and repair of fistula was first suggested by Holz[30] in 1929 and later by Fraser[31] in 1954 and Welch and associates[32] in 1957, each reporting a single case. The rationale was to prevent recurrent gallstone ileus, cholangitis, carcinoma of the gallbladder and other biliary tract problems, reported to occur in up to 30% of patients after enterolithotomy alone.[10-16] Between 1962 and 1975, seven more papers[8,17-22] appeared, supporting the "one-stage" procedure, but they totalled only 23 cases. In the largest of these series, Cooperman and associates[20] reported one death in eight patients who underwent the "one-stage" procedure and no deaths (but three recurrences) in six patients who underwent enterolithotomy alone. Kasahara and colleagues[24] reported 66 patients of whom 50 underwent enterolithotomy alone and 16 the "one-stage" procedure; the death rates were 12% and 19% respectively. Of the patients who underwent enterolithotomy alone, 14% had recurrent biliary tract problems, which, as in our series, were dealt with successfully. VanLandingham and Broders[26] reported nine cases of gallstone ileus in which the only death, as in our series, was a patient who underwent the "one-stage" procedure. However, their collected literature of 191 cases (35 "one-stage" procedures) failed to show a statistically significant difference in mortality between enterolithotomy (11%) and "one-stage" procedure (20%) ($p < 0.2$). Deitz and colleagues[29] carried out four "one-stage" procedures with no deaths and reported three deaths amongst 18 patients who underwent enterolithotomy alone.

Proponents of the "one-stage" procedure stress careful patient selection so that only those able to withstand the more extensive surgery will be considered. Given the age of the patients, concomitant medical illnesses and frequent delay in presentation, few would be suitable candidates. One must also bear in mind that the majority of patients do not have further problems after enterolithotomy and that those problems that do develop can usually be dealt with later, successfully, under more favourable conditions. This relatively benign course, coupled with the often precarious physiologic status of the elderly patient who has acute obstruction, argues strongly for enterolithotomy alone as the standard of care for gallstone ileus, with cholecystectomy and repair of the fistula done later and only for continuing symptoms.

The advice and support of Drs. Ken O'Brien, E.J. Thomas and Caroline Tallmadge are gratefully acknowledged.

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BOOK REVIEWS

continued from page 60

that it guides the reader through all the stages of hair transplantation from the initial interview, through harvesting and planting of plugs, to postoperative care and problems. I found Alt's contribution on the donor site to be exhaustive and most useful. Also, Unger's excellent chapter on the recipient site has been enlarged to include hair transplantation in early androgenetic alopecia, in women, in blacks and in orientals. The most important recent advances in hair transplantation, including alopecia reduction, unigrafts, micrografts, and quarter-grafts are well reviewed. The alternative to hair transplantation, flap surgery, is discussed thoroughly.

The generous use of photographs and diagrams enhances the reader's understanding of the text. The only error I found was in Table I on page 119.

I highly recommend this textbook for both the novice and expert hair transplant surgeon. Let us hope that we will not have to wait another 9 years for the next edition.

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MANAGEMENT OF ABDOMINAL HERNIAS. H. Brendan Devlin. 222 pp. Illust. Butterworth & Co. (Publishers) Ltd., London, 1988. Price not stated. ISBN 0-407-00348-7.

Brendan Devlin is a general surgeon at Stockton-on-Tees in northeast England. His stated intention to produce "a neat, practical book on hernia, not an exhaustive text" is fulfilled, although it is not clear for which audience this book is intended. As a result of large type, logical British style and multiple clear illustrations, this book is easy to read. Although it is only 200 pages long, it covers a large volume of material and at a size of 23 × 28 cm it will not likely fit into the pocket.

The book gives a brief but useful history of hernia surgery and includes, at the end, biographical notes on pioneers in the field such as Bassini, Cooper and McVay. Canadians will be pleased to observe the credit given to Earle Shouldice and Frank Glassow in the development of hernia surgery. In fact, the Shouldice repair is emphasized throughout the book. Mr. Devlin points out that hernia repair is poorly performed by many general surgeons and that recurrence rates are unacceptably

continued on page 73

Popliteal Aneurysms: an Index of Generalized Vascular Disease

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A review of 59 popliteal aneurysms in 38 patients seen over 10 years revealed that 34 (58%) aneurysms were symptomatic. Symptoms included gangrene (15%), ischemia due to thrombosis (38%) and embolism (5%). Patients with unilateral aneurysms (45%) were a median of 7 years younger than those with bilateral lesions (55%). The latter group had more frequent manifestations of occlusive disease, which included previous myocardial infarction, coronary artery bypass grafting and stroke. They also had more concomitant aneurysms, those of the abdominal aorta and femoral and iliac arteries being the most common. Management consisted of bypass grafting in 34 limbs and immediate amputation in 9; 16 inoperable limbs remained viable. At last follow-up (median 32 months) or time of death, 30 of 34 grafts were patent. Four grafts occluded, one perioperatively and the others at 4, 5, and 32 months respectively, resulting in two amputations. The cumulative patency rate in the asymptomatic group was 94% compared with 81% in the symptomatic group. These data illustrate that patients with popliteal aneurysms may have associated vascular disease, the likelihood of which is increased when aneurysms are bilateral.

La revue de 59 cas d'anévrismes poplités observés chez 38 patients au cours d'une période de 10 ans révèle que 34 (58%) de ces anévrismes étaient symptomatiques. Gangrène (15%), ischémie post-thrombotique (38%) et embolies (5%) faisaient partie des symptômes. Les patients souffrant d'un anévrisme unilatéral (45%) avaient un âge médian de 7 ans plus jeune que ceux qui avaient des lésions bilatérales (55%). Ce dernier groupe présentait plus fréquemment des manifestations de maladies ischémiques comprenant infarctus du myocarde anciens, pontages aortocoronariens et accidents cérébrovasculaires. Ils avaient également plus souvent des anévrismes concomitants, ceux de l'aorte abdominale et des artères fémorale et iliaque étant les plus fréquents. Il y eut 34 pontages de 9 amputations immédiates; 16 membres inopérables furent conservés. Au dernier examen de surveillance (médiane de 32 mois) ou au moment du décès, 30 des 34 greffes étaient perméables. Quatre dérivations se sont bouchées, une durant la période peropératoire et les autres après respectivement 4, 5 et 32 mois, entraînant deux amputations. Le taux cumulatif de perméabilité était de 94% pour le groupe asymptomatique, comparativement à 81% pour les patients symptomatiques. Ces résultats illustrent que les patients souffrant d'anévrisme poplité peuvent avoir des vasculopathies associées avec une probabilité qui croît en présence d'anévrismes bilatéraux.

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Presented at the 9th annual meeting of the Canadian Society for Vascular Surgery, held in conjunction with the 56th annual meeting of the Royal College of Physicians and Surgeons of Canada, Winnipeg, Man., Sept. 12, 1987

Accepted for publication Aug. 12, 1988

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With justification, popliteal aneurysms have been termed the "sinister harbinger of sudden catastrophe".[1] Left untreated, the majority will cause complications, and in roughly one-third of patients, limb amputation, usually above the knee, will be required.[2] Management of a patient with bilateral popliteal aneurysms, one of which is thrombosed, presents the surgeon with a dilemma concerning the order of surgical treatment, because the asymptomatic aneurysm may thrombose while attention is focused on the other limb. This dilemma prompted us to review our experience with popliteal aneurysms to clarify our approach to this clinical problem.

Patients and Methods

Most authorities[1-4] accept that a vessel diameter of more than 2 cm is diagnostic of an aneurysm of the popliteal artery.

Thirty-eight patients (1 woman, 37 men) with 59 popliteal artery aneurysms were treated at the Ottawa Civic Hospital between 1976 and 1987; the aneurysms were documented by angiography or ultrasonography in all cases.

Comparison of reported series is difficult because of patient classification according to complications and symptoms.[1] In this study it was not always possible to identify the initial complaint, so patients were classified according to the complications that had developed when the

popliteal aneurysm was diagnosed. A classification of asymptomatic was applied to patients who had only local discomfort or a popliteal mass, the aneurysm being unrecognized by the patient before it was discovered by the physician.

Follow-up was by regular clinic visits using noninvasive Doppler pressures and waveform analysis in most cases. When travel or distance was a problem the information was acquired by telephone.

Findings

Of the 59 aneurysms, 25 were asymptomatic; they included 1 that had thrombosed, presumably for some time before the patient sought help for symptoms in the opposite limb. Thirty-four aneurysms were symptomatic. The symptoms or signs included gangrene in 9, ischemia due to thrombosis in 22 and distal ischemic changes as a result of emboli originating in the aneurysm in 3.

The cumulative graft patency rate in asymptomatic limbs was 94% and graft failure did not lead to amputation. In contrast, there was a graft patency rate of 81% in symptomatic limbs, with two amputations.

Follow-up was complete for 31 patients (50 popliteal aneurysms); the other 7 (9 popliteal aneurysms) were lost to follow-up after several months.

Of the 38 patients, 17 had unilateral and 21 bilateral aneurysms. Patients with unilateral aneurysms were a median of 7 years younger than those with bilateral aneurysms (63 years versus 70 years). In two patients who had unilateral aneurysms, another aneurysm developed in the opposite leg, after 5 and 7 months respectively; they are included in the bilateral group. Associated occlusive vascular disease and additional aneurysms were more common in those who had bilateral popliteal artery aneurysms than in those with unilateral lesions (Table I).

Unilateral Aneurysms

Three of the 17 unilateral popliteal artery aneurysms were thrombosed, two patients requiring above-knee amputation; the other limb remained viable although functionally impaired. Eleven symptomatic and 3 asymptomatic limbs were suitable for bypass grafting (Table II). Patency rates of grafts to asymptomatic aneurysms were superior to those of symptomatic aneurysms. Two grafts occluded, one at 5 months resulting in a below-knee amputation and the other at 32 months resulting in a compromised but viable limb. Both grafts were of reversed saphenous vein.

Bilateral Aneurysms

In this group of 21 patients, treatment generally was directed first to the symptomatic limb.

The aneurysm was asymptomatic on one side in 12 patients and on both sides in 6. Two asymptomatic aneurysms, though not thrombosed, were associated with severely impaired circulation in the tibial vessels and were unsuitable for bypass grafting; neither aneurysm was symptomatic on follow-up averaging 44 months. Bypass grafts were inserted in 5 of 24 asymptomatic limbs because the symptomatic limb was not amenable to vascular reconstruction. One of the five grafts (saphenous vein) occluded in the perioperative period, but did not lead to amputation.

After surgical treatment on the symptomatic limb, 17 opposite asymptomatic limbs were subjected to a period of observation. Bypass grafting was later carried out on 10 of them; 6 remained under observation for a variety of reasons relating to the general health of the patient or an unwillingness to undergo surgical repair. In one case an asymptomatic aneurysm thrombosed while the patient recovered from bypass surgery for a thrombosed aneurysm in the opposite limb; this resulted in a below-knee amputation of the previously asymptomatic limb.

Table I. Associated Vascular Occlusive Disease and Other Aneurysms

Associated disease/ aneurysm	Patients, %	
	Unilateral aneurysm (n = 17)	Bilateral aneurysms (n = 21)
Myocardial infarction	24	33
Coronary artery bypass grafting	6	10
Stroke	12	19
Abdominal aortic aneurysm	24	38
Femoral/iliac aneurysm	18	29

Table II. Cumulative Graft Patency Rates After Bypass of Popliteal Artery*

	Asymptomatic		Symptomatic		Total patients/ total grafts
	Vein	ePTFE	Vein	ePTFE	
Unilateral	3/3	–	9/11	–	12/14
Bilateral	13/14	1/1	3/4	1/1	18/20
Totals	17/18		13/16		30/34
Patency, %	94		81		88

*Follow-up ranged from 3 to 112 months (median 32 months). Vein = reversed saphenous vein, ePTFE = expanded polytetrafluoroethylene.

Three patients had thrombosis of both popliteal aneurysms and two required bilateral above-knee amputation; one had inoperable yet viable limbs despite bilateral vascular impairment. Seven patients had anticoagulation therapy until elective angiography could be done to determine their suitability for surgical treatment; 5 of the 14 limbs were treated with bypass grafting, the remainder were not suitable. Five of the latter eventually required amputation some months later. Graft material was saphenous vein in four and expanded polytetrafluoroethylene (ePTFE) in one.

Three of nine patients who died had patent bypass grafts at the time of death, and graft failure led to an above-knee amputation in another but was not a direct cause of death.

Discussion

Aneurysms occur in the popliteal artery with a frequency that is second only to those of the abdominal aorta, and their presence indicates the high probability of another aneurysm, either in the contralateral popliteal artery or elsewhere.[1-13] This study and others (Table III) support this observation, and the fact that bilateral aneurysms increase that probability. Data show that the coronary or cerebral circulation is more likely to be occluded in patients with bilateral lesions and should the popliteal trifurcation be similarly affected, it is considered a predictor of myocardial infarction after vascular reconstruction.[14] Therefore, patients who have popliteal aneurysms should undergo careful cardiac and cerebrovascular assessment. In this study, the difference in median age of 7 years between the two groups is probably only one of several factors,[1] including a strong genetic predisposition to affect men.[4]

Our experience with respect to graft patency rate is consistent with that of other series[4,9,13] and reaffirms that the results of surgical treatment are substantially better when undertaken before thrombosis or embolism limits the outflow bed distal to the aneurysm. Once the popliteal aneurysm has thrombosed, the need for eventual amputation may not differ whether the limb is suitable for bypass grafting or not.[3] In patients with a thrombosed popliteal aneurysm and asymptomatic disease in the other limb, management must be individualized, and the indications for surgery will depend on the severity of symptoms. However, the surgeon should be alert to the perilous situation the patient may be in if the asymptomatic aneurysm thromboses while attention is focused on the symptomatic leg. When thrombosis does not produce symptoms, surgical repair is not indicated and when resulting symptoms are tolerable, without limb-threatening ischemic changes, a short delay while the asymptomatic aneurysm is dealt with will not alter the eventual outcome. Vessels patent distal to the thrombosed aneurysm will not be affected by a delay of a few weeks during which elective repair of the asymptomatic fellow may avoid thrombosis and amputation in more than one-third of cases. As a consequence of our immediate attention being focused on the symptomatic limb in patients with bilateral lesions, one patient had thrombosis of the asymptomatic aneurysm while convalescing at home after bypass grafting of the thrombosed symptomatic limb.

Ischemia due to acute thrombosis may threaten limb viability, and in such cases immediate efforts must be made to salvage the limb. Exploration of the vessel below the aneurysm and thrombectomy with a Fogarty catheter may open a major

Table III. Reported Series of Popliteal Aneurysms

Series	No. of patients	Male: female	Associated occlusive disease, %			Other aneurysms, %		
			MI	CABG	Stroke	AAA	Iliac/ femoral	Bilateral popliteal
Edmunds and associates, 1965[5]	82	–	32	–	13	36	≈15	32
Baird and associates, 1966[6]	51	–	≈30	–	22	12	≈10	42
Crichlow and Roberts, 1966[7]	42	42:0	10	–	7	14	≈12	36
Wychulis and associates, 1970[8]	152	37:1	21	–	18	35	≈50	59
Bouhoutsos and Martin, 1974[9]	71	–	–	–	10	32	13	–
Tompkins and associates, 1977[10]	18	17:1	–	–	–	28	33	45
Inahara and Toledo, 1978[11]	30	14:1	–	–	7	37	27	47
Guvendik and associates, 1980[12]	20	20:0	–	–	–	30	–	33
Szilagyi and associates, 1981[2]	62	–	–	–	–	40	≈39	40
Vermilion and associates, 1981[3]	87	–	25	–	3	40	≈55	68
Reilly and associates, 1983[4]	159	15:1	–	–	14	21	≈23	35
Whitehouse and associates, 1983[1]	61	30:1	≈33	–	5	62	37	44
Anton and associates, 1986[13]	110	54:1	–	15	–	29	32	61
Present series, 1987	38	37:1	29	8	16	32	24	55

≈Approximate determinations based on data reported. MI = myocardial infarction, CABG = coronary artery bypass grafting, AAA = abdominal aortic aneurysm.

outflow vessel[9] but does not relieve thrombosis in the capillary network. Direct intra-arterial thrombolytic therapy intraoperatively has had some success[15] and may be a helpful addition to operative thrombectomy of distal vessels; in this situation, tibial artery thrombosis is associated with a 70% limb loss.[16] However, reports of success are few and uncontrolled, and there are no long-term follow-up studies.

The rationale for an aggressive surgical approach to asymptomatic popliteal aneurysms lies in "the threat of unforeseeable grave complications"[2] associated with them. We recommend, as others[9] have, that in patients who have bilateral popliteal aneurysms, one thrombosed and one asymptomatic, the asymptomatic limb should be managed first.

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SESAP V Critique

Item 218

With rare exceptions, aneurysms of the popliteal artery occur almost exclusively among men of advanced age. Complications include thrombosis with limb ischemia, as well as distal embolization producing the so-called "blue toe" syndrome. The incidence of associated aneurysmal disease, particularly contralateral popliteal aneurysms, which may be uncalcified and asymptomatic, as well as of abdominal aortic aneurysms, is high. Spontaneous rupture and hemorrhage is rare but may occur. All popliteal aneurysms should be treated surgically if the patient's condition permits, even if they are asymptomatic, because of the high incidence of limb loss with initial symptoms. Proximal and distal ligation with bypassing of the aneurysm is preferred. The aneurysm may be resected, but injury to the popliteal vein and tibial nerve is a potential hazard.

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Complications and Functional Results After Limb-Salvage Surgery and Radiotherapy for Difficult Mesenchymal Neoplasms: a Prospective Analysis

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Wide resection with adjuvant radiotherapy is generally accepted as the optimal treatment for patients with extremity soft-tissue sarcomas. However, there is a subset of patients with "difficult" tumours who sustain such marked loss of function from limb-salvage procedures that amputation might offer a superior functional alternative. To evaluate this issue, the authors prospectively designated 19 of 52 patients registered in Toronto's Princess Margaret Hospital Prospective Sarcoma Database in 1986 as "difficult" cases, on the basis of tumour size and anatomical location. Complications and functional results of wide resection and adjuvant radiotherapy were documented. The most frequent complication was related to wound healing (8 of 19 patients). Functional analysis at 1 year follow-up demonstrated that all 19 patients had results superior to those that would be expected with amputation.

Une résection large avec radiothérapie adjuvante est généralement considérée être le traitement optimum pour les patients souffrant de sarcomes des tissus mous des extrémités. Toutefois, il existe un sous-groupe de patients porteurs de tumeurs dites "difficiles" qui subissent une telle perte fonctionnelle à la suite d'une intervention visant à sauvegarder le membre, que l'amputation pourrait offrir une alternative supérieure. Afin d'étudier cette question, les auteurs ont désigné, de façon prospective, 19 des 52 patients inscrits en 1986 au Registre prospective des sarcomes du Princess Margaret Hospital de Toronto, comme des cas "difficiles" d'après la taille et l'emplacement anatomique des tumeurs. Les complications et les résultats fonctionnels de la résection large avec radiothérapie adjuvante ont été évalués. La complication la plus fréquente se rapportait à la cicatrisation de la plaie (8 des 19 patients). L'analyse fonctionnelle effectuée après 1 an de surveillance démontre que chacun des 19 patients présente des résultats supérieurs à ceux qu'on aurait pu anticiper d'une amputation.

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Accepted for publication Aug. 12, 1988

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Surgical treatment of patients having locally aggressive mesenchymal tumours has improved substantially in the past 15 years. Enneking's original anatomical studies of soft-tissue sarcoma demonstrated that its characteristic invasion of peripheral muscle resulted in microaggregates of malignant cells penetrating beyond the pseudocapsule of the primary lesion.[1] This meant that potentially contaminated tissue had to be resected if local control was to be achieved by surgery alone. According to Enneking, this necessitated removal of the entire limb compartment involved by tumour, either by radical resection or amputation proximal to the origin of muscles inside the fascial compartment.[1-3]

Recognition that high-dose radiation can eliminate microscopic spread of soft-tissue sarcoma has modified the surgical management of this disease. Several studies have demonstrated that resection of the gross tumour mass with a limited margin of normal tissue (wide resection) combined with adjuvant radiotherapy is adequate for local control.[4-9]

Despite the obvious functional benefits of conservative, limb-sparing surgery, combined treatment

(surgery and high-dose radiotherapy) can result in considerable immediate local disability,[9,10] especially after extensive surgical dissection because of the anatomic site or size of the lesion. Indeed, it has been suggested that the soft-tissue disability after the combined treatment of soft-tissue sarcoma can be so severe that primary amputation may have provided a superior functional result.[10]

In this paper we consider the complications and functional results after surgery combined with the radical radiotherapy, by prospectively reviewing the clinical course of 19 patients with large aggressive mesenchymal neoplasms. Because of tumour size or its anatomic location these patients might be considered candidates for amputation.

Patients and Methods

There were 19 patients in the study (11 men and 8 women). They ranged in age from 20 to 70 years (mean 45.2 years). All were followed up after operation for at least 16 months (range from 16 to 26 months).

Patient Selection

All cases of soft-tissue sarcoma or aggressive fibromatosis, treated by members of the University of Toronto Sarcoma Group, are registered prospectively in The Princess Margaret Hospital Prospective Sarcoma Database. During 1986, 19 of 52 patients registered (11 men, 8 women) were characterized as having "difficult" tumours, based on the following criteria:

- Tumour size more than 20 cm.
- Tumour extension within the true pelvis.
- Encasement of the iliac or common femoral vessels.
- Tumour origin distal to the knee or elbow, with involvement of bone, muscle and skin that would necessitate extensive tissue transfer and skeletal reconstruction after adequate wide resection.
- Axillary location with invasion of the chest wall.

In the literature there are no accepted characteristics to define a subset of "difficult" or virtually unresectable lesions, but the criteria listed encompass tumours that require long, complex procedures for limb salvage.

Pathological Analysis

The protocol for pathological examination of the resected specimen, established by the University of Toronto Sarcoma Surgery Group, has the following guidelines, adhered to in all cases to determine if local resection has been adequate:

- Preoperative evaluation of the diagnostic biopsy and computed tomogram by the surgical pathologist managing the case.
- Examination of the resected specimen in the operating room for orientation by the surgeon and pathologist.
- Painting of the resection margins.
- Sectioning of the tumour in the pathology suite adjoining the operating room.
- Oriented frozen section from any resection margin with less than 1 cm of normal tissue covering the pseudocapsule.
- Extensive sampling of the margins for permanent sections to determine whether microscopic disease was present at any resection surface.

Representative samples from the diagnostic biopsy and resected specimens were reviewed by an experienced musculoskeletal pathologist (V.L.F.) who determined both the histologic subtype and grade of the tumour. The Musculo-Skeletal Tumour Society definition of histologic grading was used.[1]

Radiotherapy

The protocol for radiotherapy at The Princess Margaret Hospital consists of radical treatment of 55 to 65 Gy at 10 Gy/wk, five fractions per week, for soft-tissue sarcoma. Treatment is either preoperative (40 to 50 Gy in 4 to 5 weeks before surgery, with any remaining dose administered postoperatively using a shrinking-field technique) or wholly postoperative after wound healing is complete. Aggressive fibromatosis is generally treated with a total dose of 55 Gy. Part of the circumference of the limb should be excluded to reduce the risk of encircling fibrosis and distal edema.

Postoperative Complications

Soft-tissue complications were defined as necrosis of the wound edge, dehiscence or drainage that required dressings for longer than 7 days. Wound drainage was cultured and isolation of the same organism on more than one sample was accepted as evidence of infection. Vascular, neurologic and skeletal complications were also included in this review.

Function

A detailed functional analysis rating (modified from that of the Musculo-Skeletal Tumour Society[1]) was determined prospectively, before surgery and at follow-up 3, 6, 12 and 18 months after. For the purpose of this presentation, only the ambulatory status of patients with lower extremity tumours and the presence of pain persisting more than 3 months after the completion of treatment will be considered.

Results

Pathologic Features and Treatment

Sixteen patients presented with high-grade sarcomas: malignant fibrous histiocytoma in 9, synovial sarcoma in 2, liposarcoma in 2, fibrosarcoma in 1, soft-tissue chondrosarcoma in 1 and a chondrosarcoma originating in bone with massive soft-tissue extension in 1. Three patients had aggressive fibromatosis that had recurred locally at least twice before the described operative procedure. Ten patients presented with extensive thigh sarcomas; 3 of them required intraoperative vascular resection and reconstruction. Three patients had pelvic sarcomas and four distal tumours involving bone, muscle and skin that required composite resection and reconstruction using skeletal stabilization and microvascular free tissue transfer. Two patients who had axillary tumours required composite en-bloc resection of the chest wall.

Of the 19 patients, 11 had previously undergone incomplete tumour resection. In each case gross tumour remained at the end of the procedure. Six of these had resection and irradiation at the time of local recurrence; the other five underwent further resection immediately and received radiotherapy.

The operative procedures were long and complex; those for thigh tumours averaged 5.8 hours, for pelvic tumours 8.2 hours, for distal extremity lesions 4.2 hours and for axillary lesions 8.2 hours.

Three patients had undergone radical radiotherapy for residual gross disease more than 1 year before definitive management. Eight patients received preoperative radiotherapy (40 to 50 Gy) with a postoperative boost to 55 to 65 Gy. Six patients underwent postoperative radiotherapy only.

Complications

Eight of 13 patients with thigh or pelvic sarcomas suffered major wound complications that required secondary procedures. In two, small areas (less than 5 × 5 cm) of skin necrosis developed but healed rapidly after split-thickness skin grafting. Three patients had larger areas of necrosis (greater than 10 × 10 cm) that required débridement and grafting; of these, wounds were healed in two 3 months and in the third 9 months after surgery. The patient with delayed healing had chemotherapy postoperatively for a lung metastasis.

Three patients with thigh and pelvic sarcomas required vascularized tissue transfer for extensive wound dehiscence which developed after vascular reconstruction in two.

None of the patients who had axillary or distal extremity tumours managed by primary reconstruction with free tissue transfer suffered wound complications.

The timing of radiotherapy and surgery did not seem to affect the incidence of wound complications; 6 of 13 patients who had preoperative radiotherapy suffered wound complications compared with 2 of 6 patients who had postoperative radiotherapy.

All wound complications were treated immediately and aggressively.

Vascular complications occurred in five patients. One who had a large thigh tumour, sustained thrombosis of the superficial femoral artery immediately after resection of the lesion; thrombectomy was successful. Two patients who underwent vascular resection and reconstruction suffered major wound dehiscence which required débridement and vascularized tissue transfer for limb salvage. Chronic arterial insufficiency was not encountered. Two patients now suffer from chronic venous insufficiency and wear compression hose while walking.

Six patients had neurologic complications postoperatively. Three had complete, permanent, motor lesions of the sciatic nerve, requiring the use of an ankle–foot orthosis. Two required a cane when walking. Three other patients had substantial loss of the femoral nerve during anterior thigh resections. Two of these required a drop lock knee brace for stability while walking and the third learned to walk with a knee recurvatum gait.

Three patients who underwent bone resection during tumour removal later suffered pathologic fractures in the area. Two required reoperation and internal fixation; the third fracture healed in a cast.

Function and Follow-up

All but one patient, who had a pathologic fracture of the tibia, had stopped the regular use of narcotic analgesics within 3 months of surgery. Two who had pelvic resection required codeine when active and two (one who underwent thigh resection and the other a distal extremity resection) required anti-inflammatory medications regularly. The others, including the patient with a pathologic fracture, required no analgesics at 1 year.

All of the 16 patients who had lower extremity lesions were fully ambulatory within 6 months. Eight of the 10 patients who had resection of a thigh sarcoma were community ambulators and required no walking aids; two required a cane. Because the abductor musculature had been resected, two of three patients who had pelvic tumours excised required two canes for walking; the third walked without aids.

It should be remembered that

alternative procedures in these patients would have been hemipelvectomy or hip disarticulation. Adults rarely accomodate to prostheses after such amputations and generally use either a wheelchair or two crutches for walking.[14] All patients who had distal lower extremity tumours resected were able to walk without aids.

Of three patients treated for upper extremity tumours, two returned to work that would have been impossible after amputation — a chef and a welder. The third who had a soft-tissue sarcoma of the axilla had insufficient active shoulder movement to resume work as a hairdresser but since her elbow and hand function was virtually normal she retrained as a secretary.

No patients had local recurrence. Relapse occurred at distant sites in six patients (five with thigh tumours). Two died of metastatic disease. At the time of writing one was alive with extensive metastases and three had undergone resection of the metastases and were disease free.

Discussion

The goal of treatment in soft-tissue sarcoma is to provide local control of the lesion yet maintain function. Over the past 25 years, treatment has progressed from simple excision with a 60% to 70% local relapse rate[11,12] to radical resection,[1,3] to conservative surgery with high-dose adjuvant radiotherapy.[3] Several studies[4–9] have demonstrated that a combination of surgery and radiation has eliminated local disease in more than 90% of patients treated. Data from our institution suggest that the most important factor in determining local control is the adequacy of the local resection.[13]

If it is accepted that conservative resection combined with radiation offers a reasonable chance of local tumour control in soft-tissue sarcoma, then associated complications and residual function become important secondary considerations. There is no point in saving the limb if the patient is left with chronic pain, a draining wound or a useless extremity. The high early postoperative complication rate with combined treatment has been cited as a reason for performing primary amputation.[10] In this review, we have attempted to identify, prospectively, patients with difficult soft-tissue sarcomas who would have such severe complications and poor function that limb salvage should be avoided and amputation proposed as primary management.

Our patients in this study represent the most difficult subset of soft-tissue sarcomas, those most prone to postoperative complications, of which a delay in wound healing was the most common. Indeed, wound complications were found in 8 of 13 patients with lower extremity or pelvic tumours. This is not surprising, since adequate tumour resection required that large skin flaps be lifted off the deep fascia, interrupting the myocutaneous vessels that provide skin vascularity.[14] Added insults are the effects of radiation on skin healing[15] and dermal vascularity.[16,17] However, the high incidence of soft-tissue complications did not detract from the eventual functional results obtained in this study. All patients had healed wounds at 1-year follow-up.

Neurovascular involvement was not a contraindication to limb salvage. Although patients requiring vascular reconstruction frequently underwent a secondary procedure for wound complications, the end result was a functional limb in each case. It should also be noted that resection of the femoral or sciatic nerve, sometimes necessary for wide resection, was compatible with reasonable ambulatory function.

The results of this review suggest that almost all soft-tissue sarcomas can be managed by limb-salvage techniques with reasonable functional outcome. In our current consecutive series of 86 patients with the disease, the only amputation performed was for a tumour involving the entire brachial plexes. This aggressive approach to limb salvage has also been reported by Karakousis and associates,[4] with similar reasonable functional results.

It should be emphasized that, before referral, 11 of the 19 patients in this series had undergone one or more inadequate surgical procedures which markedly increased the difficulty of definitive surgery. We suggest that before operating on a subfascial mass, the surgeon should:

- Carry out local and systemic staging studies and discuss combined management of the case with a radiation oncologist skilled in sarcoma management before performing a biopsy.
- Determine a strategy to ensure adequate wide resection.
- Consider appropriate techniques for soft-tissue or skeletal reconstruction.
- Ensure that pathology facilities suitable for both the interpretation of biopsy and assessment of resection margins are available.

If these criteria cannot be met, we recommend that the patient be referred to a multidisciplinary management team before the first surgical procedure is done.

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BOOK REVIEWS

continued from page 64

high in many centres. The success rate depends more on the operator than the technique, and he sets out to improve the techniques and results.

The 20 chapters cover all aspects of hernia repair. Anatomy of the abdominal wall and epidemiology and etiology of hernias are covered well. There is a good section on outpatient management and on general principles of hernia repair. The coverage of suture and mesh materials is good. There is a short section on anesthesia. Although the author favours the Shouldice technique, he and his patients prefer general anesthesia, and this would likely reflect the Canadian experience. However, techniques of local anesthesia are well described. The chapters on groin and umbilical hernias in children and on the differential diagnosis of groin lumps are useful and practical.

The section on inguinal hernias in adults covers the topic well and again emphasizes the Shouldice repair. The McVay repair is described more briefly and the use of Marlex mesh is also summarized. Older studies of hernia repair are analysed to show that follow-up was usually poor and yet complete information is essential for determining true recurrence rates. Results in many large centres are often poor, especially when operation is carried out by inexperienced surgeons. There is a short but useful section on the truss. Repair of femoral, umbilical, epigastric and incisional hernias is well described. A number of rare hernias are also considered and there are short chapters on Spigelian hernia and parastomal hernia. In a chapter on extraperitoneal or preperitoneal repair with mesh, the author recommends that only experienced surgeons use this technique in cases of very large or recurrent hernias. The list of 679 references is exhaustive but might be more helpful if a few key references were highlighted.

This text does not detail the work on hernias by Nyhus. Although the illustrations are useful teaching aids, the book contains too much detail for most medical students. Residents in general surgery would benefit from reading this book early in their training and keeping it for later reference. Although the emphasis is on hernia repair, there is much useful information on groin anatomy, wound healing and choice of sutures. It could also serve as a useful review and refresher course for the general surgeon who repairs hernias as part of a varied pratice. The emphasis on the Shouldice repair, on outpatient surgery and local anesthesia is useful for surgeons trained on a steady diet of Bassini and McVay repairs. The importance of long-term follow-up should be noted by all who repair hernias.

One may question a few details, such as the need for extensive shaving before hernia repair, the use of adherent plastic during operation, or the avoidance of sutures for wound closure, but overall this is a brief, clear and logical review of hernias.

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TOTAL HIP ARTHROPLASTY. Robert E. Booth, Jr., Richard A. Balderston, Richard H. Rothman. 310 pp. Illust. W.B. Saunders Company, Philadelphia, 1988. $108.00. ISBN 0-03-013328-9.

"Total Hip Arthroplasty" is a delight to read. It is concise and informative.

continued on page 79

Surgical Treatment of Fungal Mycetoma

R. Visvanathan, BM, BCh, FRCS(Ire), FRCS, FRCS(Edin), FWACS, FICS

Chemotherapy for chronic fungal infections is often ineffective, and the associated delay in surgical treatment may result in radical procedures being performed to effect a cure. The author describes four patients with chronic fungal lesions, three involving a foot and one the abdominal wall, all of which failed to respond to antifungal chemotherapy. The lesions were excised, using procedures aimed at preserving function. Infection recurred in two patients during a 9-month follow-up. The author concludes that surgical therapy should be instituted early in the disease to forestall spread to deeper structures and preserve functional integrity of the affected parts.

La chimiothérapie des infections fongiques chroniques s'avère souvent inefficace, et il en résulte un retard de chirurgie pouvant conduire à effectuer des interventions radicales dans le but d'obtenir la guérison. L'auteur décrit quatre patients souffrant d'infections fongiques chroniques, du pied dans trois cas et de la paroi abdominale dans un, chez qui la chimiothérapie antifongique avait échoué. Les lésions furent excisées par une technique visant la préservation fonctionnelle. Au cours d'une période de surveillance de 9 mois, il y eut récidive infectieuse chez deux patients. L'auteur conclut à la nécessité d'opérer tôt dans l'évolution de la maladie si l'on veut empêcher sa dissémination à des structures plus profondes et conserver l'intégrité fonctionnelle des organes touchés.

Chronic fungal infections of the skin and subcutaneous tissue respond poorly to antifungal chemotherapy. In most instances, the lesions progress during such treatment and operative intervention is delayed with the result that radical surgical measures are often necessary to achieve a cure. This is a report on four patients with fungal mycetoma (eumycetoma) in whom surgical therapy aimed at conserving function was undertaken when chemotherapy was found to be ineffective.

Case Reports

Case 1

A 27-year-old farm labourer was admitted to hospital with an 8-year history of progressive, relatively painless ulceration over his abdominal wall. There were fleshy, confluent, ulcerating lesions with multiple sinuses and plaque-like thickening of the subcutaneous tissue extending over the affected area (Fig. 1). Loss of serosanguineous fluid from the ulcerated surface reflected on his hemoglobin (78 g/L) and serum albumin (29 g/L) levels. Multiple tissue biopsies revealed mycelial elements suggestive of *Madurella mycetomi* in a granulomatous inflammatory process with leukocytic cellular aggregations and giant cells. There was no indication of malignancy. He had no bowel symptoms and barium x-ray studies of both the small and large bowel were normal. The following treatment

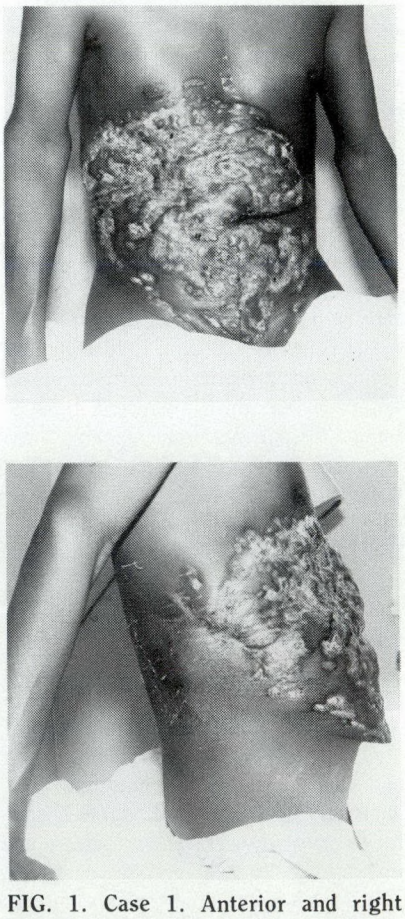

FIG. 1. Case 1. Anterior and right lateral view of abdominal lesion. Previous biopsy scars are visible on flank.

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Accepted for publication July 5, 1988

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was begun: a 6-week course of procaine penicillin G 600 000 units and streptomycin sulfate 1 g intramuscularly daily; a 6-month course of Bactrim, two tablets orally twice a day (one tablet contains 80 mg trimethroprim and 400 mg sulfamethoxazole); dapsone 100 mg/d, which was reduced to 50 mg/d after 2 months, and griseofulvin 1 g/d which also was reduced after 2 months to 750 mg/d.

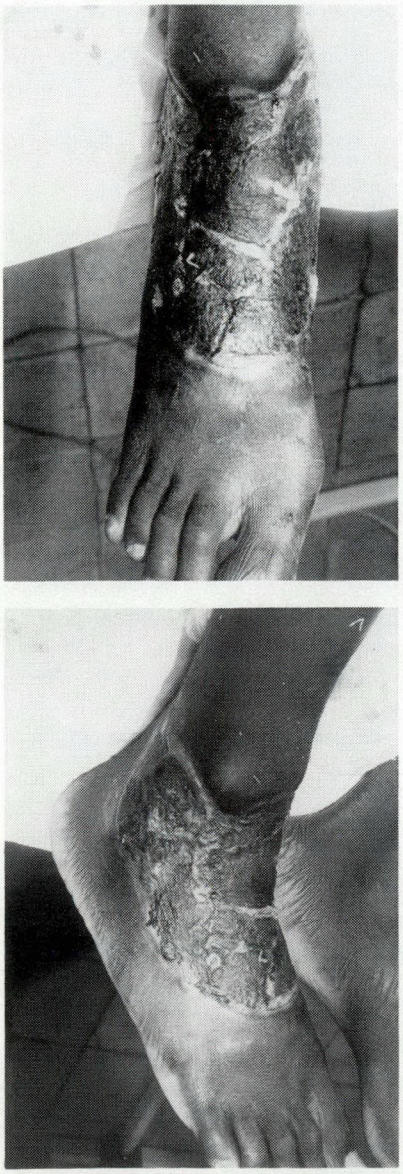

FIG. 2. Case 2. Anterior and lateral views of right foot showing nodular recurrence 5 weeks after excisional surgery and skin grafting.

The anemia was corrected and his nutritional state improved during 3 months in hospital, but there was no visible response to the chemotherapy regimen at the end of 6 months.

Under general anesthesia the ulcerated surface and subcutaneous tissue were removed en bloc from the anterior rectus sheaths and uninvolved external oblique aponeuroses. The denuded area was covered with meshed autologous skin grafts harvested from both thighs. He was discharged home 4 weeks after operation with satisfactory healing of the grafted areas. Within 9 weeks of his discharge three isolated recurrences in the form of small nodules appeared on his right flank and hypogastrium. These were widely excised and he has remained free of further infection during a 9-month follow-up.

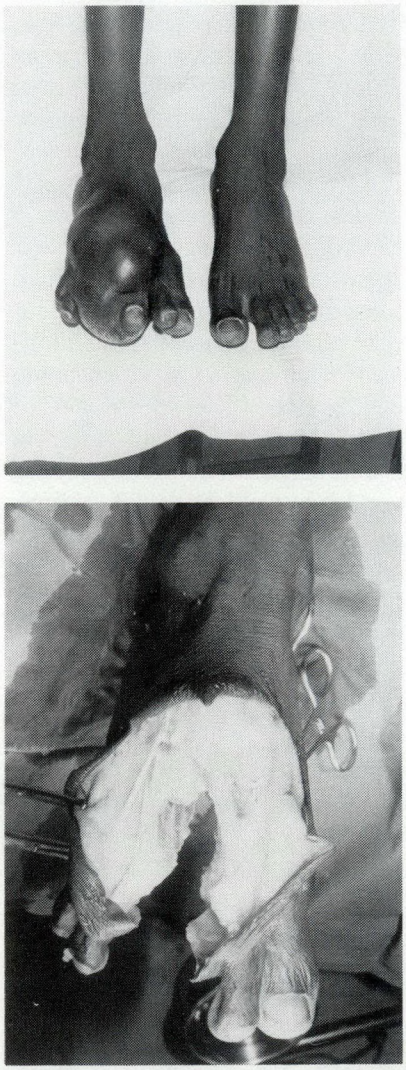

FIG. 3. Case 3. Tumour-like mycotic lesion in right foot (top) and resulting defect following its removal (bottom).

Case 2

A 34-year-old man presented with a 4-year history of progressive ulceration of the skin over the front of his right foot and ankle. The area involved was approximately 90 cm^2 with swelling, induration, ulceration and discharging sinuses affecting the skin and subcutaneous tissue. Tissue biopsies revealed hyphae consistent with *M. mycetomi.* There was no bony involvement and he had satisfactory extension of his toes. A 4-week course of daily intramuscular injections of procaine penicillin G and streptomycin was instituted and a 4-month course of oral dapsone, Bactrim and griseofulvin in dosages similar to those in case 1. He failed to respond to this regimen, so the lesion was excised using an Esmarch bandage to reduce blood loss. Dissection was carried down to the tendo-osseous plane and the diseased tissue removed en bloc, preserving the extensor tendons. After adequate granulation, the residual area was covered with split-thickness autologous skin grafts. A nodular recurrence seen 5 weeks later was excised with 1 cm skin clearance (Fig. 2). A second recurrence occurring after 3 weeks was similarly excised. No further recurrence was observed during the first 6 months of follow-up.

Case 3

A man in his early twenties was admitted with a 3-year history of

painless swelling of his right forefoot and discharging sinuses in the clefts on either side of his third toe, which was also very swollen (Fig. 3). Because previous broad-spectrum chemotherapy had had no effect, an Esmarch bandage was applied and the mass removed en bloc with the third metatarsal bone and the involved toe (Fig. 3). The reconstructed foot healed well. The surgical specimen was a granulomatous inflammatory mass with leukocytic cell infiltrate and sinus tracts similar to those seen in the two previous patients. However, no fungus was isolated from the specimen. The patient remained recurrence-free 9 months later.

Case 4

A 23-year-old man presented with a 3-year history of an ulcerating swelling on his right foot, similar to, but less extensive than, the lesion in patient 2; it covered an area of 55 cm^2 on its dorsal and lateral aspects. Dark fungal particles were seen in the discharge and *M. mycetomi* was isolated. He was started on an initial 4-week course of intramuscular procaine penicillin G and streptomycin and a 4-month course of dapsone, Bactrim and griseofulvin, orally, in dosages similar to the first two patients. There was again no response to treatment. The lesion was excised and the denuded area grafted. The patient was free of recurrence for 6 months after operation.

Discussion

The causative agent of a chronic fungal lesion may elude detection.[1] Previous chemotherapy or an overgrowth of secondary invaders may suppress the proliferation of fungal elements. The morphologic picture of granulomatous changes with inflammatory and giant cells, along with the characteristic clinical picture, usually suggests a fungal cause.

The poor response of fungal mycetoma (eumycetoma) to chemotherapy has led to the recommendation of surgical measures.[2,3] The timing of surgery, either in conjunction with or after drug therapy, has yet to be clarified, though some guidelines have been drawn up.[4] Broad-spectrum antimicrobial agents in conjunction with antifungal therapy are aimed at reducing the secondary invading organisms, though their effect was not dramatic in the patients studied. The antifungal agents dapsone and griseofulvin have some effect on eumycetoma.[5-7]

Newer agents, clotrimazole and ketoconazole, have been shown to be more effective and their toxic effects are being evaluated.[7-9] Ketoconazole in combination with surgery has been used to treat fungal mycetoma and has given encouraging results.[10] The effectiveness of these agents in reducing postoperative recurrence is, however, undetermined. Until their effectiveness and safety are established, surgery for fungal mycetoma should be carried out as soon as the diagnosis is made.

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Correction

On page 415 of the November 1988 issue, in the paper "Unusual gastric foreign body: a case report" by W.M. Kuzon, Jr., C.A. McFadyen and F.L. Moffat, there are two lines missing from the bottom of the middle column as follows: "and oversewing of the ulcer seemed justified. It could be argued that". The two sentences involved should read, "Therefore, removal of the mass with partial thickness excision and oversewing of the ulcer seemed justified. It could be argued that, since this was a gastric foreign body, a more aggressive attempt to dislodge and remove the components of the mass endoscopically should have been attempted first." We apologize to Dr. Kuzon and his colleagues and to our readers for this error.

Anteromedial (Perineal) Dislocation of the Hip: a Case Report

J.C. Burrell, MD, FRCSC;* J.K. Lipinski, MD, FRCPC, FRCR(Lond)†

Anteromedial (perineal) dislocation of the hip is rare. The authors describe the case of a 13-year-old girl whose femoral head was dislocated into the vagina as a result of a motor vehicle accident. The hip could not be reduced by traction but was pushed through the vagina with moderate ease. When the patient was placed in the lithotomy position, the hip redislocated and further reduction was required. The vagina and soft tissues were repaired and the hip joint was irrigated and closed over a drain. Antibiotics were given for 10 days. The girl recovered completely.

La dislocation antéromédiane de la hanche est rare. Les auteurs décrivent un cas chez une fillette de 13 ans dont la tête du fémur avait perforé le vagin lors d'un accident d'automobile. La hanche ne put être replacée par traction, mais elle fut poussée à travers le vagin avec relativement de facilité. Quand la patiente fut placée en position de lithotomie, la hanche se disloqua de nouveau et la luxation dut encore être réduite. On répara le vagin et les tissus mous, et la hanche fut refermée après la pose d'un drain. Des antibiotiques furent administrés pendant 10 jours. La guérison fut totale.

Anterior dislocation of the hip is uncommon; when it occurs, the femoral head usually lies in the periarticular position. We report a rare case of traumatic anteromedial dislocation of the hip in which the femoral head punctured the vaginal wall.

Case Report

A 13-year-old girl was seen 8 hours after she had been involved in a motor vehicle accident. She had multiple injuries including a right brachial plexus palsy, fractures of the mandible and the right first rib and a closed head injury resulting in a decreased level of consciousness.

The left leg was abducted and externally rotated at the hip. Swelling and bruising were evident above the perineum on the left side and the skin was tense and discoloured (Fig. 1). There was moderate bleeding from the vagina. The examining physician interpreted this finding as indicating a fracture of the pelvis. On retraction of the labia (Fig. 2), however, the femoral articular surface was clearly seen with the ligamentum teres protruding through the introitus. A pelvic x-ray film confirmed the anteromedial position of the femoral head (Fig. 3).

Initial resuscitation was carried out in the emergency department. In the operating room under general anesthesia, the presenting ligamentum teres and the attached fragment of bone were excised. No amount of traction would reduce the hip; however, a moderate push on the femoral head through the tear in the vagina reduced the head quite easily. Stability of the hip was good in all positions except abduction and external rotation. When the patient was placed in the lithotomy position to repair the vagina the hip redislocated. After further reduction, the leg was held in internal rotation which kept the joint reduced.

The soft tissues of the vagina and rectum were repaired and the patient was prepared and draped for an anterior approach to the hip joint. The joint was irrigated thoroughly and then closed over a drain. In addition to cefazolin, which was started in the emergency department, tobramycin and metronidazole were given in appropriate dosage for age and weight. The antibiotic therapy was continued for 10 days. The drain was removed 4 days after operation.

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The immediate postreduction films showed a near-anatomic position of the greater trochanter and an acceptable position of the lesser trochanter fragment. Films obtained 2 weeks after injury showed healing, callus formation and periosteal reaction, and the hip was in a normal location (Fig. 4).

When the girl was last seen, 6 months after her accident, she had a full range of movement of the hip and a normal gait. Radiologically, there were no signs of avascular necrosis.

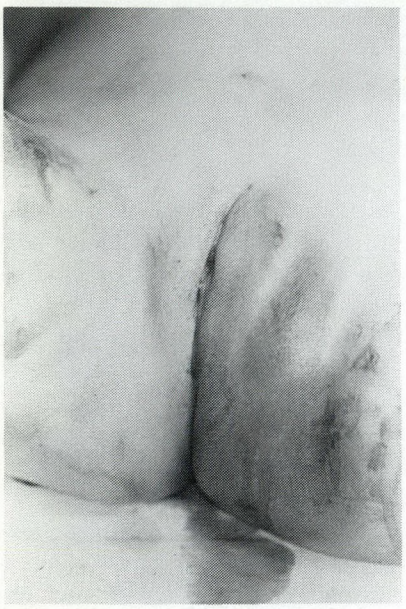

FIG. 1. Bruising and discolouration of left aspect of perineum.

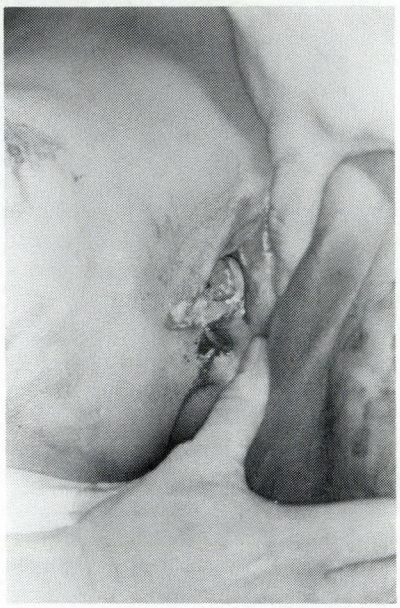

FIG. 2. Femoral head and ligamentum teres are evident at introitus.

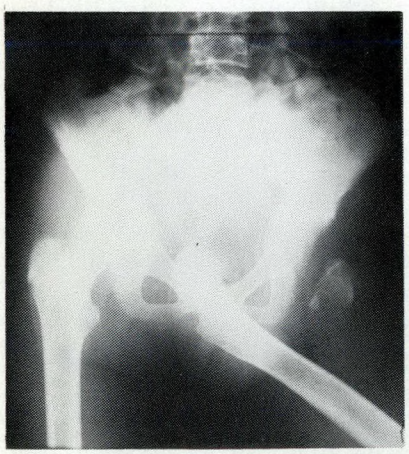

FIG. 3. Anteromedial dislocation of left hip. Lesser and greater trochanters are in near-anatomic position.

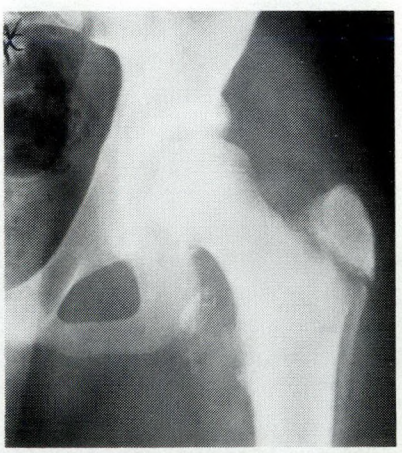

FIG. 4. Normal anatomic position of femoral head with healing of avulsed greater and lesser trochanters.

Discussion

Dislocations of the femoral head are classified as posterior, anterior and central; the posterior type is the most common, accounting for 85% of dislocations.[1] Anterior dislocations are usually pubic or inferior. We could find only one other report of a perineal dislocation.[2] For such a displacement the mechanism would have to be external rotation and flexion, associated with a medial blow to the femur. The avulsions of the lesser and greater trochanters and disruptions of the soft tissues are an obvious association.

In our case, the joint was open and because of the vaginal and rectal disruptions, contamination was likely. Furthermore, separate drainage was considered indicated as a precautionary measure. One complication of these dislocations is avascular necrosis, which occurs much less frequently (less than 10%) than in posterior dislocations.[3] The avascular necrosis may not be apparent for up to 24 months, so a long follow-up is necessary for these patients.

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continued from page 73

The book reflects the bias of the authors who are followers of the Charnley school of hip arthroplasty. For example, they still recommend the transtrochanteric approach for this procedure even though it is almost obsolete in North America. The series on which they base their conclusions is small, comprising only about 600 cases, but the follow-up is long and thorough.

The authors have no experience with bipolar prostheses and freely admit it. The section on hip revision is somewhat dated and mentions little of the serious problems currently being experienced in the revision of noncemented implants and the bone loss encountered in arthroplasties being revised for the third or fourth time. Similarly, the section on noncemented hips reflects little of the recent advances in this field such as modular hip stems; comment is made on obsolete implants such as the original Lord prosthesis which Lord himself abandoned 3 to 4 years ago. This section also contains a few errors. The screw cup shown on page 269 is an Anderson cup on the x-ray film, but the illustration is of a Richards cup. Also, a number of chapters were obviously written some time ago. A 2-day admission before hip surgery is recommended. In Canada, a 1-day admission is more usual and the advent of diagnostic related groupings (DRGs) has made same-day admission common in the United States.

Apart from these criticisms, I found this one of the best surgical texts I have seen. It is well written, lavishly illustrated and clearly thought out. The authors are to be congratulated. The section on radiologic patterns of osteoarthritis, which contains a thorough survey of the literature and the complications and results achieved in hip replacements for rare conditions such as Gaucher's disease and osteopetrosis, is of particular value.

The chapter on the patient/surgeon interview should be mandatory reading for all undergraduates and surgical residents. Indeed, this chapter could, with advantage, be reprinted separately and circulated to all surgeons. The subject is a harsh and uncomfortable one for both the surgeon and the patient. The patient must be viewed in a global sense not simply as an arthritic hip. We surgeons are not gods and without the patient's cooperation we can only do so much. As the authors of this book put it "denying hip replacement to an undependable, poorly motivated substance abuser is not an uncharitable act but rather an act of good judgement preventing him from years of potential complications that would leave him more disabled in the future". Those of us who must carry out revision on such patients know well the truth of this statement.

I heartily recommend this book for all surgeons who practise hip replacement.

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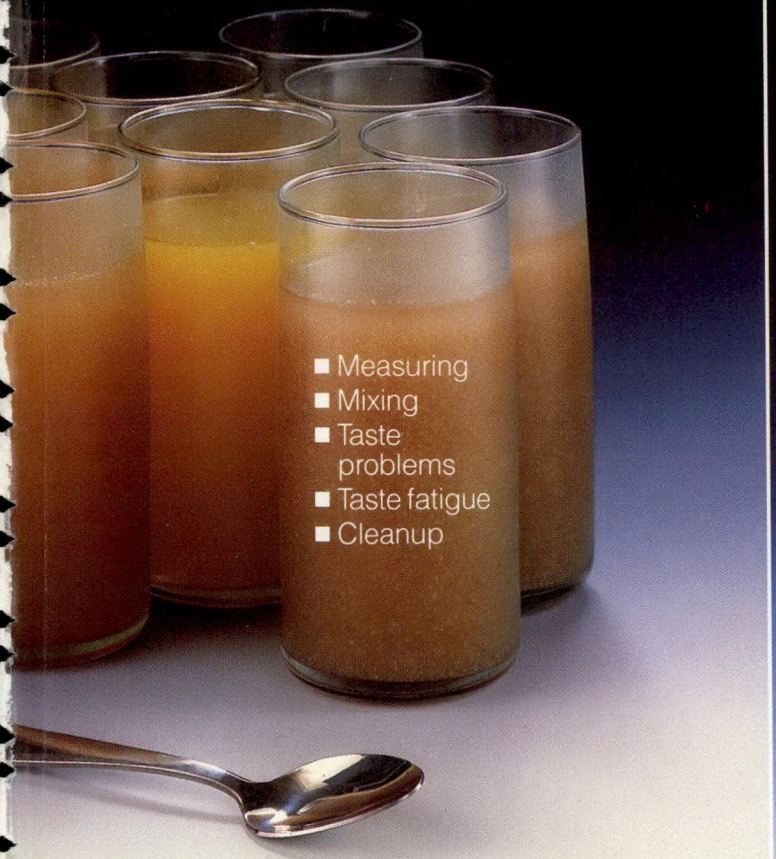

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