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Canadian Medical Association

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

The Urology Papers

On several occasions, the Canadian Academy of Urological Surgeons discussed the scarcity of urological articles published in the *Canadian Journal of Surgery*. The academy recognized that urological investigators had a natural tendency to publish their work in journals that were more likely to be read by their peers in the specialty, but it also believed that its responsibility towards the only national surgical journal was not being discharged. Probably other surgical bodies have addressed themselves to the same issue.

In the present era of specialization there is a risk that specialists will become increasingly less aware of progress made in other disciplines. Although it is impossible to keep abreast of all the new discoveries in all the disciplines, specialists would be deficient if they did not attempt to be apprised of pertinent developments, particularly by their colleagues. Several institutions have journals that tie their members together and allow communication and exchanges between the members, and "Canadian surgery" as an institution is no exception. Obviously some discretion should be applied by individuals submitting articles in selecting appropriate topics that are of wide interest, in order to have a larger number of readers and to give credence to their work.

Because of the concerns expressed above, it was suggested that the initial step could be more readily accomplished if it was undertaken collectively. This notion met with success and most urologists who were approached showed an immediate willingness to contribute. The articles submitted were too numerous to be included in one issue and the coeditors have decided to split them between the current issue and the November issue.

Although the collective spirit of this project generated enthusiasm, the success of the *Canadian Journal of Surgery* will depend on the initiative of individual investigators and their continuing support.

Besides being a vehicle for the publication of scientific articles, the *Canadian Journal of Surgery* is a forum for discussion of subjects of mutual interest to many Canadian surgeons—undergraduate and postgraduate teaching, continuing education and research, for example. It would be a sad reflection on "Canadian surgery" if this journal was not adequately supported and we, the urologists of Canada, show our support through the publication of the articles that appear in this issue and in the November issue.

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Prognostication or Biology: Acquired Abnormalities of Host Defence Mechanism in Surgical Patients

When discussing the role of acquired defects in host defence in the development or prediction of clinical outcome one must question which came first, the septic process or the defect in the immune system. It is increasingly apparent that sepsis can be both the cause and the result of acquired defects in host defence.[1-3] The value of any measurement which predicts patient outcome is twofold. First, particular measures can be taken to improve results in an individual patient. Second, certain patients known to be at risk can be assessed to determine the biologic processes that contribute to their poor outcome. It is only by defining specific defects that an approach to management can be developed which will contribute to improved survival.

In this issue (page 447), McCredie and colleagues have described some immunologic abnormalities in patients with sepsis who subsequently died. Their results demonstrate that the activity of K cells (nonimmune lymphocytes) as measured by an antibody dependent cellular cytotoxicity (ADCC) test is reduced, as is the total number of lymphomononuclear cells, and that adherence of polymorphonuclear leukocytes is decreased in all patients with sepsis, particularly in those who died. It appears therefore that patients with these markers should be watched particularly closely and treated urgently for all correctable causes of possible morbidity. These are interesting results and may help to clarify why some patients do poorly. The balance of McCredie's study indicates a number

of negative findings, not all of which are in agreement with data in the literature.

The design of the study has some worrisome aspects. The study population, consisting of 34 patients all of whom are stated to have had sepsis, is not well defined. A description of the nature and type of their infections and the microbiologic causes would have been interesting. Ten of these 34 patients were not receiving antibiotics although that may have been the case only at the time the investigation was carried out. In the study of patients with sepsis, it is critical that strict criteria (e.g., a positive blood culture, a confirmed abscess or other totally objective assessment) be utilized so that data from one series can be compared with those from another.

The definition of the numbers of B and T cells is occasionally confusing. With lymphocytopenia the numbers of B and T cells circulating are reduced. The ADCC test is a complicated test to do and to interpret. It depends upon the recognition of an Fc fragment by an Fc receptor on the specific K cell. Cells that contain these Fc receptors include neutrophils, monocytes, B and T lymphocytes, basophils and possibly eosinophils. Therefore, unless the cell populations are highly purified and defined, the number of lytic units demonstrated by ADCC testing may not reflect lymphocyte function but rather the function of an altered Fc receptor or any number of leukocytes. This would suggest that a circulating factor was affecting this receptor, a finding which would be consistent with immunosuppressive factors reported by others.[3-5]

The data on neutrophil adherence are at variance with those of MacGregor's group[6] and of our own.[7] There does not seem to be an explanation for this and it may depend entirely upon the definition of the patient population. The neutrophil bactericidal studies against *Pseudomonas aeruginosa* may be statistically different but it is hard to be convinced that they differ biologically. The percentages of colony forming units at 120 minutes were 97.7% versus 99.3%. This difference of approximately 1.6% or 32 000 colony forming units is not large when the original population was 2 million bacteria. Most laboratories performing bactericidal assays require a difference in killing of at least half a log to ascribe any statistical significance to it.[8] In the chemotactic studies a relatively nondiscriminating end point (i.e., the number of cells on the far side of the filter) was used, which may account for the differing results obtained by McCredie and associates from those of other laboratories.[9-11]

The ADCC test appears to be the most discriminating. The mechanism for reduction is not clear since drugs may also affect Fc receptor function. The question arises: Were patients in McCredie's study treated differently (i.e., 10 patients did not receive antibiotics, 7 patients received steroids and 9 patients had total parenteral nutrition)? The use of the term predictive in this setting without graphic presentation of the actual data is difficult as the sensitivity of the test cannot be evaluated. To be effectively predictive, a test must be sensitive as well as discriminating. Regardless of their prognostic value, the ADCC abnormalities provide data that are useful in defining acquired host defects in surgical patients. The results of the test suggest that there is a factor either circulating or upon the cell membrane which affects the Fc receptor.

It is unfortunate that skin testing with a variety of recall antigens was not performed. This approach to the identification of the patient with altered host defences and as a predictor of outcome is becoming well established.[1,3,12,13] The specific value of skin testing is twofold. First, it is prognostic, it identifies the patient at risk of sepsis and death. Second, and perhaps more important, when the population at risk has been identified, the biology of the increased frequency of sepsis and mortality in this group can be intensively studied to define the acquired defects and to develop therapeutic approaches. The causative factors contributing to anergy include sepsis, hemorrhage, trauma, surgery, malnutrition, cancer and a variety of other factors.[2,4] The relating of clinical events with biologic processes in anergic patients has facilitated the development of therapeutic strategy. Malnutrition clearly plays a role but is not the only factor. Drainage of sepsis, biliary tract surgery, resection of colonic cancer, restoration of blood volume with control of hemorrhage are all associated with rapid restoration of skin test responses and improvement of neutrophil chemotaxis.[2] Levamisole, effective in vitro against circulating inhibitors of neutrophil chemotaxis,[14] can in vivo reduce morbidity from sepsis but could not be shown statistically to have an effect upon mortality, anergy or neutrophil chemotaxis.[2]

It is only by defining immunologic processes, as McCredie and his group have done, that ultimately the biology of altered host resistance to infection can be adequately described and treatment delineated. There are a number of areas to which much research must be directed. These include: circulating factors; the speed with which these defects can appear following sepsis or trauma, or both; whether or not plasmapheresis or the administration of anti-inhibitors may play a role; pharmacologic manipulation with drugs such as levamisole, aspirin and other presently unidentified drugs; and a preoperative method to assess accurately the risk and to pinpoint its correction.

Prognostication is important for the individual patient. However, it is only by description and definition of the altered biology of patients with acquired defects in host resistance to infection that therapeutic strategies can be developed to improve the prognosis.

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Early Surgical Management of Acute Cholecystitis

The object of therapy in acute cholecystitis is definitive treatment with minimal mortality and morbidity. Over the years, considerable literature has accumulated concerning both merits and disadvantages of early versus delayed cholecystectomy for acute cholecystitis.

According to Hinchey, Elias and Hampson,[1] a survey of American surgeons showed that 70% favoured early operations for acute cholecystitis.

In this issue of the Journal (page 464) Archibald, Colapinto and Frost confirm that early cholecystectomy in acute cholecystitis can be done safely with low morbidity and mortality. Unfortunately, because it is not a prospective randomized study, this paper does not analyse many aspects of the preoperative, intraoperative and postoperative complications (e.g., jaundice, liver profiles, cultures of bile and gallbladder wall, frequency of explorations of the common bile duct that yield no abnormality or of retained stones in the common bile duct). The clear advantage shown by this study is the economic one: the patient's stay in the hospital is shorter with early operative intervention.

The authors are to be congratulated on the low mortality and complication rate they achieved for the entire group, particularly since approximately 40% of the patients belonged to groups 2 or 3, in which the operation was performed 72 hours after admission, regardless of when the symptoms began.

Some workers[2-7] have reported an increased frequency of major intra-abdominal complications (bacteremia, wound infection or dehiscence, or both) when cholecystectomy is delayed or when bile or gallbladder-wall cultures have given positive results. Interestingly, this correlation was not found in Archibald's paper, and the obvious and important message is the insignificant increase of major complications in patients who underwent cholecystectomy up to 7 days after admission.

Cholecystostomy has been advocated for patients deemed to be too ill for cholecystectomy, usually the elderly with decompensated heart disease, poorly controlled diabetes, pulmonary or renal insufficiency, or evidence of cerebrovascular disease in association with acute gangrenous or perforated gallbladder. The authors have reaffirmed that the mortality associated with cholecystostomy is 5 to 10 times higher than that for cholecystectomy. A cholecystectomy can be completed safely on most occasions.

It is important to emphasize the frequency of false-negative results of intravenous cholangiography in the presence of acute cholecystitis. Although 3.6% of Archibald's patients had false-negative results of cholangiography, the diagnosis of acute cholecystitis was confirmed at operation. In one study,[8] 80 of 152 patients with no opacification of the gallbladder on two consecutive oral cholecystograms, and evidence of disease at operation, also underwent intravenous cholangiography. In 14 (approximately 17%) the gallbladder filled and was interpreted as normal, an obviously erroneous diagnosis in view of the subsequent findings of cholelithiasis in 12 patients, chronic cholecystitis in 1 and acute cholecystitis in 1.

Previously we[7] reported a 6% frequency of normal oral cholecystograms in patients with acute cholecystitis, confirmed by pathological examination of the resected gallbladder. This and other studies[8,9] demonstrated that a substantial number of patients with cholelithiasis or acute cholecystitis, or both, show no abnormality on cholecystography. In order to avoid an erroneous diagnosis, the suggested alternative method at present is ultrasonography[10] or technetium scanning[9] of the gallbladder, which has a diagnostic accuracy of 95% to 98%.

Treatment of patients with acute cholecystitis should include administration of fluids intravenously and routine use of broad spectrum antibiotics, urinary monitoring by means of a Foley catheter if necessary, recording of central venous pressure and an intensive effort to evaluate and treat associated diseases. The operation should be considered urgent but seldom an emergency measure. The degree of risk associated with cholecystectomy is small and it is the procedure of choice in the absence of signs or symptoms of common duct stones or cholangitis, both of which require, in addition, common bile duct exploration or decompression.

Should the patient's clinical condition deteriorate, cholecystostomy can be a safe operation if the following precautions are taken: there can be no free perforation of the gallbladder; clear bile must be seen returning through the cystic duct and if not, the common bile duct must be decompressed; the common bile duct must also be decompressed in all patients with jaundice, chills and fever, and those in whom common bile duct stones are demonstrated.[11]

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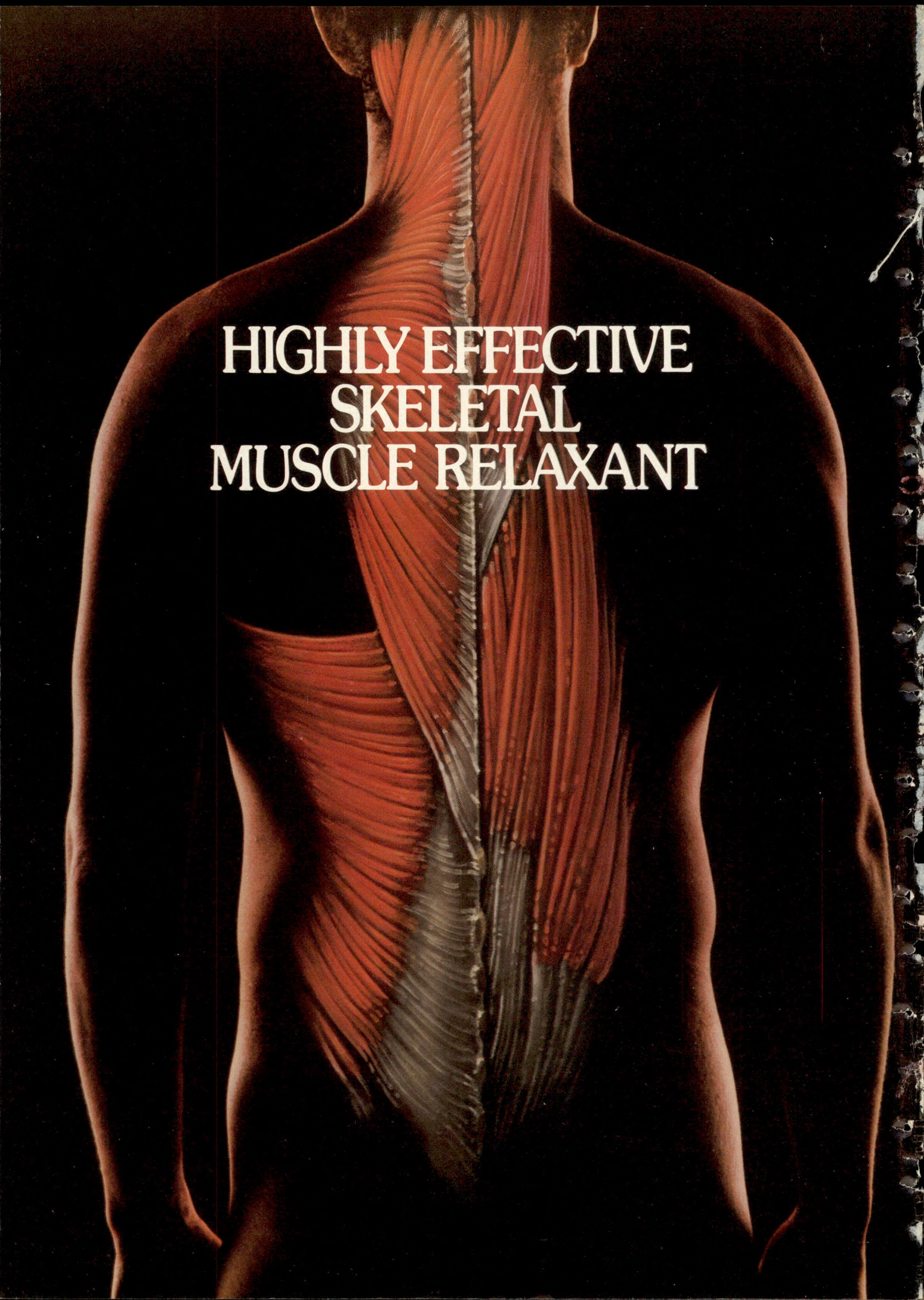
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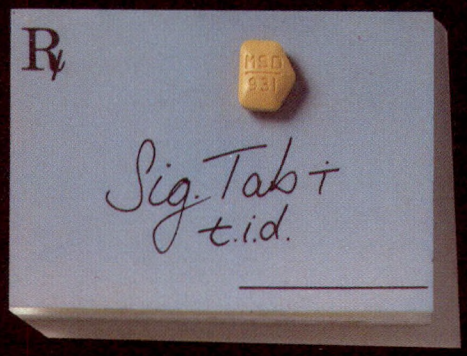

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NOTICES

Symposium on Vascular Surgery

The vascular surgical service of the department of surgery, and extended programs in medical education of the University of California School of Medicine, San Francisco, will present a conference on vascular surgery from Feb. 7-9, 1980. This course has been designed to focus on and elucidate areas of current controversy in the field of vascular surgery. There will be discussions on surgical shunting in portal hypertension, the surgical approach to vascular disorders of the abdominal aorta and its branches, femoropopliteal occlusive disease and the surgical management of cerebrovascular insufficiency. The guest faculty includes Dr. Allan Callow, chief, general and vascular surgical services, Tufts New England Medical Center, Boston; Mr. H.H.G. Eastcott, consultant surgeon, St. Mary's Hospital, London, England; Dr. Jesse E. Thompson, surgeon, private practice, Dallas; and Dr. Robert Zeppa, professor and chairman, department of surgery, University of Miami. Registration will take place on Thursday morning, Feb. 7, 1980, from 700 to 800 hours in the Emerald Ballroom, Golden Gateway Holiday Inn, 1500 Van Ness Ave., San Francisco. The fee is $185 for physicians and $95 for non-UCSF interns, residents and fellows with letter of verification. It is recommended that registration be made in advance. For more information address inquiries to: Extended Programs in Medical Education, University of California, 1308 Third Avenue, San Francisco, CA 94143.

The 5th International Symposium on Atherosclerosis

This conference will be held in Houston, Texas, from Nov. 6-9, 1979. Registration takes place on Monday, Nov. 5, 1979 from 1200 to 2100 hours at the Shamrock Hilton Hotel. The registration fee is $100 for active participants, $25 for students and $10 for accompanying guests. For more information on topics for plenary sessions, workshops and oral presentations, address correspondence to: Dr. A.M. Grotto, The 5th International Symposium on Atherosclerosis, Department of medicine, Baylor College of Medicine, The Methodist Hospital, 6516 Bertner Ave., Mail Station A 601, Houston, TX 77030.

Results of Radical Nephrectomy in 178 Cases of Renal Cell Adenocarcinoma

J.A. OLIVER, MD, FRCS[C], M.P. LAPLANTE, MD, FRCS[C], E.C. REID, MD, FRCS[C] AND R.S. SCHUAL, MD

One hundred and seventy-eight patients with renal cell adenocarcinoma were classified by stage and treated by radical nephrectomy. A transabdominal approach was used in 92% of cases and lymphadenectomy was not performed unless ipsilateral hilar nodes were involved. Survival rates are presented in the form of life-table curves. These curves indicate that survival depends on the stage of the disease at the time of initial treatment; about 80% of patients with stage 1 lesions (tumour confined to the kidney) survived for 10 years compared with only 30% to 35% of stage 2 (involvement of perinephric fat) and stage 3 (involvement of renal vein or regional lymph nodes) patients and less than 10% of stage 4 (metastatic spread) patients. Radical nephrectomy appears to be the best method of treatment for patients with stage 1, 2 or 3 lesions. Simple palliative nephrectomy may be indicated in selected patients with stage 4 lesions.

Cent soixante-dix-huit patients souffrant d'un adénocarcinome des cellules rénales ont été classifiés pas stade clinique et traités par néphrectomie radicale. Un abord transabdominal a été utilisé chez 92% des cas et une lymphadénectomie n'a pas été pratiquée à moins qu'il n'y ait une atteinte ipsilatérale des ganglions hilaires. Les taux de survie sont présentés sous forme de courbes actuarielles. Ces courbes indiquent que la survie dépend du stade de la maladie au moment du traitement initial; environ 80% des patients ayant une lésion de stade 1 (tumeur limitée au rein) ont survécu 10 ans, comparativement à seulement 30% et 35% pour les patients de stade 2 (atteinte du tissu adipeux périnéphrique) et de stade 3 (atteinte de la veine rénale et des ganglions lymphatiques régionaux), et moins de 10% pour les patients de stade 4 (envahissement métastatique). La néphrectomie radicale semble être la meilleure méthode de traitement pour les patients ayant des lésions des stades 1, 2 ou 3. Une néphrectomie palliative simple peut être indiquée chez des patients choisis ayant des lésions de stade 4.

Between Jan. 1, 1965 and Dec. 31, 1977, 178 patients with renal cell adenocarcinoma were treated by radical nephrectomy at two McGill University teaching hospitals. This paper presents the clinical aspects and relates the results of radical surgery to the stage of the disease using life-table survival curves.

Patient Data and Methods

Staging of the disease was by the Robson modification[1] of Flocks and Kadesky's classification as follows: stage 1—tumour confined to the kidney, stage 2—perinephric fat involved but tumour confined to Gerota's fascia, stage 3—involvement by tumour of renal vein or regional lymph nodes

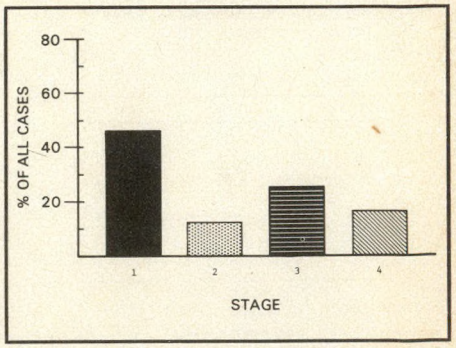

FIG. 1—Distribution of patients by stage.

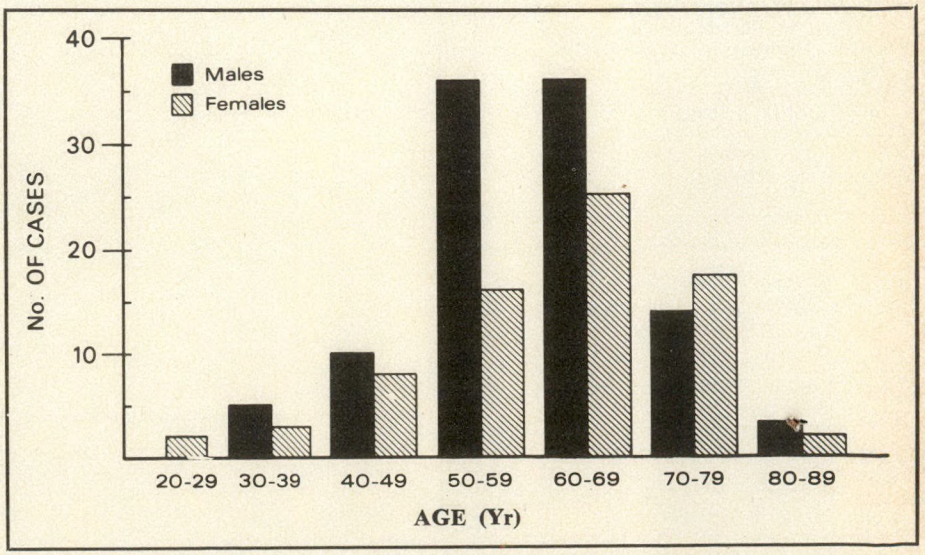

FIG. 2—Age and sex distribution. Male:female ratio was 1.4:1.

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with or without involvement of vena cava and stage 4—metastatic spread distantly or to adjacent visceral structures. Fig. 1 illustrates the percentage distribution by stage of the 178 patients and is in keeping with that reported in other large series.[1-3] There were 82 patients with stage 1 lesions, 22 with stage 2, 45 with stage 3 and 29 with stage 4 disease.

The age and sex distributions are shown in Fig. 2; they correspond to those reported in other series.

Table I lists the major presenting signs and symptoms. Renal cell adenocarcinoma may present in a variety of ways, and while the members of the "clinical triad" (hematuria, pain and palpable mass) were often noted, 24% of patients presented with nonspecific systemic symptoms such as fever, weight loss, anorexia and severe malaise. In 17% of the patients there were no presenting symptoms or signs and the tumour was discovered during other surgical procedures or as an incidental finding on intravenous pyelography done for other reasons.

The abnormal laboratory findings at the time of presentation are shown in Table II. Although these findings may alert the clinician to the possibility of a serious pathologic condition, no relationship has been reported between abnormal laboratory findings and survival rate[3,4] and this was supported in our series.

Surgical Treatment

In radical nephrectomy a "pedicle first" approach is used in which the renal vein is mobilized and the underlying renal artery is ligated primarily, followed by ligature of the vein. The kidney, and sometimes the adrenal gland, is removed leaving overlying peritoneum and Gerota's fascia intact. Hilar nodes are dissected, but if spread to these nodes is not evident, complete

Table I—Presenting Signs and Symptoms

Sign or symptom	Cases, %
Hematuria	53
Pain	24
Mass	19
None, but incidental finding of mass on intravenous pyelography	17
Systemic	24

Table II—Percentage of Patients with Abnormal Laboratory Findings

Laboratory finding	Patients, %
Hemoglobin, >16 g/dl	8
<10 g/dl	12
Lactic dehydrogenase (elevated above upper limit of normal)	18
Alkaline phosphatase (elevated above upper limit of normal)	16
Proteins, increase in α_2 globulin	41
Calcium, >11 g/dl (2.74 μmol/l) or <9 g/dl (2.25 μmol/l)	26
Serum glutamic oxaloacetic transaminase (elevated above upper limit of normal)	1

Table III—Sites of Metastases in the 29 Patients with Stage 4 Lesions at the Time of Nephrectomy

Site	Patients, %
Lung	48
Bone	31
Liver	14
Brain	3
Other	7

Table IV—Cause of Death by Stage

Cause of death	Stage, no. (%*) 1	2	3	4	Total
Operation	1 (1)	0	2 (4)	4 (14)	7 (4)
Cancer	9 (11)	7 (32)	20 (44)	23 (80)	59 (33)
Other	6 (7)	2 (9)	3 (7)	0	11 (6)
Alive	66 (81.8)	13 (59)	20 (44)	2 (6)	101 (57)

*Crude percentages, not based on life-table curves.

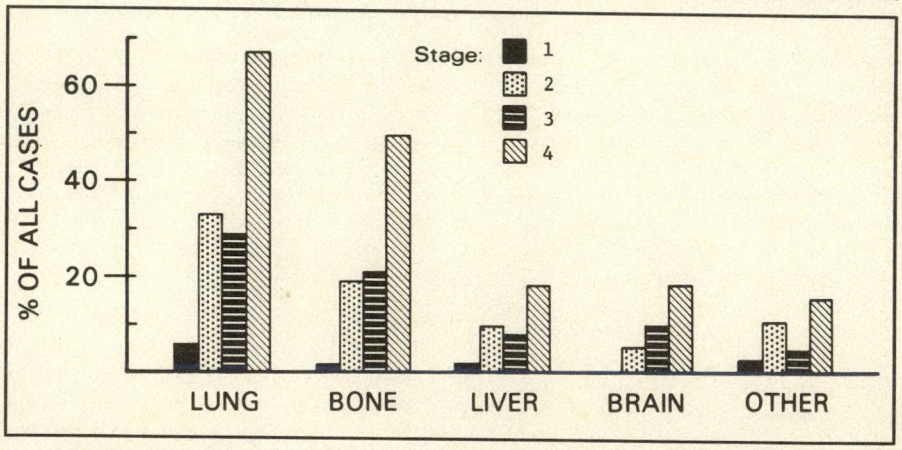

FIG. 3—Sites of late metastases developing in each stage expressed as percentage of cases in each stage.

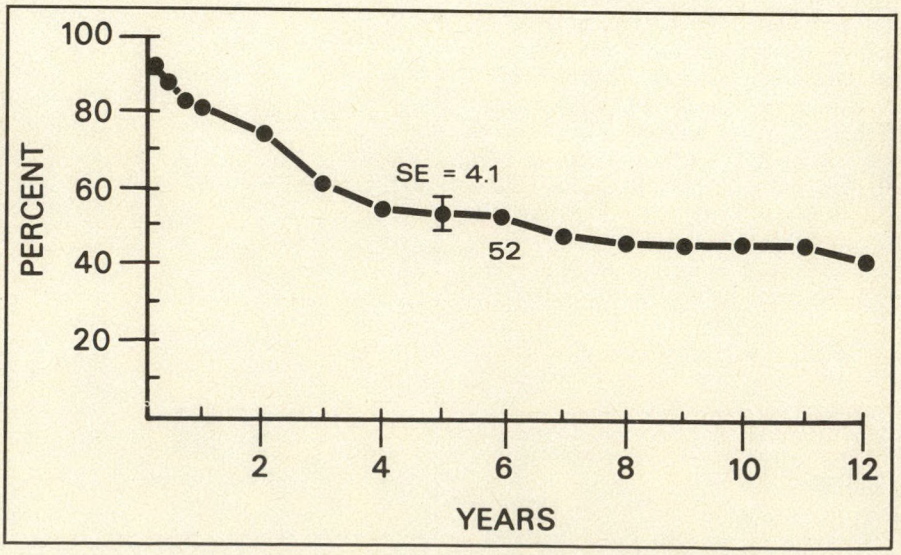

FIG. 4—Life-table survival curve for all stages (SE = standard error).

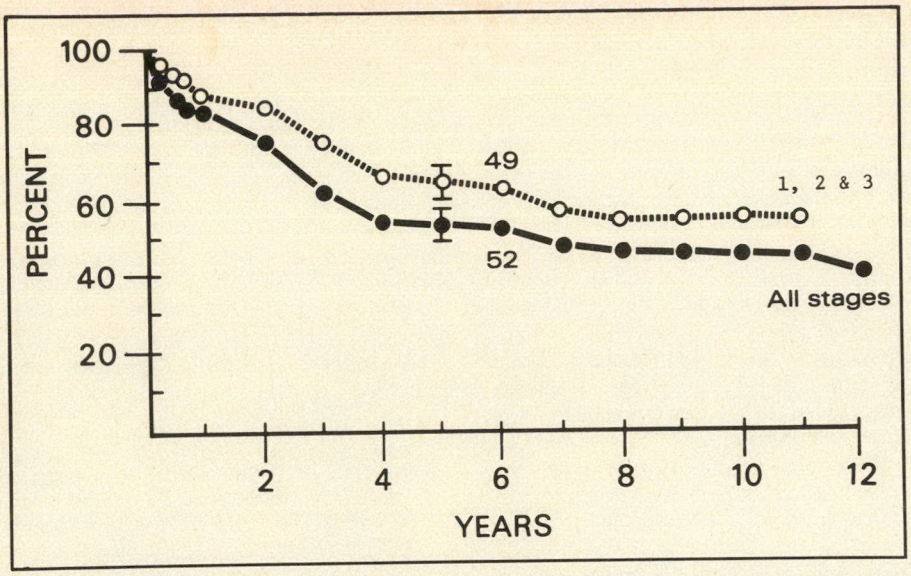

FIG. 5—Comparison of survival curves of stages 1, 2 and 3 patients with that of entire series (49 and 52 = number of patients at risk at 6 years).

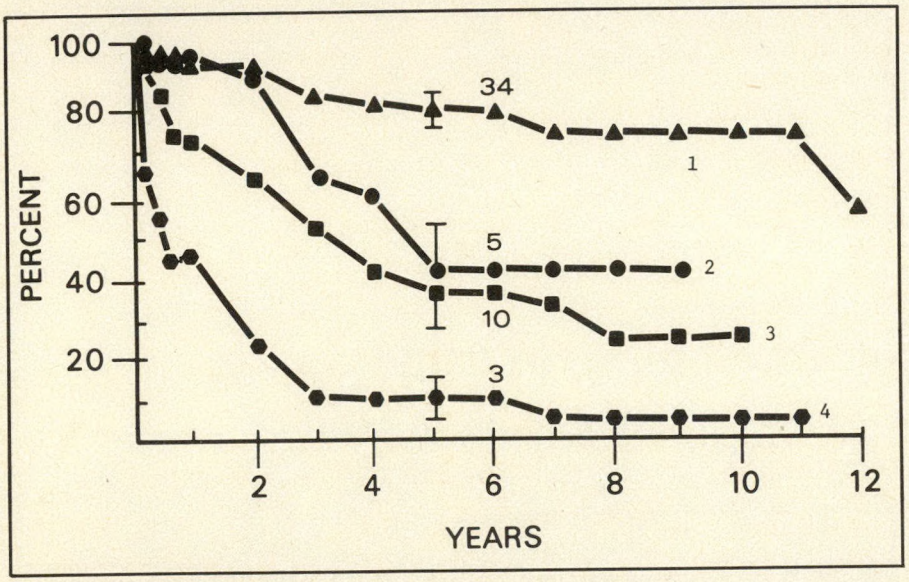

FIG. 6—Life-table survival curves plotted separately for each stage. Numbers at risk at 6 years are shown by figures above curves themselves.

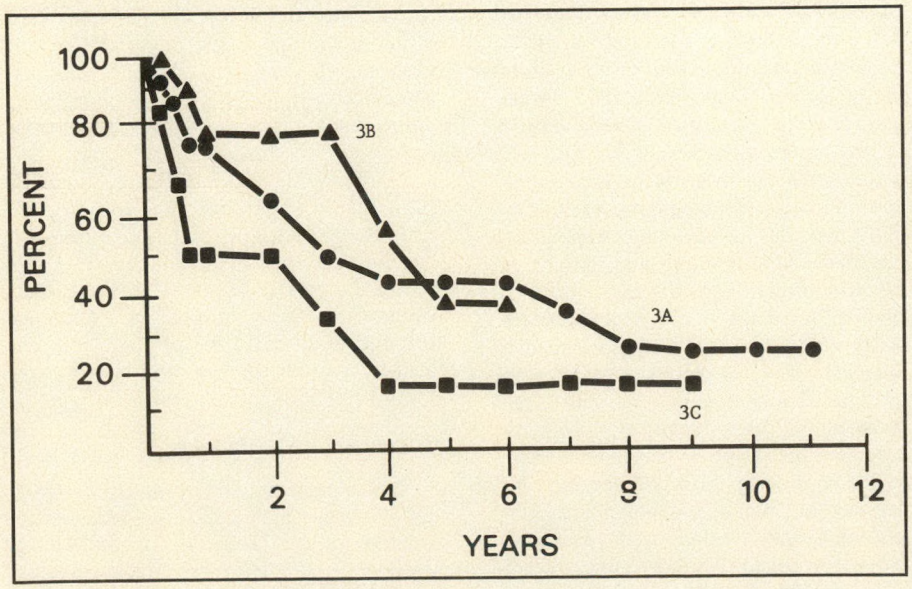

FIG. 7—Comparison of survival curves for stages 3A, 3B and 3C.

para-aortic or paracaval node dissection is not routinely done. In our hospitals, a transabdominal incision is generally used with full kocherization for right-sided tumours and preaortic dissection for left-sided lesions as described by Scott and Selzman.[5] When necessary, the inferior mesenteric vein is divided together with the ligament of Treitz. This approach provides good exposure for most tumours although for large upper pole lesions, the thoracoabdominal technique is used.[6,7] In our series the transabdominal approach was used for 165 patients and the thoracoabdominal for the remaining 13.

Results

The sites of metastases in the 29 stage 4 patients are shown in Table III; late metastases developing in each stage are shown in Fig. 3 and are expressed as a percentage of all cases in each stage. As expected, lesions classified clinically as stage 1 rarely metastasized, and these rare instances of metastasis were attributable to staging errors. Stage 2 and stage 3 lesions showed little difference in their metastatic activity either in site or in frequency.

The causes of death by stage are shown in Table IV. Operative death refers to that which occurred while the patient was still in hospital following nephrectomy, regardless of length of stay and cause of death. The overall operative mortality was 3.9% but, when the stage 4 patients were excluded, it was 2.2%.

Survival Figures

The survival figures were evaluated from the life-table curves. The survival curve for all stages (Fig. 4) shows a flattening at 4 years with a slight fall-off between 6 and 7 and 11 and 12 years. Fig. 5 compares the survival of patients with stages 1, 2 and 3 (potentially "curable") lesions with that of the entire series. Given the poor prognosis of stage 4 patients, the improvement in the mortality when these patients are excluded is expected.

The survival curves for each stage are shown in Fig. 6. The curve for stage 1 patients indicates an extremely good prognosis. The fall-off at 11 years represents death from causes other than cancer. There was no statistically significant difference in the survival of stage 2 and stage 3 patients in this series. The curve for stage 4 patients was predictable.

Stage 3 patients were subdivided for analysis as follows: stage 3A—disease involving the renal vein with or without vena caval extension (30 patients),

stage 3B—disease involving the lymph nodes (8 patients), and stage 3C—disease involving both the renal vein and the lymph nodes (7 patients).

The survival rate of these patients is shown in Fig. 7. There was no significant difference between these curves. It is worth noting, however, that whereas the overall survival of patients in stages 2 and 3 was not significantly different, the curve for stage 3C does suggest a significant difference in prognosis between those having involvement of both the vein and regional lymphatics (3C) and stage 2 patients. Certainly invasion of the renal vein by tumour leads to a significant reduction in estimated survival compared with stage 1 patients; this is the finding of most series though it is contrary to that of Skinner, Vermillion and Colvin.[3]

Discussion

The prognosis in this series of patients conforms fairly closely to that of other comparable series. Survival depends on the stage of the disease at the time of primary management. Patients whose tumours are diagnosed and treated in stage 1 do well and have an estimated 10-year survival rate of approximately 80%. Barely 35% of patients with stage 2 and stage 3 tumours survive 10 years and, for the stage 4 patients, less than 10% survive that long.

The average duration of symptoms for patients with stage 1, stage 2 and stage 3 lesions was almost identical which is discouraging in terms of improving overall survival rates, particularly since, given the great difference in survival between stage 1 patients and those in more advanced stages, improved techniques for early diagnosis are of greatest importance.

As far as operation is concerned, radical nephrectomy results in higher survival rates in stages 1, 2 and 3 than any other method. Radical nephrectomy is not indicated in stage 4 and simple palliative nephrectomy in selected cases is the most that should be done. The surgical approach, either transabdominal or thoracoabdominal, depends on the size and location of the tumour. The transabdominal approach gives excellent results in most cases. Node dissection in the absence of positive hilar nodes does not improve survival rates. Despite the low mortality associated with the procedure, it is not a necessary part of radical nephrectomy.

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Renal Cell Carcinoma in Children

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The authors reviewed the records of eight children with renal cell carcinoma and correlated the clinical presentation, pathological and radiologic findings, stage and treatment of the disease with patient survival. Angiography revealed tumours of sparse neovascularity, associated with varied histologic patterns. Patient survival was dependent on the stage of the disease at the time of treatment; treatment of localized disease was effective but of metastatic disease was generally poor. Tumour staging appeared to be the only reliable indicator of prognosis. Children with renal cell carcinoma differ from adults in that a palpable mass in a child does not necessarily indicate that there is metastatic disease.

Les auteurs ont étudié les dossiers de huit enfants ayant un carcinome des cellules rénales et ont établi une corrélation entre le tableau clinique, les observations pathologiques et radiologiques, le stade et le traitement de la maladie d'une part, et la survie du patient d'autre part. L'angiographie a révélé des tumeurs ayant une néovascularité rare, associées à des morphologies histologiques variées. La survie du patient a été dépendante du stade de la maladie au moment du traitement; le traitement d'une tumeur localisée a été efficace mais celui d'une atteinte métastatique a généralement été pauvre. L'établissement du stade de la tumeur a semblé être le seul indicateur fiable du pronostic. Les enfants ayant un carcinome des cellules rénales diffèrent des adultes en ce que la présence d'une masse palpable chez l'enfant n'est pas nécessairement l'indice d'une maladie métastatique.

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Renal cell carcinoma in children is rare. In the review by Riches, Griffiths and Thackray[1] of 1500 cases of kidney tumour, only 0.5% of the patients were children; others have reported an incidence of 2.3% to 6.6%.[2] We can trace fewer than 100 well-documented cases reported since 1934 in which the follow-up was longer than 5 years.

In reviewing the records at the Hospital for Sick Children in Toronto, we found eight patients in whom renal cell carcinoma had been diagnosed. This report correlates survival of these children with their clinical presentation, tumour stage and treatment, and describes similarities to and differences from renal cell carcinoma in adults.

Patients and Methods

Eight patients (five boys and three girls) with renal cell carcinoma were treated at the Hospital for Sick Children or at the Princess Margaret Hospital, Toronto, between January 1961

and December 1977. Age at presentation ranged from 5 to 15 years (mean 9.75 years). The tumours were left sided in six of the children; no patient had bilateral tumours. All underwent routine investigations for metastases. Intravenous pyelography (IVP) was performed in all patients, arteriography in five, radionuclide renal scanning in three, inferior vena cavography, cystoscopy and retrograde pyelography in two each, and computerized axial tomography in one.

Primary treatment was radical nephrectomy in seven cases and simple nephrectomy in one, with ipsilateral lymph-node dissection in three. Five children received radiation therapy (3500 to 4500 rads) to the abdomen and affected kidney bed postoperatively. Chemotherapy was not used routinely, although one child, thought initially to have a Wilms' tumour, was given actinomycin D, 300 μg/d for 5 days, starting 1 day before operation. In two other patients who had metastatic disease, chemotherapy was started shortly before they died.

All surviving patients are being followed up.

Findings

Clinical

The presenting symptoms and signs, and their relation to survival, are shown in Table I. Two patients (nos. 1 and 5) had sustained trauma to the flank, resulting in retroperitoneal rupture of the tumour. Of the two patients with fever, one (no. 2) had a localized tumour and one (no. 1) had metastatic disease. Two of the three patients who had a palpable mass on presentation have survived for more than 5 years (nos. 2 and 3).

Radiologic (Table II)

Intravenous pyelography demonstrated a mass in seven children and decreased renal function in one; calcification was seen in only one patient. Retrograde pyelography, performed in two cases, confirmed the IVP findings. Radionuclide renal scanning showed filling defects in all three cases in which it was done, including the patient (no. 8) whose IVP demonstrated decreased function. Computerized axial tomography was also performed in this patient and showed enlargement of the affected kidney.

Arteriography demonstrated sparse neovascularity in three patients and none in two. Inferior vena cavography showed compression by the tumour in one of two patients.

Laboratory

Two patients were anemic due to blood loss after trauma (nos. 1 and 5) and in one child (no. 8) with metastases, the erythrocyte sedimentation rate was 69 mm/h. Results of all other hematologic, renal and liver function tests were normal.

Pathological

The staging system used is shown in Table III and its relation to pathological findings and survival in Table IV.

Tumour size did not correlate with survival: two survivors had large tumours (diameter, 10 cm in patient 2 and 8 cm in patient 3) and both had stage I disease on presentation. All survivors had better differentiated tumours with clear cell elements as well as pseudocapsules; however, these characteristics were also seen in nonsurvivors.

Treatment

Three survivors had disease confined to the kidney and one had positive hilar lymph nodes. Each had a radical nephrectomy; two (nos. 4 and 6) underwent lymph-node dissection, and two (nos. 3 and 6) had radiation therapy.

Table III—Tumour Staging* and 5-Year Survival in 30 Children

Stage	Survival at 5 yr, %
I – Intrarenal tumour	79
II– Extrarenal tumour with local extension	
a – direct extension	80
b – vascular extension	30
c – local lymphatic (lymph-node) extension	75
III– Extrarenal tumour with distant metastases	10

*From Castellanos, Aron and Evans.[2]

Table II—Roentgenographic Findings

No. of patients	Investigation	Case no.	Findings
8	Intravenous pyelography	1 – 7	Mass
		8	Decreased renal function
2	Retrograde pyelography	2	Mass
		8	Thin calyces, upper pole
3	Radionuclide renal scanning	4, 6, 8	Filling defect
5	Arteriography	5 – 7	Hypovascular tumour
		4, 8	Avascular tumour
2	Inferior vena cavography	6	Normal
		8	Compressed by tumour
1	Computerized axial tomography	8	Enlarged affected kidney

Table I—Relation between Clinical Presentation and Survival

Patient no.	Age, yr	Sex	Symptoms and signs				Other features	Duration of symptoms	Outcome	Duration of follow-up
			Pain	Mass	Hematuria	Fever				
1	13	M	+	–	–	+	Trauma, weight loss	Acute, 3 mo	Dead	3 mo
2	6	F	+	+	–	+		Pain for 1 yr	Alive	14 yr
3	5	F	–	+	+	–		Acute	Alive	11 yr
4	6	F	–	–	+	–		2 mo	Alive	7 yr
5	9	M	+	+	+	–	Trauma	Acute	Dead	4 yr
6	11	M	+	–	+	–		3 wk	Alive	5 yr
7	13	M	–	–	+	–		Acute	Alive	3 yr
8	15	M	+	–	–	–	Weight loss	2 mo	Dead	2 mo

+ = present, – = absent.

Table IV—Relation of Pathological Findings to Stage, Treatment and Outcome

Patient no.	Tumour pseudocapsule	Degree of differentiation	Pattern and granularity	Stage	Extent of disease	Operation	Radiotherapy	Chemotherapy	Outcome
1	No	Moderately	Papillary, G	IIb	Renal vein	N	Yes	No	Died, 3 mo
2	Yes	Well	Alveolar, C and G	I	No metastases	RN	No	No	NED, 14 yr
3	Yes	Moderately	Papillary, C	I	No metastases	RN	Yes	Yes	NED, 11 yr
4	Yes	Well	Papillary, C	I	No metastases	RN and LND	No	No	NED, 7 yr
5	Yes	Well	Alveolar, C	IIa	Capsular lymphatics	RN and LND	Yes	Yes	Died with liver metastases after 4 yr
6	Yes, partial	Well	Papillary, C	IIc	Hilar nodes	RN and LND	Yes	No	NED, 5 yr
7	No	Moderately	Papillary and tubular, C	III	Distant peri-aortic nodes	RN	Yes	No	Alive with metastases, 3 yr
8	No	Poorly	Pleomorphic	III	Diffuse disease	RN	No	Yes	Died, 2 mo

C = clear cell, G = granular, N = simple nephrectomy, RN = radical nephrectomy, LND = lymph-node dissection and NED = no evidence of disease.

The patient with hilar node involvement (no. 6) had both node dissection and radiation therapy.

Discussion

Clinical Findings

The mean age of the children at the time of presentation in our series (9.75 years) is similar to that in a previous review.[2]

Renal cell carcinoma in children shows no bias for either sex,[2] unlike its 3:1 male predominance in adults.[3] More right-sided tumours were recorded in a 1974 review,[2] but a later report gave contrary findings[4] and the tumour was left sided in six of our eight patients. Bilateral tumours have been reported[5] but, as in adults, it is not known whether these are coexisting primaries or represent metastatic disease.[6]

No correlation has been demonstrated with developmental defects, although some patients have had urogenital anomalies such as imperforate anus with rectourethral fistula,[6] ectopic ureter[7] or horseshoe kidney.[8] Some patients have been reported to have other primary tumours, such as retroperitoneal teratoma, ependymoma[2] and neuroblastoma;[4] von Hippel-Lindau disease has been reported in some adults[3] but not in children.

One third of adult patients present with systemic symptoms such as weight loss and weakness with or without anemia and two thirds have one or more features of the classic triad of hematuria, pain and a mass. Most adults who have a palpable mass on presentation already have metastases.[3] Many children with renal cell carcinoma also have systemic initial symptoms (two of our patients presented with weight loss and two others with fever). The commonest urologic signs are a palpable mass and hematuria.[2] The major difference from adult cases is that a palpable mass is not necessarily associated with metastatic disease[9] (which may reflect the ease with which a mass in a child's abdomen and flanks can be detected by palpation[10]); indeed, two of our three patients with stage I disease had a palpable mass.

Trauma may call attention to the tumour.[2] One survivor had sustained tumour rupture secondary to trauma,[11] but in that report the follow-up was less than 5 years. Neither of our patients in whom trauma was a major feature of their presenting history survived; patient 1 died 3 months after treatment and patient 5 died with liver metastases 4 years after apparent cure.[12]

Duration of symptoms is not necessarily related to survival.[9] Patient 2 had had pain for 1 year, but had no evidence of disease 12 years after primary treatment. Others[2,4] have reported survival of patients who had had symptoms for 1 to 2 years before treatment.

Hypertension has been noted in 6% of cases[2] but was not found in our series. No endocrine effects have been recorded, but liver dysfunction has been described.[13]

Six per cent of pediatric patients[2] and a similar percentage of adults[3] present with symptoms of metastases.[2] None of our patients gave evidence of metastases initially.

Radiologic Findings

The accuracy of roentgenography in the diagnosis of renal cell carcinoma in adults is almost 95%.[3] Renal masses in children can be demonstrated by IVP and retrograde pyelography in 97% of cases,[2] but until now, diagnosis has been made at the time of operation.

In adults, arteriography is an excellent diagnostic tool. The typical appearance is of multiple tumour vessels, arteriovenous shunts and microaneurysms.[14] Hypovascular or avascular masses, which have been reported in 5% to 22%[14,15] of adult cases, reflect poor blood supply or necrosis. Until recently, tumours with poor blood supply were thought to be papillary in type,[14] but other histologic patterns have been described with this angiographic appearance;[16,17] moreover, not all papillary tumours are hypovascular.[16]

Arteriography has been little used in the diagnosis of renal cell carcinoma in children. Love and associates[18] used arteriography to diagnose renal cell carcinomas in three of five children with renal masses, and Shanberg, Srouji and Leberman[19] reported one case in which it was used. Others[2,4,20] have mentioned using arteriographic findings. Fisher and associates[8] described two patients who had renal angiography. Five of our patients had arteriography. Table V[8,18,19,21] describes the angiographic and pathological appearances in all 12 traceable patients. In only 2 patients did the tumours have the characteristic appearance seen in adults; the other 10 patients had hypovascular or avascular tumours of varied histology.

Inferior vena cavography has not previously been reported in the diagnosis of this tumour. No inferior vena caval invasion was demonstrated in our two patients who had this study, but extrinsic compression by tumour was apparent in one.

Pathological Findings

Dehner, Leestma and Price[9] showed a correlation between histology and survival. Of their few patients whose tumours were of mixed trabecular and tubular pattern with clear cells, 80%

survived. In their series the prognosis was better with clear cell tumours than with granular tumours, and a tumour pseudocapsule was a favourable sign.

In our series more survivors had clear cell tumours (Table IV) than had granular ones, but this histologic pattern did not guarantee survival. Furthermore, although all four survivors had tumour pseudocapsules, so did one nonsurvivor. Histologic grading correlated to some degree with survival: seven of the eight tumours were well or moderately well differentiated and four of the seven patients survived more than 5 years; the only patient with a poorly differentiated tumour died 2 months after admission. Thus we agree that pathological criteria are not consistent indicators of prognosis.[2] This finding is similar to that in renal cell carcinoma in adults:[22] cellular granularity and patterns of organization are not generally considered useful indicators of prognosis.[3]

Staging, Treatment and Survival

Tumour staging based on surgical and pathological criteria is at present the best method for predicting and comparing survival rates.[3] Castellanos, Aron and Evans[2] were the first to use staging to analyse reported cases. A summary of their findings in 30 patients followed up for more than 5 years (Table III) shows a good 5-year survival rate for patients with tumours localized to the kidney, with locally invasive tumours or with spread of the disease to the regional nodes only, and a poor survival rate for those with vascular permeation and distant metastases. In adults, renal vein extension is associated with a better prognosis than nodal metastases[23] and large tumours commonly are associated with a higher stage;[3] the latter does not hold for children.[10] In both age groups, stage III disease has a poor prognosis.

Additional reports of children followed up for more than 5 years are summarized in Table VI.[4,8,21,23,24] Good survival is noted for stages I and IIc, and poor survival for stages IIb and III, as in adult series.[25]

Our results in relation to stage and treatment (Table IV) show that survival usually was related to stage. The stage IIc survivor (patient 6) underwent lymph-node dissection and received radiation therapy in addition to radical nephrectomy.

Cassady and associates[4] in a series of eight cases, achieved better results than those previously reported.[2] Their survivors (the exact duration of follow-up was not specified) included some who had had vascular invasion. They treated every patient by nephrectomy, radiation therapy and long-term chemotherapy; their impressive results may be related to the intensive and prolonged use of chemotherapy.

Late recurrence after apparent cure, which is well described for adults, has been reported in some cases of renal cell carcinoma in children.[26] Also, cases of prolonged survival with disease have been reported.[16] The erratic behaviour of this tumour is therefore the same in adults and children.

Conclusions

The clinical presentation of renal cell carcinoma in children may differ from that in adults: fewer children have advanced disease when they have a palpable mass, and symptoms may be present for some time without the development of metastases. Traumatic rupture of the tumour before treatment carries a poor prognosis.

Arteriographic findings have differed in the two age groups in that neovascularity is usually sparse in children. This angiographic picture is seen with different histologic patterns.

The significance of pathological findings in regard to prognosis in both age groups is confusing. However, longer survival has been recorded with better differentiated, clear cell tumours.

Tumour staging is most reliable in predicting prognosis. Patients with intrarenal disease, minimal local extension and regional nodal disease at the time of presentation had good survival rates. Vascular extension in children, in contrast to its occurrence in adults, was an ominous finding.

Aggressive surgery has yielded good results in patients with local and regional nodal disease. The reports on chemotherapy and radiation therapy have not been detailed enough to allow comparison of their efficacy in treating distant disease.

Although it may differ in clinical presentation, renal cell carcinoma in adults and in children is similar in pathological appearance and in behaviour. In both age groups metastatic disease responds unpredictably to various treatment modalities.

Table V—Angiographic and Pathological Appearances Reported in 12 Children with Renal Cell Carcinoma

Angiographic appearance	No. of patients	Pathological findings (when stated)
Neovascular with arteriovenous shunts	2[18,19]	Papillary, glandular[19]
Hypovascular	8[8,18,21]	Papillary with necrosis[8]
		Necrosis[18]
		Alveolar (patient 5)
		Papillary (patients 6 and 7)
Avascular	2	Pleomorphic (patient 8)
		Papillary (patient 4)

Table VI—Staging, Treatment and Survival in 12 Reported Cases of Renal Cell Carcinoma in Children in Addition to Those Reviewed by Castellanos, Aron and Evans[2]

Stage	Authors	Treatment	Outcome
I	Lynne and Machiz[21]	N	NED, 8 yr
I	Nygaard and Simon[23]	RN	NED, 25 yr
IIb	Schellhammer and Smith[24]	RN	Died, 1 yr
IIc	Fisher and associates[8]	N	Alive with disease, 5 yr
IIc	Cassady and associates,[4] 2 cases	RN and LND	Case 1: NED, 10.25 yr
		CT and RT	Case 2: NED, 13.5 yr
III	Lynne and Machiz,[21] 2 cases	Biopsy only	Died in less than 1 yr
		Biopsy and RT	Died, 9 yr
III	Cassady and associates[4]	RN, CT and RT	Died in less than 1 yr
III	Fisher and associates,[8] 2 cases	Biopsy only	Both died in less than 1 yr
III	Schellhammer and Smith[24]	N	Died in less than 1 yr

CT = chemotherapy, RT = radiation therapy.

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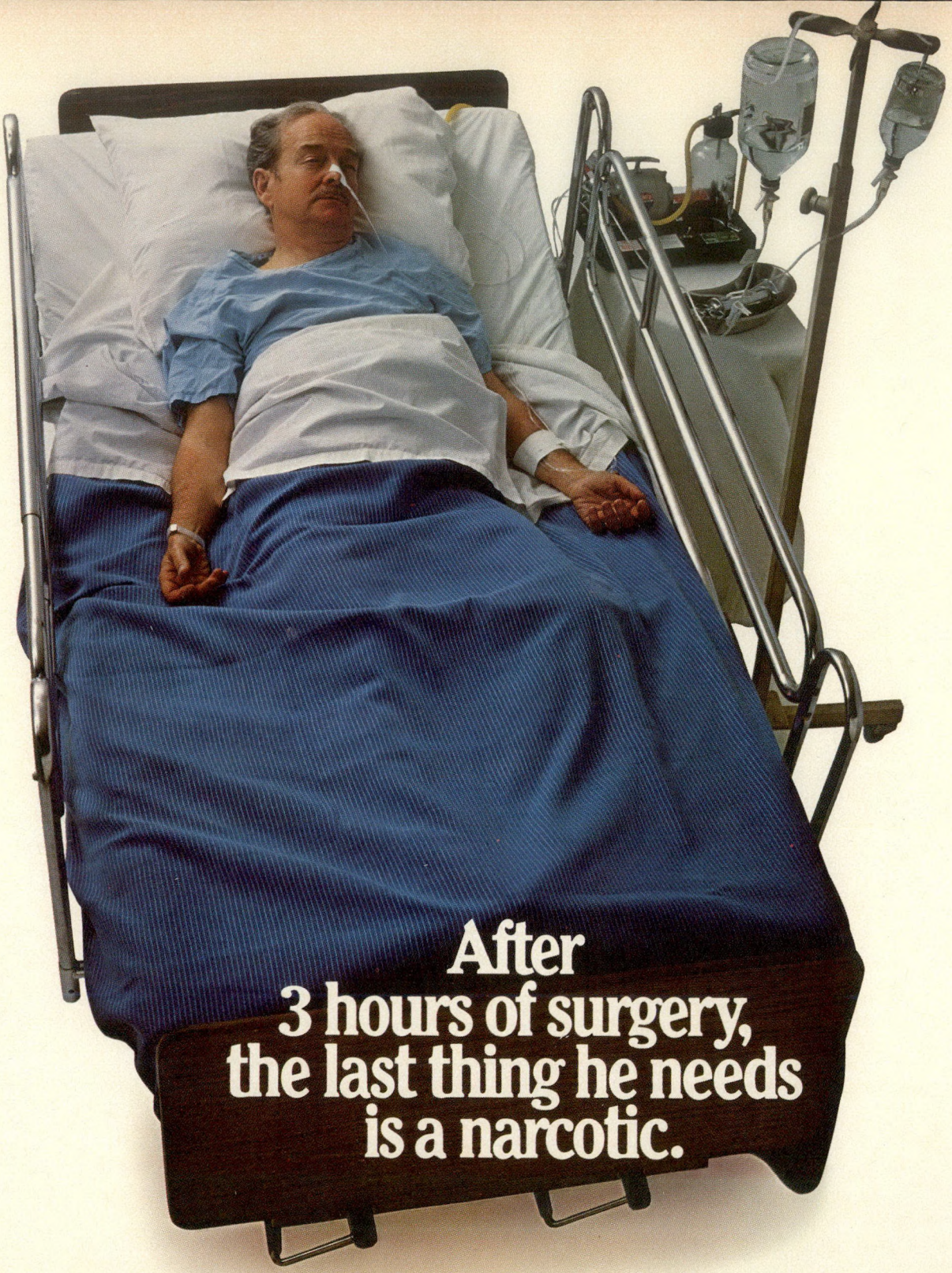

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Precautions
The lowest dosage that gives effective anaesthesia should be used, to avoid high plasma levels and serious systemic side effects. Injection of repeated doses of Marcaine may cause a significant increase in blood levels due to accumulation of the drug or its metabolites.

Tolerance varies with the status of the patient. Debilitated, elderly and acutely ill patients may require reduced doses commensurate with age and physical condition.

Safe use in pregnant women, other than in labour, has not been established.

Foetal bradycardia may follow paracervical block with local anaesthetics of the amide type and may be associated with foetal acidosis. Foetal heart rate should always be monitored during paracervical anaesthesia. Added risk appears to be present in prematurity, toxaemia of pregnancy and foetal distress. The physician should weigh the possible advantages against dangers when considering paracervical block in these conditions. When the recommended dose is exceeded, the incidence of foetal bradycardia increases. The incidence of foetal bradycardia, observed in clinical trials with Marcaine in which paracervical block was used, varied between zero and 35%.

Obstetricians are reminded that severe persistent hypertension may occur if oxytocic drugs are administered to patients who have already received a vasopressor.

Solutions containing a vasopressor agent, should be used with caution, if at all, in patients who are receiving monoamine oxidase inhibitors or tricyclic antidepressants because severe prolonged hypertension may result. Dose related cardiac arrhythmias may occur if preparations containing epinephrine are employed in patients during or immediately following the administration of chloroform, halothane, cyclopropane, trichloroethylene or other related agents.

The decision to use a local anaesthetic containing a vasoconstrictor in areas with a limited blood supply or in patients with peripheral vascular disease, will depend on the physician's appraisal of the relative advantages and risks.

Administration of Marcaine in children under 12 years is not recommended.

Caution is advised in administration of repeat doses of Marcaine to patients with severe liver disease.

Adverse reactions
Reactions to Marcaine are characteristic of those associated with amide-type local anaesthetics. A major cause of adverse reactions to this group of drugs is excessive plasma levels, which may be due to overdosage, inadvertent intravascular injection, or slow metabolic degradation. Other causes of reactions to these local anaesthetics may be hypersensitivity, idiosyncrasy, or diminished tolerance.

Excessive plasma levels cause systemic reactions involving the central nervous system and cardiovascular system. The central nervous system effects are characterized by excitation or depression. The first manifestation may be nervousness, dizziness, blurred vision, or tremors, followed by drowsiness, convulsions, unconsciousness, and possible respiratory arrest. Since excitement may be transient or absent, the first manifestation may be drowsiness sometimes merging into unconsciousness and respiratory arrest. Other central nervous system effects may be nausea, vomiting, chills, constriction of the pupils, or tinnitus. The cardiovascular manifestations of excessive plasma levels may include depression of the myocardium, blood pressure changes (usually hypotension) and cardiac arrest.

Allergic reactions are characterized by cutaneous lesions (e.g. urticaria), oedema, and other manifestations of allergy.

It should be noted that reactions due to systemic absorption may be slow or rapid in onset. Those of rapid onset include respiratory depression, cardiovascular collapse and cardiac arrest. This type of reaction necessitates a high degree of preparedness since it can occur with little warning.

In coordinated studies of 3,200 procedures carried out by 15 investigators, there were 2 severe systemic reactions. Both patients experienced convulsions as a result of inadvertent vascular injection. Foetal bradycardia has been observed with the use of Marcaine. Most cases, including a few fatalities, occurred when the paracervical route was used. (See Precautions).

In some cases Marcaine may produce marked peripheral vasoconstriction in unanaesthetized areas which may last for several hours.

Reactions following epidural or caudal anaesthesia also may include: high or total spinal block; urinary retention; fecal incontinence; loss of perineal sensation and sexual function; persistent analgesia, paresthesia, and paralysis of the lower extremities; headache and backache; and slowing of labour and increased incidence of forceps delivery.

Dosage and administration
Maximum dosage limit must be individualized in each case after evaluating the size and physical status of the patient, as well as the usual rate of systemic absorption from a particular injection site. Most experience to date is with single doses of Marcaine up to 225 mg with epinephrine 1:200,000 and 175 mg without epinephrine.

However, the recommended maximum single dose is 150 mg.

At present there is insufficient clinical evidence with multiple dosage or intermittent dose techniques to permit precise recommendations for such procedures to be given. However, limited clinical experience in this area of use indicates that Marcaine may be repeated in 3 to 6 hours up to a maximum dose of 400 mg in 24 hours. In most cases the duration of anaesthetic effect is prolonged by the addition of epinephrine.

Local infiltration: 2 to 60 mL of 0.25% solution, depending on the area and extent of the block.

Peripheral nerve block: (axillary/brachial plexus, supraclavicular, intercostal, sciatic and femoral): 5 to 30 mL of 0.50% or 5 to 60 mL of 0.25% solution, depending on the area and extent of the block.

Sympathetic: 20 to 50 mL of a 0.25% solution.

Lumbar epidural: 10 to 30 mL of a 0.25% or 0.50% solution or 10 to 20 mL of a 0.75% solution.

Caudal: 15 to 30 mL of a 0.25% or 0.50% solution.

Paracervical: 10 to 20 mL of a 0.25% solution.

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Management of Disseminated Testicular Cancer

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Thirteen patients with disseminated nonseminomatous germ cell tumours of the testis were treated with a three-drug combination (vinblastine, bleomycin and cis-diamminedichloroplatinum). Of 12 patients with measurable disease, 8 had complete and 3 partial remission. One patient with a solitary metastasis failed to respond but is disease free following surgical excision. Toxicity was moderate but no drug-related deaths occurred and there were no apparent lasting side-effects. No patients with complete remission have relapsed. Ten of the 13 patients are without evidence of disease from 9 to 36 months after treatment, 6 of these for 2 years or more. One patient died after a partial remission of 16 months. One is undergoing further treatment for relapse with liver metastases and one remains in partial remission at 30 months. These results demonstrate the efficacy of this drug combination in testicular cancer.

Treize patients souffrant de tumeurs testiculaires germinales non séminomateuses ont été traités avec une association de trois médicaments (vinblastine, bléomycine et cis-diamminedichloroplatine). Chez les 12 patients ayant une atteinte mesurable, 8 ont eu une rémission complète et 3, une rémission partielle. Un patient porteur d'une métastase solitaire ne répondit pas mais il est maintenant exempt de lésion suite à une excision chirurgicale. La toxicité a été modérée mais aucun décès attribuable aux médicaments n'est survenu et il n'y a eu aucune réaction indésirable persistante. Aucun patient ayant bénéficié d'une rémission complète n'a rechuté. Dix des 13 patients n'ont aucun signe de maladie après 9 à 36 mois, dont 6 après plus de 2 années. Un patient est décédé après une rémission partielle de 16 mois. Un patient reçoit plus de traitement pour une rechute avec métastases du foie et un autre patient est en rémission partielle après 30 mois. Ces résultats démontrent l'efficacité de cette association médicamenteuse dans le cancer testiculaire.

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Testicular cancer is the most common malignant condition occurring in men from 20 to 35 years of age.[1] It is therefore an important disease although accounting for only 1% of all cancer in males. Seminoma, which accounts for about 40% of testicular cancer, is highly radiosensitive. Cure rates approach 100% in stage I disease (confined to the testis) and are 70% to 80% in stage II (regional nodes involved).[2] Nonseminomatous germ cell tumours are less radiosensitive and the relative roles played by surgery and radiation therapy are controversial. The 3-year survival rate for patients treated by retroperitoneal lymphadenectomy or by irradiation is 80% to 90% for stage I and 40% to 80% for stage II tumours.[3-5]

Although a 5-year survival rate of 55% has been achieved for metastatic

seminoma treated by radiation therapy,[6] the majority of patients with disseminated testicular cancer require chemotherapy. Progress in the treatment of this disease has included the development of new active drugs and their use in combination. In 1976, Einhorn, Furnas and Powell[7] presented their initial results using vinblastine, bleomycin and cis-diamminedichloroplatinum (cis-platinum). In this paper we report our experience with a similar drug regimen in patients with nonseminomatous germ cell tumours of the testis.

Patients and Methods

We studied 13 patients with disseminated nonseminomatous germ cell tumours. Seven had disseminated disease at the time of initial presentation and in five metastases developed within 4 months of completing treatment to the regional nodes. One patient had had a relapse following previous complete response to chemotherapy. Six patients had embryonal carcinoma, six had embryonal carcinoma and teratoma and one had embryonal carcinoma and choriocarcinoma.

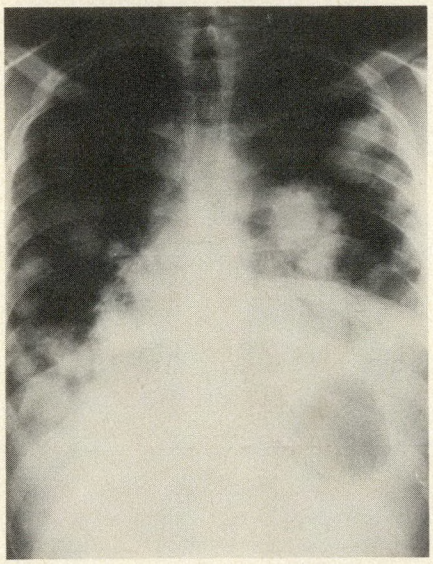

Fig. 1a

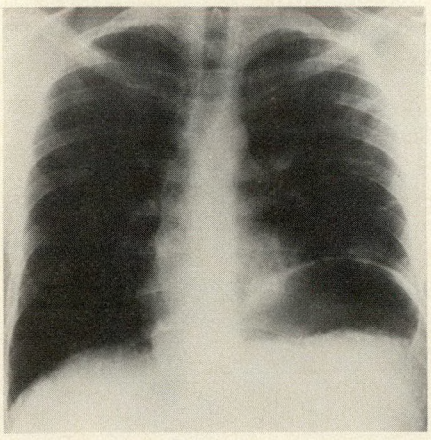

Fig. 1b

FIG. 1—(a) Chest film before treatment showing extensive pulmonary metastases and (b) 30 months later, showing partial remission of disease.

Cis-platinum was given at a dosage of 20 mg/m² body surface daily for 5 days, repeated at 3-week intervals for three courses. One patient received a fourth course. Patients were hydrated before infusion and mannitol (20 g) was given with the cis-platinum. Vinblastine (0.2 mg/kg body weight daily) was given on days 1 and 2, for a total of five courses every 3 weeks. More recently, the dose of vinblastine has been reduced to 0.15 mg/kg. Bleomycin (30 units intravenously) was given weekly for 12 weeks. During cis-platinum therapy bleomycin was given on day 2, 6 hours after vinblastine. Patients obtaining complete remission continued to receive vinblastine 0.3 mg/kg body weight every 4 weeks. Bacille Calmet Guérin immunotherapy, as initially described by Einhorn, Furnas and Powell,[7] was not used.

Results

Twelve patients had measurable disease and of these 8 obtained complete remission and 3 partial remission. None of those in complete remission have relapsed and they have remained free of disease for 9, 11, 16, 23, 25, 31, 35 and 36 months. Of the three patients in partial remission, two presented with extensive intra-abdominal and pulmonary disease and one with extensive pulmonary disease (Fig. 1). One died at 16 months from progressive intra-abdominal disease. One had complete remission of multiple lung lesions but had persistent minimal intra-abdominal disease for which he received radiation therapy. Liver metastases developed while he was completing this treatment and he is at present receiving further chemotherapy. The patient whose chest film is shown in Fig. 1 had a partial remission. He remains asymptomatic 30 months later and although he has received no therapy for 18 months his disease has not progressed.

One patient with a solitary lung metastasis failed to respond to treatment so this lesion was excised. His original testicular tumour was mainly embryonal with teratomatous elements. Only teratomatous elements were found in the metastatic lesion, this being mainly cartilage. He remains free of disease 15 months after excision of the metastatic tumour. One patient did not have measurable disease but was treated because of incomplete resection of intra-abdominal lesions. This patient with teratocarcinoma at initial presentation had a large solid mass in the pelvis, extensively involved retroperitoneal nodes and a peritoneal cavity filled with teratomatous cysts. These were all resected but fragments of tumour remained adherent to pelvis and bowel. He is without evidence of disease 34 months later.

Ten (77%) of the 13 patients have no evidence of disease at 9 to 36 months, 6 of these 2 years or more after treatment. One patient died after a partial remission of 16 months, one remains in partial remission at 30 months and one is being treated for relapse.

Eight patients had an elevated concentration of the serum α-fetoprotein, or elevated titer of the beta subunit of human urinary chorionic gonadotropin, or both. In all cases of complete remission these values returned to normal and have remained normal. In all three patients achieving partial remission, these values were grossly elevated initially, but returned to normal despite evidence of persisting disease. They have remained normal in the patient in partial remission but became elevated in the two patients who relapsed.

All patients had nausea, vomiting and alopecia during the period of induction therapy. Severe leukopenia occurred in all patients. Although three patients required hospitalization for granulocytopenia and fever, none had proven sepsis. No patients have demonstrated impairment of renal function after receiving cis-platinum or of pulmonary function after receiving bleomycin. Myalgia occurred frequently as a result of giving vinblastine and this was most severe during the maintenance phase.

Discussion

From January 1972 until May 1976, 16 patients with disseminated nonseminomatous germ cell tumours were treated at our institution with a variety of chemotherapeutic agents. Three had a complete remission and two partial remission. These results are similar to those of other reports published before 1976 (Table I[8-13]). In 1976 Cvitkovic, Hayes and Golbey[14] reported a complete remission rate of 69% using a five-drug combination of vinblastine, bleomycin, cyclophosphamide, dactinomycin and cis-platinum. Einhorn, Furnas and Powell[7] using a three-drug combination of vinblastine, bleomycin and cis-platinum reported a complete remission rate of 75%. Our present results using vinblastine, bleomycin and cis-platinum are similar and represent a notable improvement over our previous experience. None of the eight patients in complete remission have relapsed to date and five of these have been in remission for 2 years or more. Previous experience with testicular cancer indicates that most relapses occur within 2 years[15,16] so it is likely

Table I—Results of Treatment of Nonseminomatous Germ Cell Tumours before 1976

Year	Author	Treatment	No. of patients	Complete remissions,%
1960	Li and associates[8]	Dactinomycin, methotrexate, chlorambucil	23	30
1966	Mackenzie[9]	Dactinomycin ± chlorambucil ± methotrexate	154	16
1967	Wyatt and McAninch[10]	Methotrexate	10	40
1970	Mendelson and Serpick[11]	Cyclophosphamide, vincristine, methotrexate, fluorouracil	17	29
1970	Kennedy[12]	Mithramycin	23	22
1975	Samuels, Johnson and Holoye[13]	Vinblastine, bleomycin	23	39

that many of these patients will be cured.

While partial remissions resulting from chemotherapy are generally of short duration it is of interest that one patient has been in partial remission for 30 months. It seems likely that these persisting lesions have undergone maturation to a more benign form as has been previously documented.[17,18] In patients obtaining partial response an attempt should be made to eradicate residual disease by surgery supplemented as necessary by radiation therapy.

One unanswered question is, Should retroperitoneal lymphadenectomy be performed in patients who appear to be in complete remission? Two such patients in this series did not receive either surgery or irradiation to regional nodes. In the series reported by Einhorn and Donohue[19] lymphadenectomy was reserved for those with residual disease. Results to date suggest that further therapy, either surgery or irradiation, may be necessary only when residual disease is suspected or perhaps when bulky retroperitoneal disease is present initially.

Initial results with the Einhorn regimen suggested a lower response rate for teratocarcinoma compared with embryonal carcinoma.[19] Further experience has shown similar response rates.[20] The one patient who failed to respond in the present series had a primary teratocarcinoma with predominantly embryonal elements. The persisting metastatic lesion was teratomatous with no embryonal component. The one patient who died in this series had some elements of choriocarcinoma. Although choriocarcinoma in combination does not appear to worsen prognosis, results obtained in patients with pure choriocarcinoma are less good.[20] The present series did not include cases of pure seminoma. Einhorn[20] has reported complete remission in 9 of 13 patients with pure seminoma. Although irradiation remains the primary mode of therapy for such patients, these results indicate that chemotherapy for disseminated seminoma should be considered before extensive radiation therapy to bone marrow or to lungs makes it difficult to use these chemotherapeutic agents.

Impairment of pulmonary function by bleomycin or of renal function by cis-platinum was not encountered in our series. Attention to hydration and the use of mannitol helped to prevent the latter. The most serious side effect was neutropenia which occurred in all patients. Our policy was to admit and isolate only those patients who were febrile and thought to have sepsis. Aminoglycosides should not be administered in these patients as there is a risk of irreversible renal failure when used in patients receiving cis-platinum.[21]

The availability of effective chemotherapy for disseminated testicular cancer raises the question of its use as adjuvant therapy for patients with nonseminomatous germ cell tumour. The risk of recurrence must be weighed against the toxicity of adjuvant chemotherapy and the fact that over 60% of those developing metastases may be cured of their disease by subsequent chemotherapy. With possible cure rates of over 80% there is little indication for adjuvant therapy of patients with stage I disease. Recurrence is much more likely to occur in those with stage II disease. If 40% of patients with stage II disease relapse and if 60% of these can be cured by subsequent chemotherapy then an overall survival of 85% would be expected. This would prevent 60% of stage II patients from receiving unnecessary chemotherapy. To determine if adjuvant therapy can improve upon these results will require a large randomized trial.

Conclusion

Combination therapy with vinblastine, bleomycin and cis-platinum gives a complete remission rate of approximately 70% in patients with disseminated testicular cancer. Almost all the remaining patients will obtain partial remission and with adjunctive surgery or radiation therapy, or both, some may be converted to complete remission. Relapses to date have been few in those with a complete remission and eventual cure appears a strong possibility. Moderate toxicity is associated with this regimen but it was generally well tolerated and no drug-related deaths occurred. No permanent toxic effects have been noted. This combination chemotherapy represents a notable advance in the management of patients with testicular cancer.

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Surgical Treatment of Carcinoma of the Prostate

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Prostatic cancer kills more men than any other malignant condition except that arising from the lung. "Cancer Therapy: Prognostic Factors and Criteria of Response" predicted that there would be approximately 17 500 deaths due to this disease in the United States in 1978.

Surgery is only applicable in stages A and B, when the tumour, as shown by various tests, such as measurement of the acid phosphatase value, technetium scanning and radioimmunoassay, is confined to the prostate. Ideally, the lymph glands along the iliac and obturator vessels should first be removed and quick-sectioned. If malignant cells are found in the lymph glands, the disease is considered surgically incurable and the procedure should be abandoned. If, however, the glands are disease free, a total prostatovesiculectomy should be carried out.

The author also discusses the place of palliative surgery, such as transurethral resection, in the treatment of cancer of the prostate.

Le cancer de la prostate tue plus d'hommes que toute autre maladie maligne, sauf celles du poumon. "Cancer Therapy: Prognostic Factors and Criteria of Response" prédisait qu'il y aurait approximativement 17 500 décès attribuables à cette maladie aux Etats-Unis, en 1978.

La chirurgie n'est applicable qu'aux stades A et B, quand la tumeur, tel que démontré par diverses épreuves comme la mesure de la phosphatase acide, la scintigraphie au technétium et le titrage radio-immunologique, est confinée à la prostate. Idéalement, les ganglions lymphatiques le long des vaisseaux iliaques et obturateurs devraient être enlevés et mis en section rapidement. Si des cellules malignes sont retrouvées dans les ganglions lymphatiques, la maladie est considérée chirurgicalement incurable et l'intervention devrait être abandonnée. Si, toutefois, les ganglions sont sains une prostatovésiculectomie totale devrait être pratiquée.

L'auteur discute également du rôle de la chirurgie palliative, telle que la résection transurétrale dans le traitement du cancer de la prostate.

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More men die of prostatic cancer than of any other malignant disease with the exception of that arising in the lung. In those over 75 years of age prostatic cancer is the prime killer. The statistics in "Cancer Therapy: Prognostic Factors and Criteria of Response"[1] indicated that there would be approximately 17 500 deaths due to cancer of prostate in 1978.

From a different viewpoint it is estimated that 11% of all carcinomas in the male are prostatic in origin, and routine autopsies have shown that the frequency of prostatic cancer ranges from 14% to 46% even up to 90%, depending on the criteria for diagnosis as well as the thoroughness of the examination.

Regarding the management of this disease, there is no dogmatic statement which cannot be refuted by reference to the literature.

Pathology

Mostofi,[2,3] in reports of 12 000 autopsies performed on patients who had had carcinoma of the prostate, stated that 99% of the growths occurred peripherally and at least one third of these were multifocal. He also pointed out that the grade of lesion varied in the same specimen, one area showing well-defined adenocarcinoma grade I and another less well-defined tumour, grades III or IV, according to Broders' classification.[4] The growth remains localized for a time, then spreads through the capsule and hence to the lumbar spine and pelvis, usually via Batson's plexus of veins. Initial spread is by way of the pelvic and para-aortic lymph nodes and also by the blood stream to other bony sites. Indeed, the lung and brain may be involved in a carcinomatosis type of spread.

Diagnosis

Only 5% to 10% of cancers of the prostate are diagnosed when they are amenable to surgical cure or treatment. They are usually discovered by the physician who finds a nodule or induration on routine rectal examination. The remaining 90% to 95% are found because the patient has symptoms of bladder neck obstruction, which is almost always due to a stage C or D lesion (one which has penetrated the prostatic capsule), or because of symptoms due to metastases (e.g., bone pain).

In recent years we have added to our diagnostic armamentarium three aids to staging: (a) the isolation of the prostatic fraction of the serum acid phosphatase, which is almost always diagnostic when the value is elevated; (b) the estimation of the bone marrow acid phosphatase value as advocated by Veenema and associates,[5,6] who showed that elevation of the bone marrow acid value indicates extracapsular

spread of the growth some time before the serum acid phosphatase concentration becomes elevated; and (c) the radioimmunoassay for prostatic acid phosphatase as developed by Fenimore Cooper.[7-12] This assay gives positive results in 30% of cases in which the bone marrow and serum acid phosphatase values are normal as estimated by other methods. So far, this is the most sensitive test we have to detect extraprostatic spread of disease.

Normally pedal lymphangiography does not show the obturator or internal iliac nodes which are the first to be involved by cancer of the prostate. If these nodes are demonstrated, it is almost certainly by retrograde filling of these lymphatics due to obstruction of the lymph channels in the common iliac chain or possibly the para-aortic chain.

Prognosis

The prognosis depends on two factors, stage and grade, in addition to the immune response of the host to tumour.

Stage

There are four stages of carcinoma of the prostate which may be numbered 1 to 4 or, as in this paper, lettered A to D. In stage A the diagnosis is made by microscopic examination alone. The serum acid phosphatase values are normal. The lesion cannot be detected clinically. In stage B1, the lesion is less than 2 cm in diameter. The serum phosphatase values are normal. In stage B2 lesions the growth is confined within the capsule of the prostate and, on clinical examination, does not involve the base of the bladder or seminal vesicles. In stage C the growth has penetrated the capsule and invaded the base of the bladder or the seminal vesicles, or both. In this stage pelvic lymph nodes are involved in 50% to 85% of cases but the tumour is limited to the pelvis. In stage D there are metastases.

Grade

Grading of prostatic carcinoma is extremely difficult because of the wide variation within the same specimen.[13] It is therefore impossible to grade a prostatic carcinoma accurately from two or three small needle biopsy specimens. This has been a serious problem in assessing the importance of grading in various series. Unquestionably, grading of a tumour should be on the basis of the highest grade within the specimen and this can only be assessed accurately from the whole specimen.

Treatment

Carcinoma of the prostate may be divided into two main clinical groups. The first comprises stages A and B, the second, stages C and D. Tumours in stages A and B are potentially curable by total prostatovesiculectomy, with or without lymph-node dissection. As a result of this procedure, 95% or more of patients may become impotent and 10% to 20% will have some degree of urinary incompetence.

Stages A and B

Stage A.—The management of patients with stage A lesions is controversial. Many urologists believe that the large majority of patients with a tumour of this stage will not die of their disease and that their life expectancy is equal to a similar age group without the disease. We do not subscribe to this belief. We believe that stage A tumours should be treated like any other operable cancer. Some urologists actually base their treatment on the percentage of tissue with malignant change and are of the opinion that if it is less than 30%, the patient should be treated expectantly. Recently, the grade of the lesion has been shown to have a very important effect on the prognosis.[13-15] If the tumour is a well-differentiated adenocarcinoma and repeat biopsy specimens of the prostatic capsule after 1 month and a transrectal needle biopsy specimen of the posterior lobe fail to show any remaining disease, then these patients should not be subjected to total prostatectomy. On the other hand, if the lesion is of high grade (and 20% to 50% of them are), we agree with Bauer, McGavran and Carlin[16] that the prognosis even with endocrine therapy is poor and that these patients should be treated by total prostatovesiculectomy if they have no serious concomitant disease and have a life expectancy of 10 years or more.

Stage B1.—In a patient with this stage of tumour who is younger than 70 years and who is otherwise in good health, the optimum cure rate will be achieved by total prostatovesiculectomy if the lymph nodes taken from the internal iliac and obturator areas show no tumour.

Stage B2.—Autopsy series show that 6% of patients with these tumours have positive nodes (stage C lesions). Because of the complications of impotence and incontinence, there are two groups of urologic surgeons who advocate widely divergent treatment. One group advocates expectant treatment, in stages A and B lesions, with the exception, perhaps, of introducing iodine-125 needles directly into the gland or of external irradiation in cases of high-grade tumour.[17] For tumours of lower grade, therapy is withheld until symptoms develop on the premise that many carcinomas of the prostate are extremely slow growing.[18] Unfortunately, at present, we cannot predict the behaviour of such tumours. Grading may be a guide but, as already noted, is not dependable in biopsy specimens. This is the approach now recommended by Whitmore,[18] but considerable time is necessary before a thorough assessment of this approach can be completed. On the other hand, Jewett[19] and workers from the Mayo Clinic,[20,21] amongst others,[22] believe that the disease merits a radical operation and that the 10- to 15-year survival justifies this despite the complications. It is generally agreed that radical or total prostatectomy should be reserved for patients who normally have at least a 10-year life expectancy from the time of operation. It is of interest that supplying estrogens after total prostatectomy does not improve the prognosis.[23]

Stages C and D.—The second clinical group of cases, stages C and D, may require palliative surgery, such as a procedure to relieve bladder neck obstruction (usually with some degree of benign prostatic hypertrophy) which has not been relieved by estrogen therapy. In some relatively healthy patients with stage C tumour, the disease may have extended to the base of the bladder and involved the lower ends of the ureters producing hydroureter and hydronephrosis and life threatening renal failure. In such cases, bilateral reimplantation of the ureters to a higher site in the bladder may be of value.

Surgical Approach

The ideal surgical approach to the malignant prostate should: (a) allow sampling of the internal iliac and obturator lymph nodes, because if these nodes contain malignant cells the disease is surgically incurable and the operation should not be continued; (b) allow easy access to the gland itself even after a complete transurethral resection (i.e., in stage A disease); (c) permit accurate and easy anastomosis of the bladder to the urethra; (d) keep incontinence and impotence to a minimum; and (e) result in minimal morbidity, mortality and hospital stay.

Perineal Exposure

Unless this is done in two steps or by two teams, examination of the pelvic lymph nodes is not possible. It is a most difficult operation if there has

been a previous transurethral resection or enucleation. In our hands the frequency of impotence has been almost 100% and some degree of incontinence has occurred in about 50% of patients.

Retropubic Approach

This can be most difficult technically, particularly with respect to urethral anastomosis and after a previous prostatic operation. The anastomosis can be so difficult that some advocate leaving a small portion of prostate behind to facilitate it. Byar and Mostofi[23] have deplored this action because they found cancer at the prostatic apex in 75% of 208 prostates removed for early carcinoma. The incidence of impotence and incontinence is approximately the same as for perineal prostatectomy.

Total Trans-sacral Prostatectomy

This operation was originally proposed for patients who could not be put into the exaggerated lithotomy position. It allows easy access to the prostate, and visualization of the anastomosis is superior to that obtained with the retropubic approach but, like the perineal approach, it does not allow examination of the lymph nodes.

Transpubic Approach

Within the last 4 years this approach has been used almost exclusively by the staff of the Toronto General Hospital. It allows the extraperitoneal removal of the iliac and obturator nodes for quick section before manipulation of the prostate. It allows excellent exposure of the prostate for its removal and for anastomosis of the bladder to the urethra under direct vision. The procedure can be carried out by one team. It is the exposure of choice, particularly when a prostatic procedure has been done previously. There is some morbidity due to pain in the adductor regions on walking, but this has seldom persisted more than a few weeks; by leaving a small bridge of symphysis, this pain can be almost eliminated. Stress incontinence has been a problem but has been solved by fashioning a bladder tube to anastomose to the urethra after the method of Flocks and Culp.[24]

From Aug. 1, 1974, to Dec. 31, 1978, 42 patients with carcinoma of the prostate considered to be either stage A or B were operated on at the Toronto General Hospital. Six of the patients had malignant cells in the nodes on quick section and the procedure was terminated; three were clinically stage A and three stage B. Two of these tumours were highly differentiated adenocarcinomas, two moderately well differentiated and two were anaplastic. There were therefore 36 patients who underwent radical transpubic prostatovesiculectomy. It is interesting that about 60% of these tumours were understaged, although pathologically the lines of resection in all cases were clear.

Results

Follow-up on these patients is too short to be evaluated statistically, but some interesting facts have emerged: (a) after the operation 35 of the 36 patients walked without difficulty. Leaving a bridge of symphysis may have helped; (b) 3 of the 36 patients have persistent stress incontinence requiring a clamp or collecting apparatus. Anastomosis using a bladder tube, as described by Flocks and Culp, should eliminate this problem; and (c) 3 of the 36 patients were potent.

Conclusions and Summary

Carcinoma of the prostate is fatal for about 17 500 Americans each year, and with increasing longevity this incidence will increase. In men who have a life expectancy of 10 years from the time of presentation and who have a lesion which is clinically stage A, B1 or B2, the treatment of choice is surgical. In the case of a stage A tumour, if the repeat transurethral and needle biopsy specimens after 1 month fail to show any tumour and the tumour was of low grade, then watchful waiting is probably permissible. On the other hand, no matter what size the tumour may be, if it is of high grade or if repeat biopsy specimens show that the tumour is still within the capsule, then serious consideration should be given to performing a total prostatectomy. We believe that surgical extirpation is the treatment of choice in patients with stage B lesions, either B1 or B2.

The transpubic approach for prostatovesiculectomy is the best one with minimal morbidity and complications.

At present we are understaging about 60% of our cases of carcinoma of the prostate.

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Radiation Therapy for Adenocarcinoma of the Prostate

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Forty-eight patients with different stages of adenocarcinoma of the prostate were treated by external beam therapy. Biopsy results are correlated with stage of disease, original grade of tumour and with the findings on examination. The authors discuss the significance of histologic progression of the disease particularly in relation to prognosis. They review the place of staging lymphadenectomy before radiotherapy and the overall morbidity associated with treatment.

Quarante-huit patients souffrant d'adénocarcinomes prostatiques à différents stades ont été traités par faisceau de rayonnement externe. On a fait la corrélation entre les résultats de biopsie et le stade de la maladie, le grade initial de la tumeur et les constatations de l'examen rectal. Les auteurs discutent de la significativité de l'évolution histologique de la maladie en relation, particulièrement, avec le pronostic. Ils revoient le rôle du classement du stade clinique de la maladie par lymphadénectomie avant la radiothérapie, et la morbidité globale associée au traitement.

Surgical extirpation of early intracapsular adenocarcinoma of the prostate is associated with unavoidable morbidity.[1,2] Furthermore, all forms of hormonal therapy provide control rather than cure of this malignant condition. Over the past 15 to 20 years there has been increasing interest in the role of radiation therapy in the treatment of patients with potentially curable prostatic cancer and as a form of palliation for patients with bone metastases associated with localized pain. Adenocarcinoma of the prostate is a radiosensitive tumour and the introduction of external beam therapy and interstitial irradiation allow the delivery of a tumoricidal dose of radiation to the prostate without damage to the skin and other normal tissue. Acceptable long-term survival statistics are becoming available from centres using external beam therapy.[3] In addition, encouraging results of treatment with interstitial irradiation have been reported.[4]

The method of assessing local response of tumour to radiotherapy is still controversial and requires clearer definition. The inadequacy of rectal examination in the follow-up of patients with adenocarcinoma of the prostate is not well recognized. Despite the drawbacks of biopsy this form of assessment provides more objective evidence of tumour response to radiation therapy. We present biopsy data in a selected series of patients with carefully staged adenocarcinoma of the prostate treated by external beam therapy, to review early clinical results, particularly in relation to biopsy findings, and to report on the morbidity associated with this particular form of radiation therapy.

Methods

A modification of the American Urological System of staging[5] was used (Table I) to record the extent of the disease. Staging procedures included rectal examination, prostatic biopsy, technetium-99 bone scanning, radioimmunoassay to measure serum and bone-marrow acid phosphatase values[6] and pelvic lymphadenectomy. Patients have to be carefully selected for staging lymphadenectomy, which was employed in 63% of the patients studied (Table II). Routinely, four biopsy specimens (two from each lobe) were obtained from the prostate before and after treatment. Pathological grading of the tissue was carried out using a modification of the method recommended by the Veterans Administration Cooperative Urological Research Group.[7] The grading was performed under low magnification (40 to 100×) and a histologic description was given of the primary and secondary histologic patterns, the primary pattern occupying more than 50% of the malignant area. Each specimen was assigned two numbers, ranging from 1 to 4 representing the primary and secondary histologic fields. These two numbers were then combined to give an overall pattern score. When the pattern score was less than 4, the tumour was described as being well differentiated, when 5 or 6 moderately differentiated and when 7 or 8 as being anaplastic.

External beam therapy (with cobalt-60) was used to treat all patients. In those without evidence of lymphatic spread the prostate and periprostatic area were irradiated with up to 6000 rads. In patients with positive lymph nodes (D_1), the whole pelvis was irradiated to a dose of 4000 rads, and the prostate and periprostatic area were given a further 2000 rads. Both forms of treatment were delivered over a 6-week period.

Table I—American Urological System for Staging Adenocarcinoma of the Prostate

Tumour stage	Description
A	Incidental finding
A_1	Focal
A_2	Diffuse
B	Confined to prostate
B_1	Small, discrete nodule
B_2	Large or multiple nodules
C	Localized to periprostatic area
C_1	No involvement of seminal vesicles
C_2	Involvement of seminal vesicles
D	Metastatic disease
D_1	Pelvic lymph-node metastases
D_2	Bone or distant lymph-node or soft tissue metastases

Patients

Forty-eight patients were treated as described above. Their average age at time of treatment was 65.8 years (range 49 to 79 years). These patients did not receive adjuvant therapy and additional treatment was withheld until clinical progression was evident.

Following irradiation, biopsies were done annually; 105 specimens were available for study in addition to the original 48 (average 2.2 post-treatment biopsies per patient). The mean follow-up was 40 months (range 14 to 81 months). The distribution of patients

Table II—Data on 48 Patients with Cancer of the Prostate Treated by External Beam Therapy

Stage	No. of patients	No. of laparatomies	Average pattern score
A_2	8	2	4.9
B_1	13	10	3.9
B_2	12	9 (3*)	4.9
C	15	6 (3*)	5.3

*Patients with lymph-node metastases, average pattern score 5.5.

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by stage is shown in Table II. Following lymphadenectomy, six patients were restaged D_1, three from B_2 and three from C categories. The average pattern score for each stage is also given in Table II.

Results

As of Dec. 31, 1978, eight patients have died, four from progression of their prostatic cancer and four of unrelated causes (two of coronary thrombosis, one of atherosclerosis and one of lung cancer). One patient was lost to follow-up after 46 months. In addition to the four patients who died of adenocarcinoma of the prostate, five patients have shown either extension of local disease or the development of metastases, or both. Table III lists in detail the clinical status of these nine patients. Seven of the nine patients did not have the benefit of a staging lymphadenectomy and this may be of significance in three of the patients who later had metastatic disease and in two of the four patients who died. In three of these four patients, biopsy specimens obtained prior to death showed anaplastic carcinoma and the fourth patient probably had metastases at the time of treatment (common iliac lymph nodes showed metastatic disease). Two of the eight patients with A_2 disease had metastases. Of the 12 patients with B_2 disease, 2 had extension of disease, and 5 of 15 patients with stage C disease (2 with lymph-node metastases) also failed to respond to radiation therapy. No patient in stage B_1 had progression of disease.

A comparison was made between rectal examination and follow-up biopsy findings. There was an overall disagreement between rectal examination and histologic information in 38% of the biopsy specimens studied. There was a false-positive rate of 47% (normal biopsy result associated with clinically positive rectal examinations) and a false-negative rate of 33% (biopsy specimens showing tumour associated with clinically normal rectal examinations).

The initial stage of the disease was compared with the post-treatment biopsy findings at 1-year, 2-year and 3-year intervals (Table IV). The six patients with lymph nodes containing malignant cells were included and reported under their initial clinical stage. At 1-year follow-up, 43% (17 of 40) of the biopsy specimens failed to show any malignant lesion but after 2 years, only 33% (11 of 33) of biopsy specimens were cancer free and after 3 years, only 28% (5 of 18). Although the numbers are small, patients with A_2 and B disease appeared to respond more effectively to radiation therapy than those with stage C disease.

The original histologic grade of the tumour was also compared with the post-treatment biopsy findings (Table V). Patients with well-differentiated neoplasms appear to have a better prognosis than those with either a moderately well differentiated or an anaplastic lesion. The 13 patients with B_1 disease had a pattern score under 4 indicating a well-differentiated tumour and, as previously noted, in no patient has the disease progressed.

The clinical response of the patient in relation to change in biopsy findings was also studied. The grading method used allowed a quantitative evaluation

Table III—Clinical Status of Patients Who Had Extension of Prostatic Cancer or Died of the Disease

Original clinical stage	Laparotomy	Control of primary tumour	Metastases	Death due to prostatic carcinoma	Remission time, mo	Biopsy pattern score	
						Original	Follow-up
A_2	No	No	Yes	—	31	5	7
A_2	No	Yes	Yes	Yes	24	4	8
B_2	No	Yes	Yes	—	54	4	Neg
B_2	No	No	No	—	23	7	6
C	No	No	No	No	16	4	5
C	No	No	Yes	—	24	8	7
C	No	No	Yes	Yes	21	7	8
C	Yes*	Yes	Yes	Yes	28	4	Neg
C	Yes*	No	Yes	Yes	24	4	8

*Lymphnodes positive.

Table IV—Comparison of Initial Stage of Disease and Postoperative Biopsy Findings at 1, 2 and 3 Years after Treatment

Initial stage	Follow-up, yr; no. tumour-free biopsy specimens /total no.(and %)		
	1	2	3
A_2	4/6 (67)	5/6 (83)	2/4 (50)
B	9/21 (43)	5/19 (26)	3/11 (27)
C	4/13 (31)	1/8 (12)	0/3 (0)
	17/40 (43)	11/33 (33)	5/18 (28)

Table V—Comparison of Original Histologic Grade and Biopsy Findings at 1, 2 and 3 Years after Treatment

Original grade	No. of patients	Follow-up, yr; no. tumour-free biopsy specimens/total no. (and %)		
		1	2	3
Well differentiated	26	12/21 (57)	7/16 (44)	3/8 (37)
Moderately well differentiated	12	3/10 (30)	1/8 (12)	1/7 (14)
Anaplastic	10	2/9 (22)	3/9 (33)	1/3 (33)
	48	17/40 (43)	11/33 (33)	5/18 (28)

Table VI—Clinical Response in Relation to Biopsy Findings

Original biopsy	Summary of follow-up biopsy	Clinical follow-up	
		Well	Progression
Well differentiated	Improvement	6	2
	No change	13	0
	Deterioration	2	3
Moderately well differentiated	Improvement	6	0
	No change	5	0
	Deterioration	0	1
Anaplastic	Improvement	6	1
	No change	1	2

of biopsy material (Table VI). Three categories were arbitrarily chosen to summarize and compare post-treatment biopsy findings with the original histologic descriptions: (a) "improvement" represents elimination of tumour or consistent reduction in pattern score by two or more units, (b) "no change" indicates no net increase or decrease in pattern score and (c) "deterioration" means a consistent increase in pattern score of two or more units.

Of the 26 patients with well-differentiated lesions (pattern scores of 4 or less) 21 are clinically well without evidence of metastases and without evidence of local progression. Improvement was demonstrated histologically in two patients following radiation therapy yet metastases developed in one 54 months after completion of therapy. This patient did not have a staging lymphadenectomy. The other patient had metastases at the time of therapy and would now, under our present protocol, be treated by hormones. Five patients showed increasingly anaplastic biopsy specimens after treatment. Two have died of cancer, one has had a transurethral resection of the prostate and two remain well.

Of the 12 patients with moderately well-differentiated adenocarcinomas (pattern score of 5 to 6), 11 are clinically well and have shown improvement or no change in their pattern score. One patient had deterioration, demonstrated histologically, with concurrent progression of disease both locally and distally. This patient did not have a staging lymphadenectomy.

Finally, of the 10 patients with anaplastic histology (pattern scores of 7 and 8), 7 are clinically well and 3 have shown progression of disease. Two of the three have had persistently anaplastic biopsy specimens but one has shown local improvement. With an average follow-up of 40 months, 35 of 44 are clinically well.

Complications

We were impressed by the frequency of serious side effects. Irritable bladder and bowel symptoms following radiotherapy occurred in the majority of the patients, but these were generally easily controlled by simple medications and subsided after completion of therapy. We found persistent symptoms beyond the 3-month period in only five patients (10%). These were in the form of irritable bladder or bowel symptoms or some form of scrotal, penile or thigh edema. We found it hard to assess impotence but most of the younger patients were potent following therapy. However, in patients with decreasing libido prior to therapy, impotence generally followed. Our overall figure for impotence in patients who were potent before treatment was begun was 54%. We found no increase in complication rates for those who underwent pelvic lymphadenectomy prior to therapy. Lymphoceles occurred in two of the patients subjected to lymphadenectomy and drains were left in situ following the procedure until drainage had completely ceased. There were no cases of bowel obstruction. Similar findings have been reported by others.[4,8,9]

Discussion

Rectal examination is an inaccurate method of assessing the response of the prostate to radiotherapy. Kurth and associates[10] and Carlton and associates[4] have reported a 41% frequency of normal findings on rectal examination associated with positive biopsy results. A similar figure, 33%, was found in our series. On the other hand, biopsy results were negative in 47% of our patients with abnormal rectal findings. Although a proportion of this discrepancy undoubtedly results from the inaccuracy inherent in biopsy methods (15%),[11] these results demonstrate that it is most difficult to distinguish the presence of tumour from the effects of radiotherapy by rectal examination alone. In the follow-up of these patients it would appear that the only value of rectal examination is in detecting obvious clinical progression of disease.

There have been a number of reports related to biopsy findings following radiotherapy for localized adenocarcinoma of the prostate. As shown in Table VII[4,10,12-15] there are considerable differences in tumour-free biopsy rates —from 81% to 35%. Such a large difference is difficult to explain on the basis of either biopsy or radiotherapy techniques. Furthermore, Cox and Stoffel[12] reported an increasing number of negative biopsy results—from 34% to 81% over a 30-month period, whereas Nachtsheim and associates[14] found the opposite response (71% to 41% over a 36-month period). Our data also showed a decrease in the number of negative biopsy results with time.

When the initial grade of the tumour was compared with subsequent histologic patterns, we found that the well-differentiated tumour had a much greater chance of being eliminated by radiotherapy (Table IV). Furthermore, although a high percentage (70%) of our patients with anaplastic tumours showed improvement in grade, total elimination of tumour cells was not achieved. This result varies, however. Kurth and associates[10] reported no relationship in response to radiotherapy with different grades of tumour whereas McLoughlin and associates[16] found that the results with anaplastic lesions were better.

There has been much discussion on the prognostic importance of biopsy findings. Kurth and colleagues[10] found a positive correlation between the persistence of tumour cells in biopsy specimens and the development of metastases. However, Cox and Stoffel[12] found no relationship between positive biopsy findings and progression of disease. In our series, of the nine patients whose follow-up biopsy specimens either remained anaplastic or became more anaplastic, progression of disease was observed in six. On the other hand, of the 39 patients whose follow-up biopsy specimens showed improvement or remained well or moderately well differentiated, progression was noted in only 3. Deterioration of histologic pattern or persistence of anaplasia in biopsy specimens as distinct from a merely positive biopsy result would appear to be a poor prognostic index.

It should be noted that although both Kurth and associates[10] and Cox and Stoffel[12] reported on stage C disease, in the former series less than one third of the patients had staging laparotomies and in the latter study no patient underwent this procedure. In the present report, of the seven patients in whom distant bone or soft tissue metastases developed, only two had lymph nodes assessed by laparotomy before radiotherapy. In both of these cases lymph-node metastases were discovered at operation. Whenever possible, pelvic lymphadenectomy should

Table VII—Biopsy Findings after Radiotherapy for Localized Adenocarcinoma of the Prostate

Series	No. of patients	Tumour free rate	Follow-up, mo
Carlton and associates[4]	34	65	12 - 30
Kurth and associates[10]	53	43	32
Cox and Stoffel[12]	37	81	30
Mollenkamp, Cooper and Kagan[13]	76	42	12
Nachtsheim[14]	17	41	36
Sewell and associates[15]	17	35	4 - 38

be carried out as a staging procedure prior to curative radiotherapy.

Unfortunately, it is difficult to compare survival statistics obtained from the various treatment modalities (radiotherapy, surgery, endocrine therapy), because of (a) inadequate staging, (b) different methods of statistical analysis, (c) the lack of results from radiotherapy beyond the 10-year period, (d) the use of adjuvant therapies in many series and (e) the long history of carcinoma of the prostate. At present no one treatment method appears to offer a clear advantage over others. On the other hand, radiotherapy is potentially curative, is associated with fewer complications than surgical procedures and is suitable for the management of older patients with localized disease. These advantages are appealing to many. However, the persistence of positive biopsy results following therapy is worrisome, and opinion varies as to the clinical importance of this finding and whether additional treatment is necessary. Several of our patients had positive biopsy results but no evidence of clinical progression of disease at periods varying from 56 to 61 months. At present, additional therapy is not given unless there is objective evidence of extension of disease locally or distally. More study is required to define clearly the place of radiation therapy in the treatment of adenocarcinoma of the prostate.

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Surgical Management of Renal Cell Carcinoma at the Vancouver General Hospital: 20-Year Review

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Over a 20-year period 143 patients with renal cell carcinoma were treated surgically at the Vancouver General Hospital. The results of simple nephrectomy are compared to those of radical nephrectomy. The authors conclude that radical nephrectomy (including node dissection) is a useful staging procedure but provides little or no long-term therapeutic benefit over simple nephrectomy. They stress the need for new adjunctive therapy.

Au cours d'une période de 20 ans, 143 patients souffrant d'un carcinome des cellules rénales ont été traités chirurgicalement au Vancouver General Hospital. Les résultats de la néphrectomie simple sont comparés à ceux de la néphrectomie radicale. Les auteurs concluent que la néphrectomie radicale (incluant la dissection ganglionnaire) est une intervention utile pour classifier le stade clinique de la maladie mais qu'elle offre peu d'avantage thérapeutique et aucun de longue durée par rapport à la néphrectomie simple. Ils insistent sur le besoin de nouveaux traitements d'appoint.

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This study was undertaken to evaluate the possible therapeutic benefits of adding ipsilateral node dissection (radical nephrectomy) to the standard en bloc total resection of the contents of Gerota's fascia (termed a "simple" nephrectomy in our hospital). We found the node dissection to be an excellent staging procedure, but it did not substantially improve survival in our series.

Patients and Methods

Of 243 patients with renal cell carcinoma seen at the Vancouver General Hospital between Jan. 1, 1957 and Dec. 31, 1976, 143 were treated surgically by either simple or radical nephrectomy.

Before 1967, surgical treatment of renal cell carcinoma consisted of simple nephrectomy (in 55 patients) with removal of the contents of Gerota's fascia. In a few patients, some regional nodes were examined.

Since 1967, the standard surgical procedure for the condition has been radical nephrectomy (in 88 patients), emphasizing early ligation of the renal vessels, with en bloc dissection of the lymphatics from the diaphragm to the bifurcation of the aorta and vena cava.

The male:female ratio was 5:2. The mean age of patients treated by simple nephrectomy was 62 years and by radical nephrectomy was 56 years. All patients were followed up for at least 2 years and 80% were followed up for 5 years.

Staging

Standard staging studies, including angiography, were performed in all patients who underwent radical nephrectomy. In recent years chest tomography has been added to these studies.

The Robson staging method was used.[1,2]

There were 62 patients with stage 1 (tumour confined to kidney) lesions, 24 with stage 2 (involvement of perinephric fat) lesions, 32 with stage 3 (involvement of renal vein or regional lymph nodes) lesions and 25 with stage 4 (metastatic spread) lesions.

Results

The survival at 3, 5 and 10 years for all potentially curable patients (stages 1, 2 and 3) was 66% (63 of 95), 52% (40 of 77) and 27% (19 of 71), respectively. These percentages are comparable to those in most series.[1-5]

Surprisingly, the survival for stages 1, 2 and 3 patients combined was actually shorter for those who had radical nephrectomy than for those who underwent simple nephrectomy (Tables I and II). This finding could not be explained on the basis of more extensive surgery since the operative mortality was only 1.5%, but was owing in part to the fact that only 13 stage 1 patients who had radical nephrectomy had been followed up for 5 years.

The survival for stage 2 and stage 3 patients was somewhat better with radical nephrectomy. Survival of patients with perirenal invasion (Table III) and of those with lymph-node metastases (Table IV) was slightly improved when radical nephrectomy was carried out.

For analysis of survival related to the degree of venous invasion, patients were considered in four groups: those with (a) microvenous invasion, (b) invasion of a renal vein tributary, (c) invasion of the renal vein and (d) invasion of the inferior vena cava. The 5-year survival in these groups was 16%, 20%, 27% and 16%, respectively.

There was no benefit from radical nephrectomy in patients with invasion of the renal vein or one of its tributaries.

Of six patients who had inferior vena caval invasion there was only one survivor at 5 years. This patient subsequently received irradiation for brain metastases. He is alive 7 years after operation. The mean length of survival of this group was 16 months and the 5-year survival rate was 16%.

In our patients there were 25 with stage 4 disease who underwent radical nephrectomy. In most cases a symptomatic primary tumour was the reason for operation. Seven patients in whom solitary metastases at other sites had been removed previously, were operated upon for cure. Two had solitary lung metastases that were removed following nephrectomy and one had a solitary metastasis in the left femur treated by amputation. By 5 years only four of these patients were alive and at 10 years there were no survivors.

Discussion

Several authors have evaluated the therapeutic effectiveness of radical nephrectomy with node dissection.[1,2,5] Our results suggest that there may be some benefit from node dissection in stage 2 and stage 3 disease but the overall effect is minimal (Tables I and II). In this series survival was actually shorter in those who had radical nephrectomy. This is particularly important as the operative mortality in our series was only 1.5% (one case in each group).

While prophylactic node dissection seemed to be beneficial if the patient had positive nodes the possibility remains that this procedure in the stage 1 cases may not always be beneficial. It is possible that the removal of these nodes may alter the immunologic defence mechanism. (The numbers are small and of questionable validity since they are from different eras with changing surgical techniques and pathology.)

Table I—Length of Survival of Patients Who Underwent Simple Nephrectomy

Stage	No. of patients operated on	Survival, yr; no. patients surviving/total followed up at each interval (and %)		
		3	5	10
1	30	24/26 (92)	18/24 (74)	10/21 (48)
2	9	7/ 9 (78)	6/ 9 (66)	3/ 8 (37)
3	12	2/10 (20)	2/10 (20)	0/ 9 (0)
4	4	1/ 3 (33)	0/ 3 (0)	0/ 3 (0)
1, 2, 3 combined (potentially curable patients)	51	33/45 (73)	26/43 (60)	13/38 (34)
All patients	55	34/48 (71)	26/46 (57)	13/41 (32)

Table II—Length of Survival of Patients Who Underwent Radical Nephrectomy

Stage	No. of patients operated on	Survival, yr; no. patients surviving/total followed up at each interval (and %)		
		3	5	10
1	32	15/23 (65)	4/13 (31)	3/13 (23)
2	15	6/10 (60)	6/ 7 (86)	2/ 6 (33)
3	20	9/17 (53)	4/14 (29)	1/14 (7)
4	21	5/19 (26)	4/19 (21)	0/18 (0)
1, 2, 3 combined (potentially curable patients)	67	30/50 (60)	14/34 (41)	6/33 (18)
All patients	88	35/69 (51)	18/53 (34)	6/51 (12)

Table III—Patients with Perirenal Invasion Surviving 5 Years after Nephrectomy

Procedure	5-year survival no./total (and %)
Radical nephrectomy	6/ 7 (86)
Simple nephrectomy	6/ 9 (66)
Total	12/16 (75)

Table IV—Survival of Patients with Lymph-Node Metastases after Nephrectomy

Procedure	5-year survival, no./total (and %)	Mean survival mo ± SD*
Radical nephrectomy	1/6 (17)	36 ± 35
Simple nephrectomy	0/4 (0)	12 ± 8

*Standard deviation.

Radical nephrectomy did not improve the survival of patients with involvement of the renal vein.

Since only one of six patients with involvement of the subhepatic vena cava was alive at 5 years, extending the surgery above the diaphragm and into the heart with its attendant risks would appear to be contraindicated.

Conclusions

Radical nephrectomy with lymph-node dissection remains an excellent staging procedure. Morbidity and mortality are similar to those of simple nephrectomy. The procedure may confer benefit to patients with involvement of regional nodes.

Surgical therapy seems to have reached its limits,[3,6] and further advances will depend upon the development of adjunctive systemic modes of treatment.

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Management of Primary Bladder Cancer by a Multidisciplinary Team

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Results of management of a closed series of primary bladder carcinoma over a 20-year period by a multidisciplinary team are presented. Patients were classified by the TNM method before treatment. These experiences indicate that stage and grade are relevant to prognosis and treatment. The TNM classification can be precise and practical when used diligently by a treatment team. Although no new methods of treatment are offered, the treatment now available may be utilized to better effect if programmed to allow care of the patients by a team, especially if the team explores the limits of radiation and surgery in their hands.

On présente les résultats obtenus sur une période de 20 ans, par une équipe multidisciplinaire dans le traitement d'une série de carcinomes primaires de la vessie. Les patients ont été classifiés, avant traitement, selon la méthode TNM. Ces expérience indiquent que le stade et le grade sont pertinents au pronostic et au traitement. La classification TNM peut être précise et pratique lorsqu'elle est utilisée avec diligence par une équipe de traitement. Bien qu'aucune nouvelle méthode de traitement ne soit offerte, le traitement maintenant disponible peut être utilisé avec de meilleurs effets s'il est programmé pour permettre la prise en charge du patient par une équipe, spécialement si cette équipe explore les limites de la radiothérapie et de la chirurgie entre ses mains.

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This is a report of a closed series of 807 patients treated for primary bladder cancer. Beginning in 1952, all patients who were admitted for initial treatment were included in the series. Twelve patients who had not been staged prior to treatment were excluded. All patients were managed by a treatment team consisting of urologists, radiotherapists and a pathologist.*

Method

All tumours were staged by the tumour, nodes, metastasis (TNM) classification[1] before treatment was initiated. This classification was found to be precise and practical.

At the beginning the four primary objectives were: (a) to establish the limits of transurethral excisional biopsy of the tumour; (b) to establish the limits of radiation therapy; (c) to disregard lymph nodes at surgery; and (d) when cystectomy was indicated, to use simple cystectomy and to remove the urethra at the same time.

When the data were reviewed in 1962, it was obvious that many tumours could not be handled by either transurethral resection or radiation alone. So the uniform treatment program was altered and patients with high-stage, high-grade tumours were managed by combined diversion, irradiation and cystourethrectomy.[2,3]

Since 1962, the uniform treatment program has been as follows.[2,3] In situ carcinoma (TIS) is treated by transurethral excisional biopsy. Patients with TIS who present with bladder irritation are treated by combined diversion, irradiation and cystourethrectomy. Patients with tumours classified as T1 and T2 are managed by transurethral excisional biopsy. Radiation therapy is added when the tumour is anaplastic and when there is uncertainty that the tumour has been completely excised. Patients having T3 tumours are handled by staged treatment—laparo-

*In the original team, the urologists were J.V. Berry and W.E. Collins, the radiotherapists were G. Stoddart and G.E. Catton and the pathologist was E. Liepa.

tomy with urinary diversion, followed by irradiation to the whole pelvis using 4000 rads over 28 days and, 6 weeks later, simple cystourethrectomy. T4a tumours are subjected to urinary diversion and irradiation. Total cystectomy without irradiation is used for patients with squamous cell carcinomas and adenocarcinomas of the bladder floor. Adenocarcinomas at the vault are removed by extensive partial cystectomy with excision of urachus and umbilicus.

Findings

Survival figures are relative to the survival of a normal population of the same age and sex distribution (i.e., actuarily adjusted). Survival according to cell type is shown in Table I. As seen in Table II, surprisingly few tumours, upon recurrence, shifted to a higher stage. We have data on only 74 patients on the shift in grade, which is presented in Table III; 39 recurrent tumours maintained the same grade as the primary tumour, 30 recurrent tumours were of higher grade and 5 recurrent tumours were of lower grade than the primary tumour. As seen in Table IV the age distribution was the usual one with all 10 decades represented. There did not seem to be any significant correlation of age to stage (Table V), but correlation of age to grade (Table VI) showed that the average age of patients with grade 1 tumours (of low-grade malignancy) is 64 years, of those with grade 2 tumours (of medium-grade malignancy) 69 years and of those with grade 3 tumours (highly malignant) 70 years. Survival by age is interesting (Fig. 1); the 5-year survival rate of patients younger than 40 years was 93%, patients between 40 and 49 years of age 76%, between 50 and 59 years 73%, between 60 and 69 years 66%, between 70 and 79 years 57% and of those over 80 years of age 60%. The 10-year survival rates were somewhat different: 94% of the patients younger than 40 years survived 10 years; 75% between 40 and 49 years survived 10 years, but patients older than 50 years had a 10-year survival rate which was approximately the same, ranging from 51% to 58%. The importance of this finding is not known.

Survival by grade was what one would expect (Table VII). There was a direct relationship between grade and survival over the 5- and 10-year periods. There was similar relationship of stage to survival as shown in Table VIII.

The site of the tumour in the bladder had a definite effect on survival. Of 94 patients with tumours involving the bladder neck and prostate 45% survived for 5 years and 37% for 10 years. Those with tumours elsewhere in the bladder fared much better with 69% and 57% survival rates, respectively.

The presence of metastases had a considerable effect on survival.

When patients with T1, T2 and T3 tumours without metastases (688 patients) were grouped together, the 5-

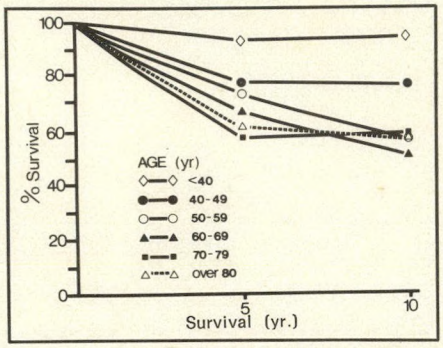

FIG. 1—Five- and 10-year survival rates by age are presented. Importance of these data is not known.

Table I—Survival Correlated with Tumour Cell Type*

Cell type	No. of patients	Survival, % 1 yr	5 yr	10 yr
Transitional cell	725	—	69	56
Squamous cell	20	—	27	17
Adenocarcinoma	6	50	0	0

*In 56 patients the cell type was not clearly stated.

Table II—Shift to a Higher Stage on Recurrence*

Classification of primary tumour	No. of patients	No. with shift to higher stage
TIS	8	2
T1	412	28
T2	159	25
T3	107	10
T4	99	0

*In 22 patients there was no clear statement of stage prior to treatment.

Table III—Shift in Grade

Grade of recurrent tumour	Grade of primary tumour NS	1	2	3	Total
NS*	56	481	127	69	733
1	0	20	4	1	25
2	0	14	15	0	29
3	0	7	9	4	20
Total	56	522	155	74	807

*Not stated.

Table IV—Age Distribution*

Age, yr	No. of patients
0 – 10	1
11 – 20	1
21 – 30	6
31 – 40	20
41 – 50	61
51 – 60	153
61 – 70	230
71 – 80	223
81 – 90	103
91 – 100	8

*Mean 66.03 yr. On the chart of 1 patient, the age was not noted.

Table V—Correlation of Age to Stage*

Classification of tumour	Average age, yr	No. of patients
TIS	66	8
T1	63	412
T2	69	159
T3	70	107
T4	68	99

*Stage not noted for 22 patients.

Table VI—Correlation of Age to Grade

Grade of tumour	Average age, yr	No. of patients
X	68	56
1	64	522
2	69	155
3	70	74

Table VII—Survival by Grade*

Grade of tumour	No. of patients	Survival, % 5 yr	10 yr
1	522	83	71
2	155	37	22
3	74	25	13

*Grade not stated for 56 patients.

year survival rate was 74% and the 10-year survival rate 62%, but when metastases were present (11 patients) there was a 2-year survival rate of only 27% and only 1 patient survived for 3 years. Similarly, patients with T4 tumours without metastases (80 patients) had a 5-year survival rate of 22% and a 10-year rate of 21%. The 19 patients with T4 tumours who had metastases had a 6% 5-year survival rate but none of the patients survived for 6 years. On the records of nine patients there was no evidence that a search was made for metastases.

In the charts of 52 patients there was no clearly stated opinion as to whether initial treatment was curative or palliative only, but in the remainder there was a clear statement. Treatment was a curative attempt in 621 patients; 79% of these patients survived 5 years and 64% survived 10 years. Survival by the different treatment methods that were used in a curative attempt is shown in Table IX. The survival rates were quite different in those who had palliative treatment only (Table X); in this group of 134 patients, 15% survived 5 years and 11%, surprisingly, survived 10 years.

When transurethral resection (TUR) was done as a curative measure 85% of the 508 patients survived 5 years and 71% survived 10 years. When radiation therapy was combined with transurethral resection, 5- and 10-year survival rates were 64% and 37%, respectively. The results of treatment by TUR related to stage and grade are presented in Table XI.

Thirty-four patients had staged urinary diversion, irradiation of the whole pelvis (4000 rads over 28 days) and simple cystourethrectomy 6 weeks later; 57% survived for 5 years and 44% for 10 years. Two of these patients had T2 tumours, 21 had T3 tumours and the remaining 11 had T4a tumours; 51% of patients with T3 tumours survived 5 years and 46% survived 10 years.

The most heartening thing about this program has been the disappearance of pain in all patients. When a cure was not possible, palliation was most effective. We have benefited from the experience of Mount[4-6] when treatment of the primary tumour is impossible. In other situations, transurethral resection of the intravesical tumour was effective. Urinary diversion almost always relieves pain. Emergency or salvage cystectomy has been necessary only three times. We have been impressed with the results of low-dose irradiation for hemostasis.

We attempted to assess residual bladder irritation in patients after treatment (Table XII). This is important because persistent bladder irritation or the appearance of bladder irritation may indicate that a recurrent in situ carcinoma is changing to multiple focal invasive cancer.[7] The indications used for cytologic examination of the urine were irritable bladder, hematuria, obvious bladder cancer, ureteral urines in bladder cancer and at follow-up of patients with bladder cancer.

The status of the 807 patients at the end of the study is set forth in Table XIII.

Table VIII—Survival by Stage

Classification of tumour	No. of patients	Average age, yr	Survival, %	
			5 yr	10 yr
T1S	8	66	59	52
T1	412	63	90	78
T2	159	69	61	61
T3	107	70	26	27
T4	99	68	19	16

Table IX—Survival after Treatment for Cure*

Treatment	No. of patients	Average age, yr	Survival, %	
			5 yr	10 yr
All procedures	621	65	79	64
TUR only	508	65	85	71
Surgery other than TUR	36	64	56	36
Radiation only	14	69	37	40
Radiation + TUR	29	65	64	37
Radiation + other operative procedure	31	61	41	50

TUR = transurethral resection.
*3 patients were lost to follow-up.

Table X—Survival after Palliative Treatment Only*

Treatment	No. of patients	Average age, yr	Survival, %	
			5 yr	10 yr
All procedures	134	69	15	11
TUR only	28	77	16	0
Surgery other than TUR	22	63	11	15
Radiation only	27	71	20	15
Radiation + TUR	24	73	12	19
Radiation + other operative procedure	31	63	17	7

*2 patients did not have either surgery or irradiation

Table XI—Survival following TUR

Stage and grade of tumour	No. of patients*	Survival, %	
		5 yr	10 yr
T1, G1	362	92	82
T1, G2	24	68	0
T1, G3	7	86	75
T2, G1	93	69	46
T2, G2	41	50	40
T2, G3	19	46	12

*In 10 patients who had TUR the intent of treatment was not stated.

Table XII—Bladder Irritation in 137 Patients following Treatment

Degree of irritation	No. of patients	Survival, %	
		5 yr	10 yr
Mild	103	28	16
Severe	34	33	20

Table XIII—Status of Patients at End of Study

Status	No. of patients
Alive and well with no disease	129
Alive with disease	15
Alive, status of disease not stated	24
Died	
of disease	222
of other causes, no bladder cancer	132
of other causes, bladder cancer present	52
of cancer, status not known	84
of metastases, no bladder cancer	18
Lost to follow-up (16%)	131
Total	807

Summary

Results of the management of a closed series of 807 patients with primary bladder carcinoma by a multidisciplinary team are presented. All patients were classified by the TNM method prior to treatment and, since 1962, uniform treatment has been used. Our experiences indicate that stage and grade are relevant to prognosis and treatment. The TNM classification can be precise and practical when used diligently by a treatment team. Although no new methods of treatment are offered, it is suggested that what is available may be utilized to better effect if programmed to allow care of patients by treatment teams, especially if the team explores the limits of radiation therapy and surgery available to them. As a result: (a) patients can face a future without pain; (b) most patients can maintain the use of their own bladder; (c) when surgery or irradiation, or a combination, is indicated, it can be carried out promptly; (d) most T1 and T2 tumours can be handled by transurethral excisional biopsy; and (e) staged urinary diversion, irradiation therapy to the whole pelvis (4000 rads over 28 days) followed 6 weeks later by a simple cystourethrectomy yield 5- and 10-year survival rates that are at least as good as more radical irradiation and more radical surgery.

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SESAP II Question

606. Six weeks ago a 20-year-old man first noted a painless scrotal mass. Examination discloses a nontender 5- by 5-cm, smooth, testicular mass which does not transilluminate. The best management would consist of

(A) an attempt to aspirate fluid from the mass to allow better palpation

(B) needle biopsy

(C) orchiectomy through an inguinal incision

(D) examination of the mass through a scrotal incision; excision if the mass proves to be a tumor

(E) administration of antibiotics and observation for two to four weeks

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

For the critique of Item 606 see page 486 of this issue.

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

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

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

Il ne faut pas qu'on puisse identifier un patient grâce à une illustration à moins qu'il n'y ait expressément consenti par écrit; faute de permission les traits de sa physionomie doivent être oblitérés.

Les illustrations en couleur ne seront publiées qu'aux frais de l'auteur. Si l'illustration provient d'une autre source, il convient d'obtenir tant de l'auteur que de l'éditeur de l'ouvrage dont elle est tirée, l'autorisation de s'en servir aux fins de la publication.

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

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

Un résumé qui ne doit pas dépasser 125 mots doit accompagner chaque article sur une feuille séparée.

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

Trans-sphincteric Approach to the Rectum

CHARLES F MCCULLOGH, MD, FRCS[C], FACS*

In 28 cases the trans-sphincteric approach has been used to remove lesions of the lower and mid-rectum; in 4 cases the combined abdominal and trans-sphincteric approach was used. Complications were minor and were easily treated and the operation was well tolerated by poor-risk patients. No patient had altered anal continence. The author emphasizes the need for careful identification and reconstruction of the anatomical structures.

The trans-sphincteric approach gives excellent exposure of the mid- and lower rectum and has been particularly useful in managing large villous adenomas. The trans-sphincteric approach alone is not adequate for the treatment of cancer, but makes possible sphincter-preserving resections of lesions that might otherwise be treated by more radical procedures.

Dans 28 cas, l'abord trans-sphinctérien a été utilisé pour l'ablation des lésions du rectum moyen ou inférieur; dans 4 cas, d'abord abdominal et trans-sphinctérien a été employé. Les complications ont été banales et furent facilement traitées et l'opération a été bien tolérée par des patients à risque élevé. Aucun patient n'a souffert d'une atteinte de la continence anale. L'auteur souligne la nécessité d'une identification et d'une reconstruction soigneuses des structures anatomiques.

L'abord trans-sphinctérien donne une excellente exposition du rectum moyen et inférieur et il a été particulièrement utile dans le traitement des gros adénomes villeux. L'abord trans-sphinctérien seul n'est pas suffisant dans le traitement du cancer. Cet abord rend possible des résections sans atteinte du sphincter, des lésions qui devraient autrement être traitées par des interventions plus radicales.

From the department of surgery, Calgary General Hospital, Calgary, Alta.

Presented at the 2nd annual meeting of the Canadian Association of General Surgeons, Montreal, PQ, Feb. 7, 1979

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Surgeons operating on a fistula in ano are careful to avoid cutting the deep portion of the external sphincter ani muscle for fear of producing anal incontinence. In this situation their fears are warranted; most of us recall patients who have been rendered incontinent following such a procedure. Excision of the septic fistula allows the muscles to retract and become nonfunctional, the defect is bridged by scar tissue and the patient is left with some degree of incontinence. However, obstetricians have noted that a complete tear through the anal sphincter, caused by uncontrolled delivery of the fetal head is usually followed by prompt healing and complete restoration of anal function if the tear is repaired immediately.

Incision through the sphincter muscles apparently does not cause incontinence if the muscles are accurately replaced and sutured. Indeed, Bevan[1] in 1917, reported a posterior midline approach to the rectum with or without removal of the coccyx, and, in 1970, Mason[2] described a trans-sphincteric approach lateral to the coccyx to expose the rectum.

Faced with the problem of managing a patient with a large villous adenoma of the mid-rectum that was too large and too high to be easily removed through the anus, yet too low to make anterior resection possible, I read Mason's accounts[2,3] with interest. Biopsy of my patient's tumour had been done on several occasions and each time the specimen had been reported as benign. An abdominoperineal resection or an abdominoendorectal resection for a lesion that was probably benign was not warranted, so the trans-sphincteric approach was used. The lesion was easily exposed and excised, and it proved to be benign. The patient made an uncomplicated recovery and was fully continent. This experience prompted use of the trans-sphincteric approach for rectal lesions in other cases.

Patients, Surgical Technique and Results

Between Jan. 1, 1973 and Dec. 31, 1978, 28 patients were operated on using this approach. Their ages ranged from 36 to 75 years. The pathological diagnosis was benign villous adenoma in 11 cases, adenomatous polyp in 8, adenomatous polyps with atypia in 2, carcinoid tumour in 2 and villous adenocarcinoma in 1. The distal margin of the lesions ranged between 3 and 8 cm from the anal verge. The size of the lesions varied from 2 cm in diameter to those completely encircling and extending along the rectum for several centimetres. The most proximal margin of a tumour resected by the trans-sphincteric route alone was 13 cm from the anal verge.

Of the 28 patients a combined abdominal and trans-sphincteric approach was used in 4. In each case the left colon, sigmoid and rectum were mobilized by the abdominal approach. The rectum and colon including the tumour were then delivered and excised through a trans-sphincteric exposure and a low end-to-end anastomosis was

easily made. This was done for carcinoma in two of the four cases. The diagnoses in the four cases were "polypoid carcinoma" in one, "malignant ulcer, 1 cm in diameter" in one, and "extensive benign villous adenoma" in two.

Twelve of the 28 patients were over 60 years of age. Some were obese and some, for other medical reasons, were not good candidates for surgery. Before admission to hospital for operation, most patients had undergone sigmoidoscopy and roentgenography after a barium enema. A biopsy of the rectal lesion had been done, and the distance of the lesion from the anal verge had been recorded. The degree of anal continence was recorded upon admission. Patients were placed on a low-residue diet without milk or milk products for 72 hours before operation. Mechanical bowel preparation was accomplished with enemas and laxatives and an antibiotic preparation was usually given—though the necessity for it is questionable. (In two cases, no antibiotic was given and no wound infection occurred.)

At operation patients are placed in the prone position with the trunk flexed (the jack-knife position). The buttocks are taped apart and the perineal area and buttocks prepared and draped. It is helpful to outline the coccyx and lower sacrum and the line of incision with a sterile marking pencil. The incision is made on the left side just lateral to the lower sacrum and coccyx and is carried down to the posterior midline at the anal verge. It is quite easy to identify each anatomical structure which is carefully tagged with a colour-coded clamp applied to a marked suture, before being incised. This is most important to ensure exact anatomical apposition of structures when the wound is being closed. If the muscle layers are not tagged at this stage accurate apposition may be difficult or impossible because the cut ends retract. The three parts of the external sphincter ani muscle are evident and are tagged. The puborectalis muscle and the lower innermost part of the levator ani muscle are identified and tagged. The fourth sacral nerve lies under the levator ani muscle and well lateral to the incision and can therefore be avoided. When the rectum is entered by incising the muscular tube and mucosa (also tagged), the exposure of the mid- and lower rectum is excellent.

On closing, each layer is apposed by approximating the colour-coded clamps. The muscle layers are closed with interrupted absorbable sutures and the skin is closed with interrupted sutures.

Postoperatively, the wound is left exposed after 24 hours and is kept dry with the use of a heat lamp for 10 minutes twice a day. Sitz baths are not given and the area is cleansed as required with a cleansing agent. Patients have noted remarkably little discomfort. They are allowed up the day following operation.

Intake is advanced from liquids to a full diet over a period of 1 week. Rectal thermometers, suppositories and digital examination are avoided in the early postoperative period. Bowel function usually begins spontaneously after 4 to 5 days. Bulk-producing laxatives may be used if necessary.

There were three complications of the operative procedure in the 24 patients whose operation was by the trans-sphincteric approach alone. One patient had a large fecal fistula which closed spontaneously after 2 weeks and two patients had superficial wound abscesses that required simple drainage.

Discussion and Conclusions

It is apparent that because of senility or local anal conditions, some patients have anal incontinence. This must be assessed preoperatively, in order to judge the effect of the operation on continence. In this study it was found that the degree of anal continence was unaltered by trans-sphincteric operations, but, since incontinence was sometimes present, had careful evaluation not been made preoperatively, the operation might have been blamed for results which, in fact, were optimal for that patient.

Before using the trans-sphincteric approach it is particularly important to evaluate carefully the rectal lesion in question. The trans-sphincteric approach with local excision is not a cancer operation. Therefore, it is important to remember that the villous adenoma may have one or more areas of invasive carcinoma within it. In assessing a villous adenoma, mobility and induration are important factors. Although multiple biopsy specimens may be reported as benign, only examination of the entire lesion by the pathologist will give the final answer. The surgeon must be prepared to do a more radical operation if he finds evidence of a malignant condition at operation. The treatment of small cancers by local excision is not a subject of discussion in this paper.

The trans-sphincteric approach makes possible sphincter preserving resection of lesions that might previously have been treated more radically. The operation is particularly well tolerated by poor-risk patients: the three complications in our series were managed without permanent sequelae.

It is emphasized that careful identification and reconstruction of the puborectalis muscle, the external sphincter, the levator ani muscle and the rectal wall will lead to primary healing and maintain continence. When attention is paid to these details, this operation is safe and well suited to the management of a select group of lesions in this area.

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

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Essential Neurology. William Pryse-Phillips and T.J. Murray. 644 pp. Illust. Medical Examination Publishing Co., Inc., Garden City, New York, 1978. $25. ISBN 0-87488-740-2.

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Randomized Sequential Trial of Parenteral Nutrition in Healing of Colonic Anastomoses in Man

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Adults who underwent elective colonic resection with anastomosis for both benign and malignant disease were randomly assigned to control or treated groups. Treated patients received daily 50 ml/kg of amino acid solution containing either 10 or 25 g/dl glucose by central or peripheral vein plus 500 ml of commercial soybean emulsion for 24 hours before operation and for 5 consecutive days after. Patients in both groups were examined by roentgenography after a water-soluble contrast enema, between 10 and 14 days after operation, and the integrity of the anastomosis was assessed radiologically without knowledge of the treatment given.

Results were assessed by sequential analysis. After 21 pairs of subjects were entered, a boundary was crossed making the area favourable to treatment inaccessible, and the trial was terminated. Forty-seven patients were included in the trial: there were four anastomotic leaks in 23 control subjects and eight leaks in 24 treated subjects. The authors conclude that intensive perioperative parenteral nutrition in patients who undergo routine elective colonic resection does not improve the rate of healing of colonic anastomoses.

Des adultes qui ont subi une résection non urgente du côlon avec anastomose pour des maladies bénignes ou malignes ont été assignés au hasard à un groupe témoin et à un groupe traité. Les patients traités ont reçu quotidiennement par une veine centrale ou périphérique, 50 ml/kg d'une solution d'acides aminés contenant 10 ou 25 g/dl de glucose plus 500 ml d'une émulsion commerciale de soya pendant les 24 heures qui ont précédé l'opération et les 5 jours consécutifs qui ont suivi. Les patients des deux groupes ont passé un examen radiologique après un lavement avec une substance de contraste hydrosoluble, de 10 à 14 jours après l'opération, et l'intégrité de l'anastomose a été évaluée radiologiquement sans connaître le traitement.

Les résultats ont été évalués par analyse séquentielle. Après l'inclusion de 21 paires de sujets, on a croisé une limite rendant inaccessible l'aire favorable au traitement, et l'essai a été interrompu. Quarante-sept patients ont été inclus dans l'étude: il y a eu quatre fuites anastomotiques chez les 23 sujets témoins et huit fuites chez les 24 sujets traités. Les auteurs concluent que l'alimentation parentérale intensive dans la période péri-opératoire chez les patients qui subissent une résection non urgente du côlon ne semble pas affecter la vitesse de guérison de l'anastomose colique.

Assessment of anastomotic integrity after colonic resection by roentgenographically opaque enemas in the postoperative period has been utilized by Goligher[1-3] to study details of the surgical technique. We have adapted this method to investigate the value of intensive parenteral nutrition in the perioperative period in patients subjected to elective colonic resection.

Patients and Methods

Eleven general surgeons at two Calgary hospitals permitted us access to patients who underwent elective colonic resection for benign and malignant disease. We excluded patients older than 75 years and patients recognized preoperatively to have signs or symptoms of congestive cardiac failure. Of 79 patients interviewed, 8 were excluded because of demonstrable cardiac failure, 7 were judged incapable of providing informed consent and 17 patients refused to enter the trial. The remaining 47 patients were assigned to treated or control groups according to the last digit of their hospital registration number: those with odd numbers were treated and those with even numbers entered the control group.

The 23 control patients were treated in the usual manner as ordered by the attending surgeon, except that roentgenography after a water-soluble contrast barium enema was performed between 10 and 14 days after the procedure. This was performed by a radiologist who had no knowledge of the treatment given. For the purposes of this study, identification of any extravasation of contrast material outside the bowel lumen in the area of the anastomosis was accepted as a "leak" and failure on the part of the radiologist to demonstrate extravasation was classified as "non-leak".

Treated patients received high volume, intensive parenteral nutrition starting 24 hours before operation and continuing for 5 days after operation. We found no difference in the frequency of contrast extravasation at the area of the anastomosis between the two groups. The solutions administered were a commercial mixture of L-amino acids (Travasol®, 2.5 g/dl) with either 10 or 25 g/dl glucose. These were administered intravenously in a dosage of 50 ml/kg body weight every 24 hours by either peripheral (10 g/dl glucose) or central (25 g/dl glucose) vein. Because of the poor quality of peripheral veins in most subjects, 21 of the 24 treated patients had a central venous catheter inserted preoperatively for the supplemental nutrition, in each case by percutaneous subclavicular puncture. Each subject in addition was given 500 ml of a commercial soybean emulsion (Nutralipid®) intravenously daily. For a 70-kg subject, the daily intake by the intravenous route was therefore 50 g of lipid, 70 g of amino acid protein, and either 350 g (peripheral vein) or 700 g (central vein) of glucose.

Finally four patients (one treated and three control) had total nitrogen balance studies performed in the perioperative period; urine, stool and nasogastric suction material were analysed for nitrogen by the micro-Kjedahl method[4] and intake was calculated from known values

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for intravenous fluids and from dietary tables.

Each subject was asked for his or her estimate of weight loss before admission, and preoperative and postoperative weights were compared. Total lymphocyte counts and hemoglobin, total protein and serum albumin values were measured before and after operation. Results were assessed as the radiologists' reports became available. Paired subjects were entered into a skewed sequential analysis:[5] boundaries were determined assuming a frequency of leaks among controls of 30% and among treated patients of 15%. A two-tailed closed design was selected with $2\alpha = 0.05$, $1\text{-}\beta = 0.95$, $\theta 1 = 0.80$, $N = 35$.

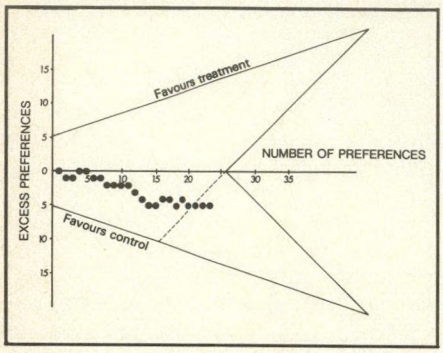

FIG. 1—Sequential analysis: pairs of subjects entered as described by Armitage.[5] Restricted skew design (two-tailed) with $2\alpha = 0.05$, $1\text{-}\beta = 0.95$, $\theta 1 = 0.80$, $N = 35$.

Results

Forty-seven patients were successfully entered into the trial and underwent roentgenography after a water-soluble contrast enema between 10 and 14 days postoperatively. A small pneumothorax developed in one patient after an attempt to insert a subclavian catheter percutaneously, but this resolved spontaneously; there were no deaths associated with the trial. In one treated patient clinical signs of anastomotic disruption developed, confirmed radiologically, which required a defunctioning colostomy. None of the other patients with roentgenographic anastomotic leaks received any specific therapy.

The trial was terminated after 21 pairs had been entered; at this point a boundary was crossed making the area favourable to the treatment inaccessible (Fig. 1) and in our opinion it was unethical to continue the trial merely to determine if the period of parenteral nutrition could be shown to be *worse* than the standard postoperative therapy. In all there were eight radiologically demonstrated "leaks" in 24 treated patients and four in 23 controls.

Further analysis of the subgroups within this trial provided no further useful information. In particular, 19 patients were identified who claimed a weight loss greater than 4.5 kg in the 6 months before surgery; as expected, most of these patients had cancer of the large intestine. Of these 19 subjects, 8 were controls and 2 of these demonstrated a leak; of the 11 patients in the treated group 3 had a leak. Mean concentrations of total protein, serum albumin and hemoglobin, and total lymphocyte counts were similar in both groups preoperatively and appear little changed postoperatively (Table I). Table II notes the details of the operative procedures performed and lesions identified. There was no appreciable excess either of patients with cancer or of low anterior resections in either group.

Fig. 2 shows nitrogen balance in four patients, one treated and three controls. As expected, the period of intensive parenteral nutrition was accompanied by a positive nitrogen balance in the treated subject, in contrast to the expected postoperative negative nitrogen balance in the three control patients.

Table I—Comparison of Preoperative and Postoperative Laboratory Values in Treated and Control Patients

Measurements	Treated (n = 24)		Control (n = 23)	
	Preop	Postop†	Preop	Postop
Total protein, g/dl	6.1 ± 0.6*	5.8 ± 0.5	6.4 ± 0.4	6.0 ± 0.9
Serum albumin, g/dl	3.7 ± 0.5	3.2 ± 0.7	3.6 ± 0.2	3.3 ± 0.8
Hemoglobin, g/dl	13.1 ± 1.3	12.6 ± 2.3	12.6 ± 1.0	12.5 ± 2.5
Total lymphocytes, $\times 10^9$/l	1.18 ± 0.28	1.35 ± 0.14	1.46 ± 0.27	1.31 ± 0.22
Body weight, kg	71.5 ± 5.7	67.6 ± 4.2	73.0 ± 2.3	70.5 ± 5.6
Age, yr	66 ± 4		69 ± 6	

*Mean ± standard error of the mean.
†Postoperative values obtained between day 7 and 12.

Table II—Operative Procedures and Diagnosis in Treated and Control Patients

Procedure	Diagnosis	Treated, no. (no. with anastomotic leak)	Control, no. (no. with anastomotic leak)
Right hemicolectomy	Cancer	7 (1)	5 (1)
	Other	1 (1)	1
Segmental resection	Cancer	3 (1)	2
	Diverticulosis	1 (1)	2
	Other		1
Anterior resection	Cancer	7 (3)	7 (2)
	Diverticulosis	4 (1)	3 (1)
	Other		1
Colectomy with ileo-rectal anastomosis		1	1
		24 (8)	23 (4)

Discussion

Major surgery is accompanied by a variable period of increased catabolism

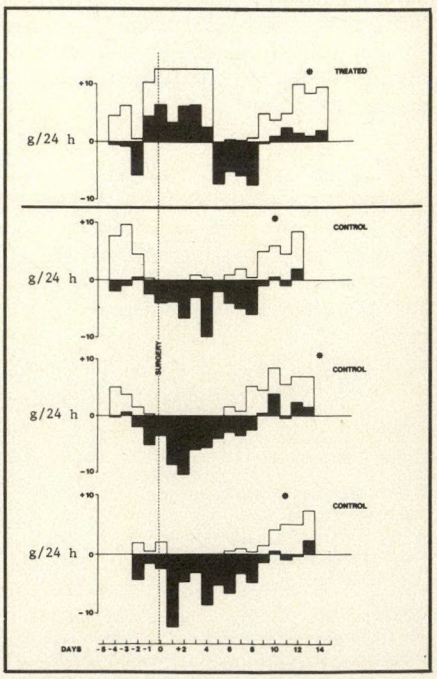

FIG. 2—Nitrogen balance in four subjects (selected at random so that one was in treated group and three in control group). Asterisk indicates postoperative roentgenography after contrast enema.

associated with a negative nitrogen balance.[6,7] It has been claimed that the negative nitrogen balance in this period can be diminished or even reversed by intensive intravenous administration of amino acids alone[8] or mixtures of amino acids plus glucose or lipid.[9] It is clear that accepted methods of preparing patients for elective colonic surgery combined with current methods of postoperative care may allow only minimal intake of protein and energy sources for as long as 7 to 10 days.

In this trial, we attempted for 6 days to give high-volume parenteral nutrition with solutions containing amino acids, glucose and soybean emulsion to modify the patient's response to major colonic resection with anastomosis. We found that the frequency of leakage from these anastomoses in the postoperative period did not differ in subjects randomly assigned to control or treated groups.

Similar trials of intensive perioperative nutrition in patients who undergo major surgery have produced conflicting results. Although Abel and colleagues,[10] by preoperatively identifying malnutrition in patients who underwent major cardiac surgery, could predict an increased frequency of complications, they could not show any change in the complication rate or the duration of hospitalization after 5 days of nutritional therapy in the postoperative period. When this study was extended to subjects with malignant gastrointestinal conditions, intensive perioperative nutritional supplementation failed to lessen the frequency of complications.[11] Collins, Oxby and Hill[12] claimed an improvement in the rate of healing of perineal sinuses after abdominoperineal excision of the rectum in patients receiving parenteral nutrition with amino acids and glucose compared with a control group of patients receiving amino acids alone, and another control group of patients who had no specific nutritional support. Each of these studies used subjective methods to identify postoperative complications, and, as far as can be determined, no attempt was made to conceal the method of treatment from the observer assessing the results. In the study reported here, the radiologic presence or absence of a leak at the site of the colonic anastomosis was made without knowledge of the patient's treatment.

Bozzetti, Terno and Longoni[13] found that the collagen content of perineal biopsy specimens after abdominoperineal excision of the rectum was increased by intensive parenteral nutrition, but they did not present clinical data to support their claim that wound healing was thereby facilitated. In malnourished rats, Steiger and associates[14] recorded an improvement in the tensile strength of colonic anastomoses when parenteral nutrition was given immediately after operation. Irvin[15] confirmed this finding in rats who were starved to lose one third of their body weight, but could find no advantage for supplemental nutrition in lesser degrees of malnutrition.

It can therefore be argued that changes in the rate of healing of colonic anastomoses might have been observed if we had selected patients who were profoundly depleted nutritionally before operation. We cannot dispute this but note that there were no differences in the frequency of anastomotic leaks in subjects who claimed a preoperative weight loss of greater than 4.5 kg whether or not they had received parenteral nutrition. It is also clear that either more prolonged or more intensive nutritional support might have decreased the frequency of anastomotic leaks in the treated group. The period of nutritional support we selected was influenced by the expense of the solutions used, and the real difficulty in deciding whether additional days of hospitalization would prove of long-term benefit to the patient. Fig. 2 suggests that the 6-day period of nutritional supplementation used was sufficient to alter favourably the nitrogen balance.

These conclusions refer only to the apparent failure of intensive perioperative parenteral nutrition to influence the number of postoperative anastomotic leaks in patients who undergo elective colonic resection and should not be construed as evidence against the use of parenteral nutrition in other circumstances.

We are grateful to the patients and surgeons of Calgary General and Foothills hospitals who permitted entry into this trial, and to the radiologists who read the postoperative contrast roentgenograms. Micro-Kjeldahl nitrogen analyses were performed by Maria Tesanovic of the special chemistry department, Foothills Hospital.

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Elastin and Granulation Tissue

C. TELFER, B SC,* G.M. LEES, MD, FRCS[C],† M. CHAMBERS, M SC‡ AND H.T.G. WILLIAMS, MB, CH B, FRCS, FACS, FRCS[C]§

The contraction of granulation tissue is an important factor in wound healing. The tract of an abdominal drainage tube closes at the rate of 1 mm/h once the tube is removed. Specialized myofibroblasts are generally believed to be responsible for this process and the presence of elastin in granulation tissue has been debated for many years.

A 3-mm polyethylene tube was inserted through the left lobe of the liver in 41 rats. A tube of granulation tissue formed around the plastic. This granulation tissue was isolated, after periods ranging from 8 to 20 days, by removing the left lobe of the liver and scraping away the surrounding liver tissue.

Biochemical assay for elastin revealed that normal hepatic tissue does not contain any detectable amount of elastin. All 41 samples of granulation tissue contained elastin with a mean value of 8.5×10^{-6} g of elastin per milligram of tissue. Normal rat aorta contains 31.4×10^{-6} g of elastin per milligram of tissue.

These tubes of granulation tissue were histologically normal and the presence of elastin was recognized using elastin stains. The exact role of elastin in granulation tissue is uncertain but this experiment clearly demonstrates its generation and presence there.

La contraction du tissu de granulation est un facteur important dans la cicatrisation des blessures. Le passage d'un drain abdominal se referme à la vitesse de 1 mm/h une fois que le tube est retiré. On croit généralement que des myofibroblastes spécialisés sont responsables de ce processus alors que la présence d'élastine dans le tissu de granulation est débattu depuis plusieurs années.

Un tube de polyéthylène de 3 mm a été inséré dans le lobe gauche du foie chez 41 rats. Un tube de tissu de granulation s'est formé autour du plastique. Ce tissu de granulation a été isolé après des périodes allant de 8 à 20 jours, par prélèvement du lobe gauche du foie et raclage du tissu hépatique environnant.

La mesure biochimique de l'élastine a révélé que le tissu hépatique normal ne contient aucune quantité décelable d'élastine. Les 41 échantillons de tissu de granulation contenaient tous de l'élastine à la concentration moyenne de 8.5×10^{-6} g d'élastine par milligramme de tissu. L'aorte du rat normal contient 31.4×10^{-6} g d'élastine par milligramme de tissu.

Ces tubes de tissu de granulation étaient histologiquement normaux et la présence d'élastine a été reconnue par des colorants de l'élastine. Le rôle exact de l'élastine dans le tissu de granulation est incertain mais cette expérience démontre clairement sa génération et sa présence dans le tissu de granulation.

John Hunter was perhaps the first to emphasize the importance of wound contraction. Since his time, and particularly in recent years, intensive investigative effort has been devoted to wound healing and early reduction (contraction) in the size of a wound.[1-6] After a brief "latent period" of 1 to 2 days, there is a progressive reduction in size of full thickness "granulating" wounds so that by 7 days after injury the wound size is reduced by 50% to 60%. This can be admirably demonstrated in the closure of tracts left after removal of a gastrostomy tube. These tracts close at the rate of approximately 1 mm/h and are effectively sealed in less than 24 hours, irrespective of the size of the tube, so that lost tissue is replaced and epithelialization completed speedily.

The power of a wound to contract rests in the granulation tissue but the mechanism is incompletely understood. Collagen has no innate contractile ability and wound contraction proceeds normally in scorbutic animals.[7] Moreover, granulation tissue contains relatively little collagen during the stage of active wound contraction.[4,8] In the myofibroblast a potential cellular mechanism of contraction exists. The evidence supporting the myofibroblast theory is strong, both on a pharmacologic and ultrastructural (i.e., electron microscopic) basis.[3-5] However, recent work by Ehrlich, Grislis and Hunt[2] suggests that the myofibroblast does not have the sole (or even dominant) contractile force.

Until recently, little attention has been paid to the part elastin and elastic fibres may play in wound contraction. Studies have concentrated on the histologic demonstration of elastic tissue in healing skin wounds.[9-11] The appearance of the first elastic fibres in granulation tissue depends upon such variables as staining technique, the nature of the tissue under study and random sampling errors. Their appearance has been reported as early as 8 days after wounding by Schwartz[10] and as late as 56 days by Williams.[11] All these studies concentrated on healing skin wounds and it is theoretically possible that "migration" of elastic fibres from more lateral unwounded skin structures may introduce a source of error. We set out to demonstrate the presence of elastin in granulation tissue from a structure which in its normal uninjured state has no chemically detectable elastin.

Materials and Methods

The formation of granulation tissue was induced in the liver of 41 adult male Wistar rats. Under intraperitoneal sodium pentobarbital anesthesia, a midline laparotomy was performed. A short piece of polyethylene tubing (diameter 3 mm) was placed through the substance of the left lobe of the liver. Following this, the liver, with the tube in place, was returned to the peritoneal cavity. At periods ranging from 8 to 20 days the animals were sacrificed and the segment of liver with the polyethylene tubing was retrieved. The core of granulation tissue which had formed around the tube was carefully dissected from the surrounding normal liver (Fig. 1).

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The isolated segment of granulation tissue was then studied by light microcopy using both elastin and non-elastin stains (hematoxylin and eosin, Masson's trichrome and Weigert's resorcin-fuchsin stains). Biochemical assay for elastin content was performed on all samples using a modification of the method of Naum and Morgan[12] (employing 5 M guanidine hydrochloride followed by enzymatic degradation and autoclaving). As a control, the elastin microassay was carried out on 13 normal uninjured rat livers. In addition, rat aorta, which has a high elastin content, was also studied. No attempt was made to correlate elastin content with the age of the granulation tissue nor to demonstrate the presence of oxytalan ("pre-elastic")[9] fibres during the early stages of granulation tissue formation.

Results

The biochemical assay when applied to specimens of *whole* isolated granulation tissue produced consistently positive results—a mean elastin content of 8.5×10^{-6} g/mg of tissue (range 0 to 21.7×10^{-6} g/mg) (Table I). In the 13 samples of normal uninjured liver no elastin could be detected. In the seven specimens of rat aorta, the mean value of elastin was 31.4×10^{-6} g/mg. The three samples with no biochemically detectable elastin were obtained at the beginning of our study when only a small portion of the tissue was assayed. We subsequently modified the technique so that the whole tube of granulation tissue was used in the assay for the remaining 38 animals. The histogram (Fig. 2) shows a bell-shaped distribution of values around the mean.

Examination of stained sections using light microscopy confirmed the presence of apparently normal granulation tissue with abundant collagen, new vessels and fibroblasts as demonstrated in preparations stained with hematoxylin and eosin and with Masson's trichrome stain (Figs. 3 and 4). Elastic fibres were identified without difficulty using Weigert's resorcin-fuchsin stain. The elastin content appeared to be most abundant in the more mature granulation tissue. The elastin fibres were not uniformly distributed throughout the entire thickness of the granulation tissue tract but were concentrated towards the outside (Fig. 5). To confirm that contraction did occur in this experimental model we inserted the polyethylene tube in the liver substance and left it in situ within the peritoneal cavity for 10 days as in the usual preparation. Two animals were then ex-

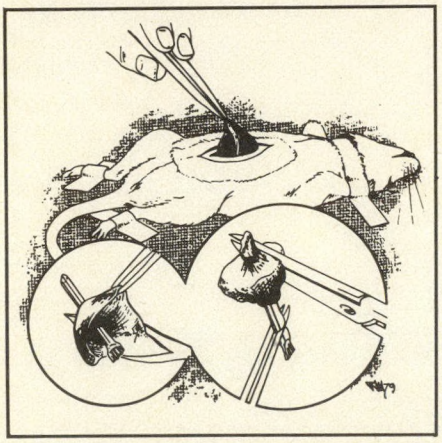

FIG. 1—Insertion of polyethylene tube in left lobe of liver. Inset to right shows isolation of granulation tissue tract from surrounding normal liver substance.

Table I—Elastin Content in Tissue from Normal Uninjured Liver, from Aorta and from Granulation Tissue Preparation

Tissue	No. of samples	Elastin content, $\times 10^{-6}$ g/mg Mean	Range
Liver	13	0	0
Aorta	7	31.4	21.5 – 37.9
Granulation tissue	41	8.5	0 – 21.7

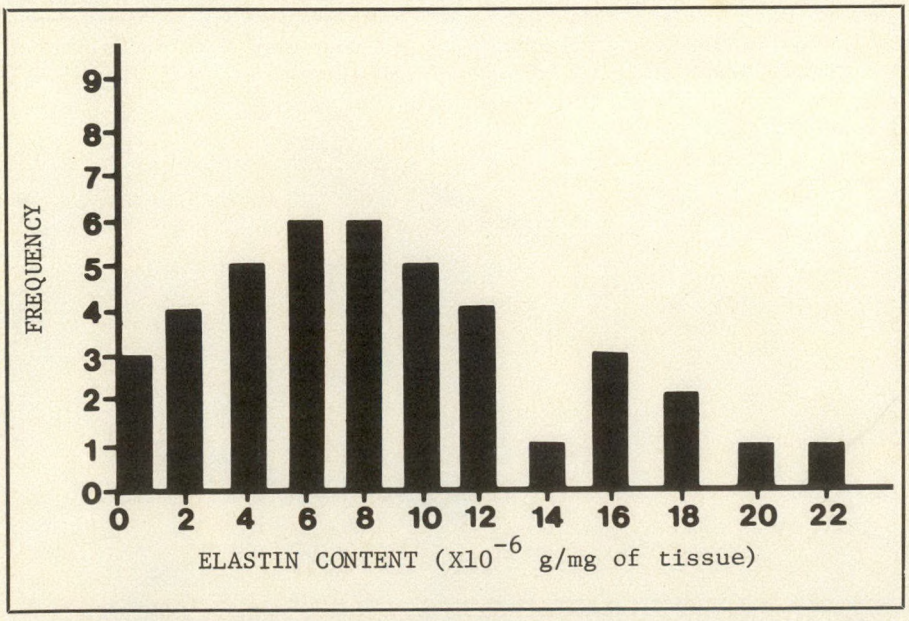

FIG. 2—Histogram depicting elastin content in granulation tissue from rat liver. Mean content of elastin was 8.5×10^{-6} g/mg of tissue.

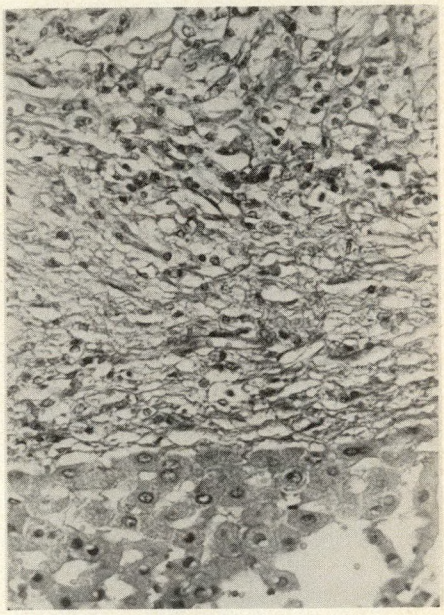

FIG. 3—Granulation tissue preparation in rat liver, showing normal hepatic parenchyma (at bottom) and granulation tissue with fibroblasts, collagen and new vessels (hematoxylin and eosin, reduced by 52% from ×250).

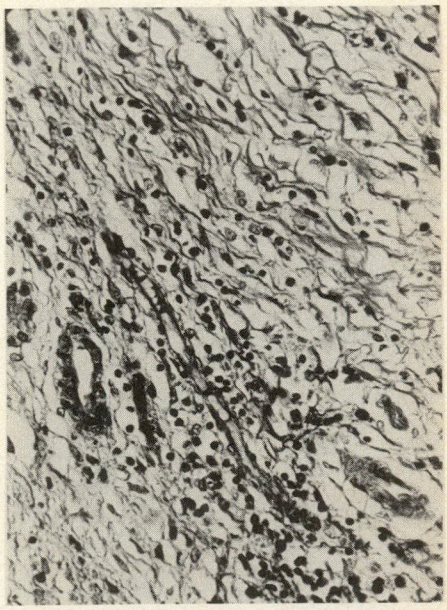

FIG. 4—Granulation tissue preparation in rat liver. Cellular elements are present including fibroblasts and endothelial cells plus collagen fibres (Masson's trichrome stain, reduced by 52% from ×250).

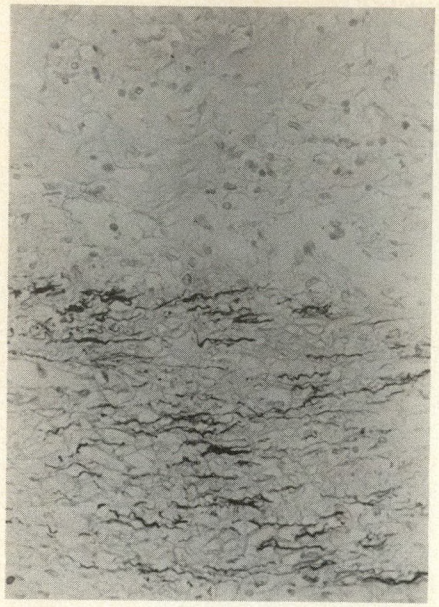

FIG. 5—Granulation tissue preparation. Darkly staining elastic fibres are evident in bottom half. Same orientation as in Figs. 3 and 4 (Weigert's resorcin-fuchsin stain, reduced by 52% from × 250).

plored under general anesthesia, the tubes were removed from the liver and the peritoneal cavity was closed. Approximately 10 hours later the animals were sacrificed and the liver wound was inspected. In both cases no residual tract could be identified thereby indicating activity of the contractile mechanism of granulation tissue.

Conclusions

Rat liver contains no biochemically detectable elastin using the modified technique of Naum and Morgan. The samples of granulation tissue formed in the liver all contained biochemically detectable elastin and overall amounts were approximately one third of the amount of elastin present in the wall of the aorta. Histologic examination showed that the elastin was concentrated in the outer one half of the granulation tissue, nearest the host tissue. The properties of resiliency, elasticity and tensile strength[13] suggest that elastin could play a role in wound contraction.

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Predictive Value for Survival of Lymphocytes and Polymorphonuclear Leukocytes in Patients with Sepsis

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To study their value in predicting prognosis, tests were performed on peripheral blood lymphomononuclear cells and polymorphonuclear leukocytes in 34 critically ill patients with sepsis. Initially, the number of lymphomononuclear cells was reduced by 32% compared with healthy control subjects and was 42% lower in those who died than in survivors. The values remained low in those who died. The numbers of T and B cells, determined by rosette formation using sheep and mouse erythrocytes, did not change during the period of observation. Initially, K cell activity was decreased by 48% compared with normal activity. In those younger than 65 years, K cell activity was 68% lower in patients who later died than in survivors. It returned to normal at 20 to 30 days and decreased in those who died. Polymorphonuclear leukocyte adherence was decreased by 50% compared with healthy control subjects and tended to be lower in those who died. Chemotactic migration of polymorphonuclear leukocytes and intracellular killing of *Staphylococcus aureus* and *Pseudomonas aeruginosa* were not impaired. It was concluded that the lymphomononuclear cell count, K cell activity and adherence of polymorphonuclear leukocytes were decreased in patients with sepsis and that the values were useful in predicting prognosis.

Dans le but d'étudier leur valeur prévisionnelle pour le pronostic, des épreuves ont été effectuées sur les cellules lymphomononucléaires du sang périphérique et sur les leucocytes polymorphonucléaires chez 34 patients critiquement malades souffrant de septicémie. A l'origine, le nombre de cellules lymphomononucléaires était réduit de 32% comparativement à des sujets témoins sains et était de 42% inférieur chez ceux qui sont morts, par rapport aux survivants. Ces valeurs demeurèrent faibles chez ceux qui sont décédés. Le nombre de cellules T et B déterminé par la formation de rosettes à l'aide d'érythrocytes de mouton et de souris n'a pas changé durant la période d'observation. Au début, l'activité des cellules K était réduite de 48% comparativement à l'activité normale. Chez les patients de moins de 65 ans, l'activité des cellules K était 68% plus faibles chez les patients qui sont décédés par la suite, que chez les survivants. Elle est revenue à la normale après 20 à 30 jours et diminua chez ceux qui sont décédés. L'adhérence des leucocytes polymorphonucléaires était diminuée de 50% par rapport aux sujets témoins sains et tendait à être plus faible chez ceux qui sont morts. La migration chimiotaxique des leucocytes polymorphonucléaires et la destruction intracellulaire du *Staphylococcus aureus* et du *Pseudomonas aeruginosa* n'étaient pas altérées. On conclut que le compte de cellules lymphomononucléaires, l'activité des cellules K et l'adhérence des leucocytes polymorphonucléaires étaient diminués chez les patients souffrant de septicémie et que ces valeurs étaient utiles pour établir le pronostic.

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Innate and adaptive humoral and cellular resistance are important in determining the establishment and course of infections. Immunoglobulins, complement and polymorphonuclear leukocytes (PMNL) play the major role in controlling bacterial sepsis, and T cell lymphocytes (T cells) and large mononuclear cells are mainly responsible for resistance to viral and fungal infections. B cell lymphocytes (B cells), on sensitization by specific bacterial cell antigens, become plasma cells and they in turn produce the immunoglobulins. Patients critically ill with severe bacterial infections have abnormalities in the number and function of lymphocytes and PMNL that could seriously affect prognosis. Meakins and associates[1] showed that surgical patients who had a decrease in cell-mediated immunity had an increase in postoperative infections and mortality when compared with healthy control subjects. They determined the delayed hypersensitivity response to five recall antigens and defined anergy as the ability to respond to only one or none of the antigens. Also, they found that polymorphonuclear chemotactic migration was decreased in anergic patients.

There is a population of non-T, non-B cell lymphocytes that lyse nonisogenic cells in the presence of anti-target cell antibody,[2] a reaction known as antibody dependent cellular cytotoxicity (ADCC). When nucleated target cells are used, this reaction is mediated by nonimmune lymphocytes known as "killer" or K cells. The role of K cells in sepsis is not known.

We have determined the number of lymphomononuclear (LMN) cells, T and B cells, the function of K cells, and adherence, chemotaxis and intracellular killing of PMNL in the peripheral blood of patients critically ill with sepsis. The values were determined during the course of sepsis to find out if they aided in predicting prognosis.

Methods

We studied 34 patients (23 men and 11 women) with sepsis who were admitted to the critical care/trauma unit of Victoria Hospital, London, Ontario. Their ages ranged from 18 to 83 years (mean 53 ± 3.2 years). All were critically ill, had a source of infection and a febrile response, and most had positive results from blood cultures. Patients with negative results of blood cultures were included when they had previously been given antibiotics. Most patients had a Swan-Ganz catheter inserted to monitor pulmonary and systemic hemodynamics. These patients had an increased cardiac output and low peripheral resistance, characteristic of sepsis.

The patients were studied from the time of admission to the unit until the septic state resolved and they were discharged from the unit, or until they died. The control group consisted of healthy individuals matched with the 34 patients for age and sex.

Lymphomononuclear Cells

The number of LMN cells in the peripheral blood was the total leukocyte count times the percentage of the cells in the differential smear. For rosette formation, lymphocytes were isolated from the peripheral blood using Ficoll-Hypaque®. Equal volumes of lymphocytes and sheep red blood cells were incubated at 37°C for 15 minutes. The supernate was removed and a portion of the residue placed on a slide and 200 lymphocytes were examined microscopically for rosette formation. A rosette was defined as the presence of three or more sheep erythrocytes in contact with a lymphocyte. The results were expressed as per cent rosette formation. Early rosettes were those present after incubation for 1 hour and total rosettes those present after 18 hours. We made this distinction because early rosettes may be a family of functional T cells while the total count identifies all the lymphocytes that have T cell markers on their surface. B cells were determined from rosette formation using mouse erythrocytes.

The ADCC test was performed as described previously.[3] Murine P-815 mastocytoma cells were incubated with sodium chromate. Antimastocytoma cell antibody was produced in the rabbit. Mastocytoma cells labelled with chromium-51, antibody and peripheral blood lymphocytes were incubated for 3 hours at 37°C. Control samples for measurement of maximal release of isotope had hydrochloric acid added. Isotope release was determined in the supernate using a well-type scintillation counter.

Lysis was calculated as follows:

$$\%\ \text{specific release of } {}^{51}\text{Cr} = \frac{ER - SR}{MR - SR} \times 100,$$

where ER is experimental release, SR is spontaneous release and MR is maximal release.

The ratio of the number of lymphocytes to mastocytoma cells required to lyse 50% of 10 000 cells was defined as 1 lytic unit. An increase in lytic units signified a decrease in the number of mastocytoma cells lysed by a given number of lymphocytes. The reciprocal of the number of lytic units to lyse 50% of 10^6 mastocytoma cells was used so that an increase in value signified an increase in ADCC activity. To correct for lymphopenia, the number of lytic units per 10^6 cells was multiplied by the ratio of LMN cells times the total leukocyte count. The results were expressed as lytic units times 10^6 mastocytoma cells per millilitre of blood.

Polymorphonuclear Leukocytes

Adherence of PMNL was determined with heparinized whole blood by the method described by MacGregor.[4] The percentage of cells that adhered to nylon fibres was determined by placing the cells in a Pasteur pipette (Scientific Products Division, American Hospital Supply Corp., McGraw Park, IL) containing 80 mg of fibres packed to a height of 15 mm. The value was calculated as follows:

$$\%\ \text{adherence} = \frac{CA - CE}{CA} \times 100,$$

where CA is the number of cells in the affluent and CE is the number of cells in the effluent.

For assays of polymorphonuclear leukocytic chemotaxis and intracellular killing, isolated cells were suspended in Krebs-Ringer phosphate (KRP) solution at pH 7.45 containing 0.006 M glucose and 0.35% bovine serum albumin (Sigma Chemical Co., St. Louis, MO).[5]

Chemotactic attractant was prepared from the bacteria-free supernatant of an 18-hour growth of *Escherichia coli* in Medium 199®.[6] It was diluted to 25% by volume with KRP solution and placed in the lower compartment of a Boyden chamber (Schleicher & Schuell, Inc., Keene, NH). Polymorphonuclear leukocytes, 2.5×10^6, were placed in the upper compartment which was separated from the lower by a membrane filter GmbH, pore size 3 mμ (Sartorius Membran Filter, Göttingen, West Germany). The chambers were incubated for 3 hours in a humidified environment at 37°C. The filters were then removed, fixed, stained and examined. The average number of cells that had migrated to the undersurface of the filter membrane was determined at a magnification of 440× in five random fields within the area of a Whipple micrometre disc (Canlab Ltd., Toronto, Ont.). This number was the chemotactic migration value.

In the bactericidal experiments, hospital strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa* were grown for 18 hours in trypticase soy broth (Difco Laboratories, Detroit, MI). The organisms were separated by centrifugation, washed and resuspended in 0.9% sodium chloride at a concentration to yield 2.0×10^7 colony forming units per millilitre. To 0.1 ml of the suspension of organisms was added 0.5 ml of PMNL (2.0×10^7), 0.3 ml of KRP and 0.1 ml of AB serum as a source of opsonins. The mixture was then placed in capped plastic culture tubes (Falcon, Oxnard, CA) and agitated at 37°C on an Ames aliquot mixer (Fisher Scientific Co. Ltd., Don Mills, Ont.). Controls did not contain PMNL cells. A zero-time specimen was taken and 0.1-ml aliquots were removed after incubation for 15, 30, 60 and 120 minutes. The specimens were diluted with distilled water and placed on pour-plates. The number of colonies was counted after incubation at 37°C for 24 hours. The assays were performed in duplicate and the results expressed as the average of the two values.

Comparisons were made between the values recorded at the time of admission to the unit when the patients were critically ill and at the time of their recovery and discharge or before death. Student's *t*-test, with Yates' correction, was used for the statistical analyses and a probability of less than 5% was accepted as significant. Values were expressed as the mean ± standard error of the mean.

Results

The most frequent origins of the sepsis in the 34 patients studied were the abdomen, burns and peripheral vascular surgery (Table I). The infections were mostly bacterial; a few were fungal but there were no protozoal or viral infections. In survivors, the mean interval between admission and discharge was 24 ± 3.4 days; in those who died, it was 14.9 ± 4.0 days. The mortality was 47% from the complications of uncontrollable sepsis, such as respiratory, renal or hepatic failure.

At the time of admission to the unit, the number of LMN cells was decreased by 32% compared with healthy control subjects ($P < 0.01$) (Table II). In survivors, the values had returned to normal by the time of discharge from the unit but they remained low throughout the illness in those who died. The proportion of monocytes present (0 to 5%) was not related to survival or death, indicating that lymphopenia was the sig-

Table I—Origin of Sepsis

Origin	No. of patients
Abdomen	6
Burns	5
Peripheral vascular surgery	5
Multiple trauma	4
Pneumonia	4
Gynecologic operations	3
Congestive heart failure	2
Other	5

Table II—Number of Lymphomononuclear (LMN) Cells, Early T, Total T and B Cells and Function of K Cells in Peripheral Blood of Patients with Sepsis

	Controls	Upon admission		Upon discharge or before death	
		Survived	Died	Survived	Died
LMN cells, no.	2200 ± 72 (34)	1906 ± 360† (16)	1102 ± 151† (18)	2476 ± 460 (16)	1210 ± 268 (18)
Early T cell rosettes, %	54.1 ± 3.5 (11)	54.6 ± 2.9 (18)	55.9 ± 3.8 (16)	62.0 ± 3.0 (18)	60.3 ± 4.8 (16)
Total T cell rosettes, %	64.9 ± 2.9 (10)	66.8 ± 2.8 (18)	63.3 ± 3.2 (16)	66.8 ± 2.8 (18)	65.9 ± 3.9 (16)
B cell rosettes, %	6.9 ± 1.1 (8)	11.6 ± 1.8 (17)	16.2 ± 2.9 (15)	11.1 ± 2.3 (16)	11.5 ± 2.8 (13)
K cell activity, lytic units × 10^6 cells/ml	16.1 ± 1.8* (34)	7.4 ± 2.1* (17)	6.5 ± 1.8‡ (16)	12.3 ± 5.2 (17)	2.0 ± 0.6‡ (16)

Probable difference (Student's *t*-test) : *P < 0.01, †P<0.05, ‡P < 0.02.

nificant prognostic factor. Early T and total T cell numbers were normal initially and did not change during the period of observation (Table II). The percentage of B cells was normal and tended to increase in those who died (Table II). The difference, however, was not significant.

K cell activity was decreased by 48% at the time of admission ($P < 0.01$) and in the group as a whole was similar in those who lived and who died (Table II). However, in those under 65 years of age, there was a greater decrease in those who later died than in those who survived ($P < 0.05$, Fig. 1). This initial value was therefore predictive of later death or survival. In survivors, there was a return to normal at 20 to 30 days; in those who died, the final values were 68% lower than the initial values ($P < 0.02$).

The first values for adherence of PMNL were decreased by 50% and values in patients who survived did not differ from those in patients who died (Fig. 2). In patients who survived, the values had returned to normal when they were retested an average of 31 days later at the time of discharge from the unit. The results were the same for both sexes and in those younger or older than 65 years. Antibiotics, large doses of corticosteroids and central intravenous hyperalimentation had no effect (Table III).

There was no change in chemotactic migration during the period of observation (Table IV). Intracellular killing of *S. aureus* was not affected by sepsis. Killing of *P. aeruginosa* remained normal when incubation was for 15, 30 or 60 minutes but was increased when the incubation time was 120 minutes ($P < 0.05$).

Discussion

We found that sepsis was associated with a decrease in the number of LMN cells in the peripheral blood. Most of the patients in whom the decrease was 55% ($1100/mm^3$) or in whom a decrease persisted ultimately died. The simple observation of the number of LMN cells in the peripheral blood was extremely useful in indicating the severity of sepsis, in predicting prognosis and in monitoring the clinical course of the patient. This finding was in agreement with the observation in untreated patients with Hodgkin's disease that patients who died had a LMN cell count of less than $1400/mm.^{3,7}$ Similarly Meakins and colleagues[1] found that the lymphocyte count was decreased in anergic surgical patients and that in this group of patients there was a high frequency of sepsis and death.

Monitoring of early and total T cells and B cells, using rosette formation, was of no value in predicting prognosis in patients with sepsis. Meakins and associates[1] found that the percentage of T cell rosettes was decreased in anergic surgical patients and that those with a decrease had a high frequency of subsequent sepsis. The two populations differed only in that our patients had established sepsis, whereas the patients in the series reported by Meakins had infections subsequently.

There are conflicting reports on the role of B cells in surgical patients. Guggenheim and Buechler,[8] working with rats, and Hill and colleagues[9] found that malnutrition caused a decrease in the number of B cells, while Wunder,

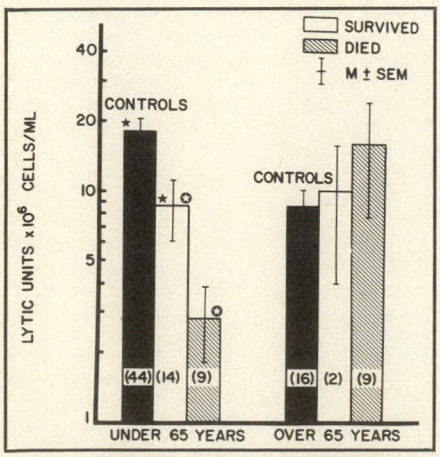

FIG. 1—K cell activity in patients with sepsis under and over 65 years of age (probable difference, Student's *t*-test, *P > 0.05, ⊛ P < 0.05).

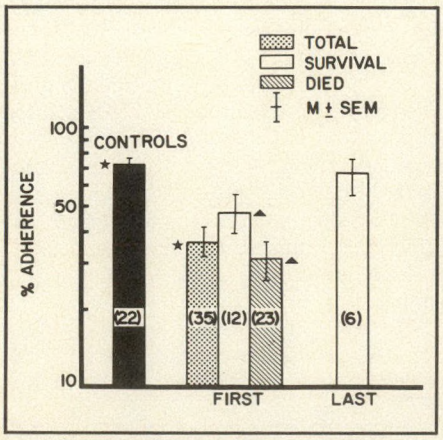

FIG. 2—Adherence of polymorphonuclear leukocytes to nylon fibres determined in patients with sepsis on admission and at time of discharge from unit or before death (probable difference, Student's *t*-test, *P <0.01, ▲ = not significant).

Table III—Effect of Antibiotics, Steroids and Central Intravenous Hyperalimentation on Percentage Adherence of Polymorphonuclear Leukocytes (PMNL) in 34 Patients with Sepsis

Treatment	Given	Not given
Antibiotics	33.7 ± 4.7 (24)	31.5 ± 11.1 (10)
Steroids	37.3 ± 6.1 (7)	27.9 ± 5.5 (27)
Hyperalimentation	35.1 ± 7.9 (9)	36.7 ± 5.2 (25)

Table IV—Intracellular Killing (%) of *Staphylococcus Aureus* and *Pseudomonas Aeruginosa* by PMNL

Organism	Time (min)	Controls	Total	Upon admission		Upon discharge
				Survived	Died	
S. aureus	15	53.0 ± 13.1	60.3 ± 5.3	57.2 ± 11.3	62.1 ± 5.8	50.0 ± 13.0
	30	77.7 ± 7.5	77.8 ± 4.0	77.5 ± 8.7	77.9 ± 4.4	73.9 ± 7.4
	60	88.4 ± 4.0	85.5 ± 2.0	83.1 ± 5.7	86.9 ± 3.5	88.9 ± 3.9
	120	96.3 ± 1.1	90.5 ± 2.1	89.0 ± 5.8	91.4 ± 1.5	95.9 ± 2.0
P. aeruginosa	15	66.2 ± 6.1	66.7 ± 3.3	65.2 ± 5.1	67.7 ± 4.5	57.2 ± 9.7
	30	85.2 ± 4.9	88.5 ± 1.5	85.4 ± 3.5	90.4 ± 1.0	72.6 ± 9.0
	60	93.7 ± 2.4	96.7 ± 0.8	94.9 ± 1.8	97.8 ± 0.5	91.9 ± 3.7
	120	97.7 ± 0.5*	99.3 ± 0.1*	99.5 ± 0.2	99.4 ± 0.1	96.5 ± 1.9

Probable difference (Student's *t*-test): * $P < 0.05$.

Stinnett and Alexander[10] found no change. Our results show that in the marked catabolic state associated with sepsis, the number of B cells is normal and does not change during the course of the disease.

In those under 65 years of age, K cell activity was decreased in patients with systemic sepsis, was lower in those who died ($P < 0.05$) and continued to decrease as the general condition deteriorated. It has already been noted that K cell activity is decreased in healthy people older than 65 years.[11] The results of our study indicated that sepsis is not associated with major defects in K cell function in the group as a whole. The decrease in critically ill patients with sepsis may be due to the direct toxic effects of the infections on the K cells or their progenitors or to the marked increase in tissue catabolism. It is not known if improvement of K cell activity will also improve the prognosis.

It has been assumed that immunologic surveillance is performed mainly by T cells. There is increasing evidence that K, natural killer (NK) and large mononuclear cells may play more important roles.[12] Athymic mice have few T cells but do not have an increase in non-lymphoreticular cancers. A greater number of malignant lymphoreticular tumours and skin cancers are found in patients with congenital deficiencies of T and B cells than in the normal population but few mesothelial or epithelial tumours are found, and patients with sarcoidosis and leprosy have fewer T cells but no increase in the frequency of cancer. If immunologic surveillance by T cells is important there should be an increase in non-lymphoreticular cancers in these patients. T cell deficiency is generally associated with an increase in fungal, viral and protozoal infections and B cell deficiency with an increase in bacterial infections. The predominantly bacterial infections seen in our study in patients with decreased K cell activity suggest that K cells may also play a role in bacterial infections, but to what extent we can only speculate.

We found that adherence of PMNL was decreased in patients with sepsis. Lentnek, Schreiber and MacGregor,[13] however, observed increased adherence in patients with inflammatory diseases, including localized sepsis. The difference in results was unlikely to be accounted for by differences in methodology. They used a lighter weight of nylon fibres than we did but this should have decreased rather than increased adherence. Treatment could affect the results. We found that results in males and females did not differ and that the use of antibiotics, steroids and central intravenous hyperalimentation had no effect on adherence, suggesting that the decrease in PMNL adherence was the direct result of sepsis and not of any coincidental treatment. Also, since the values returned to normal in survivors, it is unlikely that the impairment preceded the illness. The importance of a decrease in adherence of PMNL is not known. It may indicate that the cell is unable to adhere to the capillary endothelium prior to its passage through the wall of the vessel in response to a chemoattractant. For example, alcohol causes a decrease in adherence[14] and also inhibits migration of PMNL into Rebuck skin windows. Therefore the number of PMNL that reach a septic focus may be reduced. Additional simultaneous studies are required of adherence, migration using the skin window technique and chemotactic response.

We used heparinized whole blood for our studies on adherence of PMNL. The effect could therefore be produced by PMNL or plasma. MacGregor[4] showed that the effect of steroids on adherence is mediated by plasma, and that washed cells adhere normally. We are currently investigating the effect of plasma on adherence.

In contrast to our results, Meakins and coworkers[1] found that sepsis caused a reduction in chemotactic migration of PMNL. The techniques used were not similar. We determined the number of PMNL that had migrated to the undersurface of the chemotactic membrane after 180 minutes. Maximal migration was measured at that time.[15] Meakins and his group[1] measured the distance migrated after 120 minutes, in which case it is possible that the rate of migration was reduced yet total migration could have remained normal. Christou, Meakins and MacLean[16] found that there was a chemotactic inhibitory factor in the serum of normal and anergic patients and that there was an additional inhibitory factor in those who were anergic. They postulated that the decrease in chemotaxis they observed in anergic patients was responsible for the increase in sepsis.

Bactericidal function of PMNL in patients with sepsis may be unimpaired[1,17] or decreased.[18] We found that killing of *S. aureus* was normal and so was killing of *P. aeruginosa* when incubation was for 15, 30 or 60 minutes. It was increased, however, when incubation was for 120 minutes.

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BOOK REVIEWS

CLEFT CRAFT. The Evolution of its Surgery. III. Bilateral and Rare Deforities. D. Ralph Millard, Jr. 922 pp. Illust. Little, Brown and Company, Boston, 1977. Price not stated. ISBN 0-316-57138-5.

This book from one of the leading authorities on cleft lip and palate is advertised as authoritative, sometimes irreverent, often humorous but always sagacious in its assessment of bilateral and rare clefts. It is indeed all of that. It takes the reader through the embryology, anatomy and surgical history of the subject from its beginning to the present. It is well illustrated with diagrams, drawings and photographs, and has an excellent bibliography and index. It contains much historical information and good factual advice on the management of these difficult problems but it is not a book for the novice. For the uninitiated, the abundance of historical information and numerous viewpoints presented might confuse rather than clarify. Periodically, the author does summarize sections to give a rational approach; an excellent example of this is the chapter entitled "Outline of my approach to secondary bilateral cleft lip rhinoplasty". In the preceding 11 chapters the author has outlined in detail the problems of nasal deformity in bilateral cleft lips and the various approaches to its management. In this chapter he pulls it all together in six pages, dealing specifically with tip flatness and columella shortness, columella retraction, reduction rhinoplasty, submucous resection, shortness of vestibular lining, alar base deformities and retroposed maxilla.

Although most chapters are quite short the chapter on the projecting premaxilla is 40 pages long. This controversial subject certainly deserves an exhaustive discussion. The approaches of many prominent workers in this field are presented in detail along with the rationale of their method of management. Millard describes the period when total resection of the maxilla was used, resection of the vomer and setback, the years of disapproval of these techniques and finally presurgical orthodontic treatment for the protruding premaxilla. It is apparent that controversy still exists and that all the questions are not yet answered.

The first 31 chapters consider primary deformity and its correction. Millard makes it clear that definitive surgery on a lip should be performed at the primary operation. This is indeed a philosophy worth striving for although often difficult to achieve.

In the second section on secondary bilateral cleft deformities 23 chapters cover the management of these perplexing problems, many of which have resulted from inadequate primary surgery, but many, such as a short columella, are inherent in the anomaly itself.

The third section on rare clefts is relatively short, particularly so, considering that it deals with some of the most difficult reconstructive problems a surgeon faces. It does, however, make the book more complete and has a good bibliography to direct the reader to other original articles.

This book goes back to 1957 when the "Principles and Art of Plastic Surgery" by Sir Harold Gillies and D. Ralph Millard was published. The artistic presentation is similar in both publications and the authority of the authors comes through very strongly. Millard has given much credit to earlier workers in this field and has enriched the book with many of their pencil portraits. This book is not for the novice or uninitiated in the field but is a must for every surgical reference library and should be readily available for senior residents in plastic surgery.

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CORONARY ARTERY SURGERY. John L. Ochsner and Noel L. Mills. 275 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1978. $31.25. ISBN 0-8121-0620-2.

This book, dealing with the various aspects of coronary artery surgery, is very nicely laid out with excellent illustrations and is easily read. The 15 chapters encompass major considerations in preoperative evaluation, patient selection and preparation for surgery, the various operative techniques, the major anesthetic considerations, postoperative management, combined operations and reoperation. Accepted techniques are well described in a step-wise fashion while controversial techniques are avoided.

Cardiac surgical residents will find that the book is an excellent résumé of the subject. It also contains useful information for practising cardiovascular surgeons, cardiologists, cardiovascular nurses and paramedical personnel especially operating-room nurses.

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Treatment of Carotid Cavernous Fistula by Intravascular Occlusion Using a Balloon Catheter

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The surgical treatment of carotid cavernous fistula gradually evolved into a "trapping" technique. This technique includes ligation of the cervical internal carotid artery, clipping of the intracranial portion distal to the fistula and often embolization of the isolated segment. The development of embolization techniques using intravascular balloon catheters greatly simplified this treatment.

The authors report a case of spontaneous carotid cavernous fistula in which obliteration was achieved by an intracarotid balloon catheter. This was inserted by direct puncture of the carotid artery, which had been exposed by a simple neck incision. The patient's visual acuity was preserved. The efficacy, ease and safety of this method are emphasized.

Le traitement chirurgical de la fistule caverneuse carotidienne a progressivement évolué vers une technique de "piégeage". Cette technique comprend la ligature de l'artère carotide interne cervicale, le clip de la partie intracrânienne distale à la fistule et, souvent, l'embolisation du segment isolé. Le développement des techniques d'embolisation utilisant les cathéters intravasculaires à ballonets a grandement simplifié ce traitement.

Les auteurs signalent un cas de fistule caverneuse carotidienne spontanée où l'oblitération a été réussie grâce à un cathéter intracarotidien à ballonet. Celui-ci a été inséré par ponction directe dans la carotide qui avait été exposée par une simple incision du cou. L'acuité visuelle du patient a été préservée. L'efficacité, la facilité et la sécurité de cette méthode sont soulignées.

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The management of carotid cavernous fistula has challenged the ingenuity of surgeons since Travers[1] in 1809 first reported the successful treatment of such a case by ligation of the common carotid artery. In the ensuing years, numerous attempts have been made to devise a definitive form of treatment. These have included embolization alone,[2] or in combination with "trapping,"[3,4] electrothrombosis of the sinus[5-7] and direct repair of the fistula during cardiac standstill.[8,9] The most successful and widely practised is the "trapping" technique described by Hamby and Gardner[3] and Jaeger.[4]

The successful use of a balloon catheter to occlude a carotid cavernous fistula was first reported in 1971 by Prolo and Hanberry.[10] They used a no. 3 French Fogarty balloon catheter, passed it through the internal carotid artery to the site of the fistula and inflated it with positive contrast material thus obliterating the fistula. Others[11-14] have since reported success with this method.

The case reported here was treated in this way. The fistula remains obliterated 2 years after the procedure and the patient has had no ill effects from the permanently implanted balloon catheter.

Case Report

On July 15, 1975 a 54-year-old, right-handed woman experienced severe pain in her left eye associated with a loud "whooshing" sound in her left ear. The pain and noise persisted and after 2 days the eye began to close.

She was admitted to the St. John's General Hospital on July 25, 1975. Examination showed complete loss of function of the left third cranial nerve and dysesthesia in the distribution of the first and second divisions of the fifth cranial nerve. There was no exophthalmos. Visual acuity was normal. A loud bruit could be heard all over the head, maximally over the left orbit. A diagnosis of a spontaneous carotid cavernous fistula was made and was confirmed by bilateral carotid angiography (Fig. 1).

On Aug. 13, 1975, under general anesthesia and with electroencephalographic (EEG) monitoring, the left cervical carotid bifurcation was exposed. Tapes were passed around the internal, external and common carotid arteries. A 16-gauge Angiocath (Desereta Pharmaceuticals Canada Ltd., Port Credit, Ont.) was inserted into the proximal internal carotid artery. An 18-gauge Angiocath was then inserted into the bifurcation of the artery immediately below this. Through the 18-gauge Angiocath, 15 ml of Renografin-60® was injected and angiograms were made. A no. 3 French Fogarty embolectomy catheter was then passed by way of the 16-gauge Angiocath into the internal carotid artery.

The guide wire was withdrawn and enough Renografin-60® was injected to allow visualization of the catheter, which was maneuvered into the intracavernous portion of the carotid artery with fluoroscopic control. After the balloon was inflated with Renografin-60®, auscultation over the left orbit indicated that the bruit was no longer audible. Repeat angiography, however, showed that the fistula was only partially occluded. The catheter

was therefore withdrawn and the 16-gauge Angiocath was replaced by a 15-gauge one. Through this, a no. 4 French Fogarty catheter was inserted and threaded easily up to the fistula. Angiography after inflation of the balloon demonstrated that the fistula was totally occluded (Fig. 2).

Interestingly, the balloon had herniated into the fistula, plugging it and leaving a portion of the internal carotid artery patent. The Angiocath was withdrawn over the catheter, the end of which was occluded with two medium-sized clips (Ligaclips, Ethicon Sutures Ltd., Peterborough, Ont.). The redundant portion of the catheter was cut off. The catheter was fastened to the artery with a purse-string suture and the protruding end buried in the undersurface of the sternomastoid muscle. The common carotid artery was ligated.

Upon awakening from the operation, the patient noted that both the pain and the bruit had disappeared. After several days, the third nerve palsy began to regress, so that 1 week after the operation, the patient could open her eye. Visual acuity remained normal. Skull roentgenograms taken on Aug. 15, 1975, showed the contrast-filled balloon unchanged in size and position in the left paracellar region (Fig. 3). Antibiotic therapy consisting of ampicillin (1 g *q6h*) and cloxacillin (1 g *q6h*) was maintained for 10 days after operation. She was discharged from hospital on Aug. 30, 1975.

At follow-up examination 2 years later, all signs of the fistula were absent and there was no neurologic abnormality. Skull roentgenograms showed only a remnant of contrast material present at the site of the balloon (Fig. 4).

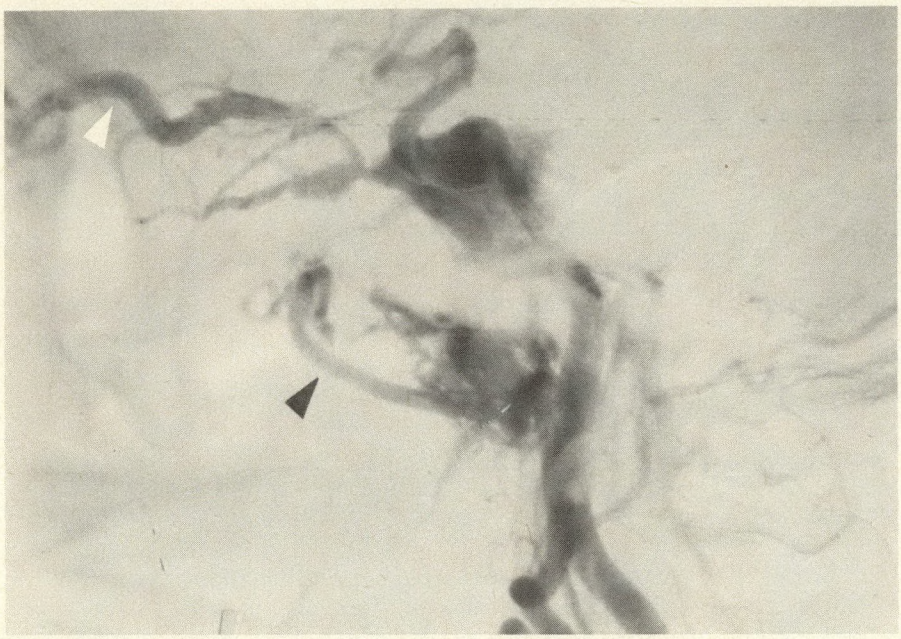

FIG. 1—Carotid arteriogram (subtraction study) demonstrating carotid cavernous fistula with brisk shunting via cavernous sinus into ophthalmic vein (white arrow). Shunting is also shown occurring through infraophthalmic vein (black arrow) into venous channels in nasopharynx.

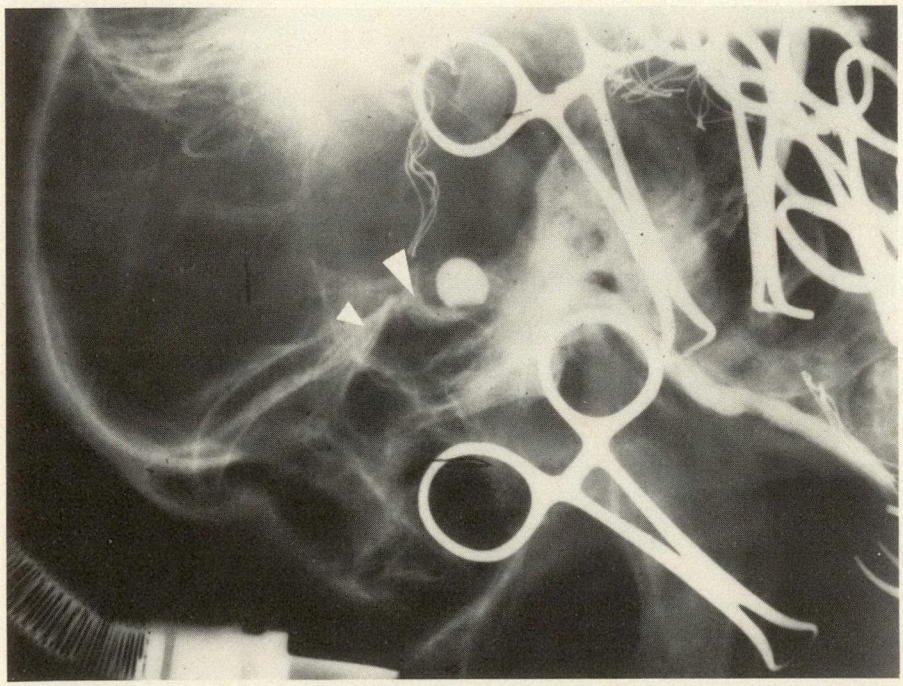

FIG. 2—Intraoperative carotid arteriogram showing contrast-filled balloon obliterating carotid cavernous fistula. There is some filling of supraclinoid carotid (large arrow) and ophthalmic (small arrow) arteries.

Discussion

The technique described above is a simple and safe way of obliterating a carotid cavernous fistula. Intraoperative fluoroscopy and angiography allow accurate balloon placement and demonstrate the degree of obliteration of the fistula. In our case, the importance of fluoroscopy and angiography is illustrated by the fact that with the initial small balloon, the fistula was not completely obliterated, even though the bruit had disappeared. In the postoperative period, the status of the contrast-filled balloon can be readily

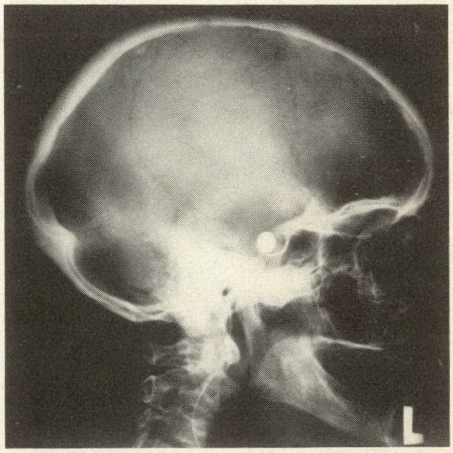

FIG. 3—Lateral skull roentgenogram showing contrast-filled balloon in place.

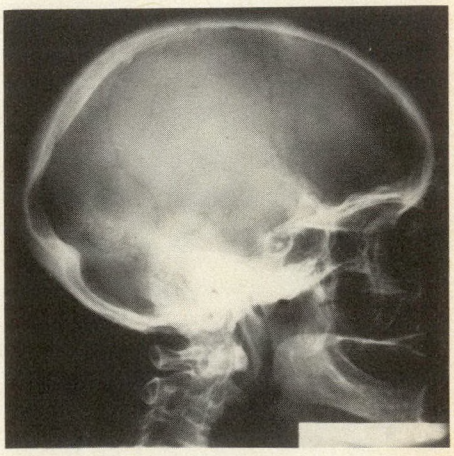

FIG. 4—Lateral skull roentgenogram taken at 2-year follow-up shows only remnant of contrast material in presumably deflated balloon.

Poulenc News

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Antiemetic Stemetil® shown to have beneficial effect on LOS tone

Aspiration of acid into the lungs remains a common cause of death associated with general anaesthesia. The lower oesophageal sphincter (LOS) is said to be a major mechanism which maintains competence of the gastro-oesophageal junction, and several drugs commonly used during anaesthesia may influence LOS tone, thereby increasing or decreasing the tendency to regurgitation.

Reporting in the July 1978 issue of the British Journal of Anaesthesia, researchers demonstrated that Stemetil (prochlorperazine) an antiemetic used commonly before and after surgery, significantly increases LOS tone without affecting oesophageal pressure. The resultant increase in Barrier Pressure (BP) decreases the tendency to regurgitation. The investigators measured an average increase of BP from 2.31 kPa to 3.36 kPa ($P<0.005$) in 8 volunteers following the I.V. administration of 12.5 mg Stemetil.[1]

This information further enhances Stemetil's reputation as a pharmacologically complete antiemetic. In addition to its effect on LOS tone, Stemetil's multi-level antiemetic action promptly stems nausea and vomiting of central or peripheral origin. Its anxiolytic action[2] inhibits cortical impulses associated with "psychological vomiting". Its C.N.S. action directly blocks the chemoreceptor trigger zone,[3,4] raising the threshold for impulses arriving at the medullary vomiting center.

Stemetil in Radiation Sickness

The results of a trial involving 45 patients who developed nausea and vomiting following radiation therapy showed that Stemetil was effective in all of the patients within 1-2 days, with good to excellent results.

Stemetil was administered in a dosage of 10 mg b.i.d. after the onset of nausea and vomiting, and was continued for 5-10 days after symptoms ceased. The only side effect was drowsiness, which might not have been drug related.[5]

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followed by plain skull roentgenograms.

We ligated the common carotid artery as described in other reports.[11,12,14] This is probably not necessary and certainly increases the risk of cerebral ischemia.[15] The catheter can be adequately fastened to the vessel with a purse-string suture and the proximal protruding end occluded by metal clips. This procedure appears to prevent deflation of the balloon, at least until thrombosis of the fistula occurs. Intraoperative EEG monitoring will warn of cerebral ischemia. Superficial temporal to middle cerebral artery bypass has been used before occlusion of the fistula to protect the blood supply to the endangered hemisphere (Ford R, Richardson P, Anderson D: Unpublished data, 1978).

Two years after operation, skull roentgenograms of our patient showed that the balloon had deflated; however, the patient remained asymptomatic, suggesting that the fistula had been obliterated by thrombus.

A detachable balloon has been developed[14,16] which can be left in the defect in the artery, obliterating the fistula while preserving the arterial lumen. This happened fortuitously in our case, the balloon actually herniating into the arterial wall defect and occluding the fistula, while sparing a portion of the lumen of the internal carotid artery.

As reported by others,[10-12] we found that the flexible catheter easily negotiated the curves of the carotid artery. Our patient's visual acuity remained normal, presumably because of the beneficial hemodynamic effect of preserving flow through the ophthalmic artery, while at the same time lowering intraocular venous pressure.[10,17]

We found that a no. 4 French Fogarty catheter passed easily through the 14-gauge Angiocath and that direct puncture of the artery with the needle was simpler than performing an arteriotomy. As we suspected, and as subsequently been shown,[13] this procedure may be performed by a percutaneous technique.

Summary

Occlusion of a carotid cavernous fistula was achieved by an intracarotid balloon catheter which was inserted by direct puncture of the exposed carotid artery. The patient's visual acuity was preserved and all symptoms and signs of the fistula were absent at follow-up 2 years later, despite collapse of the balloon. We suggest, particularly since a detachable balloon has recently been developed, that this is the preferred method of treatment for carotid cavernous fistula.

We thank Mrs. June Wheeler, RN, for her expert assistance with the procedure and Mrs. Patricia Sweetapple for typing the manuscript.

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Percutaneous Transfemoral Retrieval of the "Runaway" Ventriculoatrial Shunt

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A 22-year-old man with a ventriculoatrial shunt was admitted to hospital for investigation of headache, nausea and vomiting. During a procedure done to convert the ventriculoatrial shunt to the ventriculoperitoneal type, the shunt tubing was inadvertently cut in the neck. The atrial end was found to have migrated into the right atrium. It was recovered by percutaneous cardiac catheterization through the femoral vein. The patient tolerated the procedure well. The authors believe that this method of retrieval is easier and carries less operative risk than previously reported methods.

Un jeune homme de 22 ans porteur d'une dérivation ventriculo-auriculaire a été hospitalisé pour investigation d'une céphalée, nausées et vomissements. Au cours d'une intervention pratiquée dans le but de transformer une dérivation ventriculo-auriculaire en dérivation ventriculo-péritonéale, la tubulure de dérivation fut sectionnée par inadvertance au niveau du cou. On s'aperçut que l'extrémité auriculaire avait migré dans l'oreillette droite. Elle fut recouvrée par cathétérisme cardiaque percutané dans la veine fémorale. Le patient supporta bien l'intervention. Les auteurs croient que cette méthode de récupération est plus facile et comporte moins de risques opératoires que les méthodes préalablement décrites.

Migration of the atrial catheter into the heart is a known,[1-5] but relatively uncommon, complication of ventriculoatrial shunting. It may occur as a result of spontaneous disconnection of the catheter from the ventricular part or during revision of the shunt. In the past this complication has been left untreated in the hope that it would not cause embolization,[4] or has been retrieved by thoracotomy or more recently[5,6] by cardiac catheterization through the internal jugular vein. We present the case history of a patient in whom the atrial catheter was recovered by percutaneous transfemoral cardiac catheterization.

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Case Report

A 22-year-old man was admitted for the 10th time to the University Hospital, Saskatoon, on Jan. 18, 1978. He complained of intermittent headaches, nausea and vomiting which had started 1 month earlier. His first hospitalization had been in 1973 for treatment of a head injury resulting in intracerebral, subdural and epidural hematomas of the right cerebral hemisphere. These were removed surgically. Subsequently cerebrospinal fluid rhinorrhea developed due to a fistula, which was repaired, and later he had hydrocephalus, which was treated by inserting a ventriculoperitoneal shunt. The shunt had been revised several times over the years because of blockage of the tubing. At the time of this admission a ventriculoatrial shunt was in place.

On physical examination the Holter shunt reservoir appeared to be emptying slowly but filling rapidly, suggesting a block of the atrial end, which was confirmed by radioisotope scanning. On Jan. 23, 1978, the patient underwent operation to convert the ventriculoatrial shunt to a ventriculoperitoneal shunt. During the procedure the shunt tubing was inadvertently cut in the neck. The ventricular end was noted to be patent and leaking cerebrospinal fluid. The atrial end could not be located. A tunnel was found in the subcutaneous tissue from which the shunt tubing had retracted inferiorly. An intraoperative roentgenogram of the neck and chest (Fig. 1) showed the upper end of the radiopaque shunt tubing to be 10 cm cephalad to the right clavicle. Further dissection down the tunnel failed to discover the shunt tubing. The proximal tubing was connected to a Codman Accuflo abdominal shunt tubing (Codman & Shurtleff, Inc., Randolph, MA) and placed in the peritoneal cavity. On Jan. 25 we again attempted to retrieve the tubing by dissection in the lower part of the neck, but to no avail. An intraoperative roentgenogram showed the upper end of the tubing resting 2 cm cephalad to the clavicle (Fig. 2).

On Jan. 26 an open-tipped no. 8 Teflon catheter was introduced into the right femoral vein under local anesthesia. This was passed up to the superior vena cava under fluoroscopic control. A curved safe T-3 wire guide (Cook Inc., Scarborough, Ont.) was then bent double and the loop thus formed was passed through the catheter until about 6 cm of it protruded

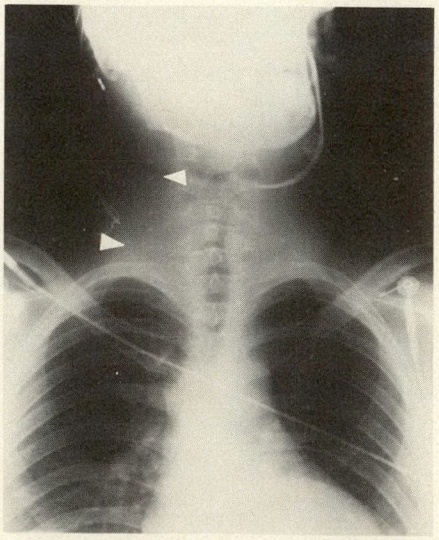

FIG. 1—Intraoperative roentgenogram of neck and chest (Jan. 23, 1978) made after shunt tubing was cut. Upper end of distal tubing is seen 10 cm above clavicle (higher arrow). New ventriculoperitoneal shunt is in situ (lower arrow).

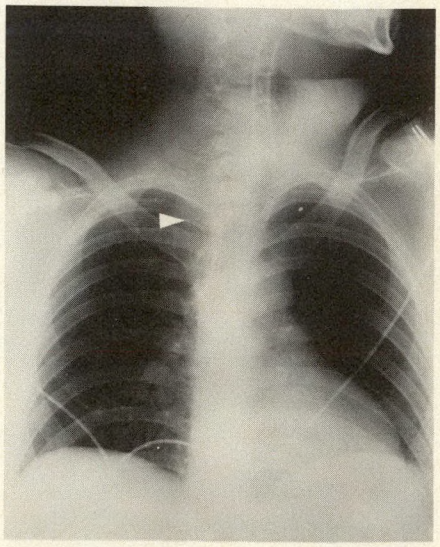

FIG. 2—Intraoperative roentgenogram of neck and chest (Jan. 25, 1978) made during second attempt to retrieve tubing from neck. Top of cut shunt tubing (arrow) is now 2 cm cephaled to right clavicle.

beyond the catheter tip. It was then maneuvered as a snare under fluoroscopic control until the shunt tubing was trapped between the wire and the Teflon catheter (Fig. 3). The catheter, wire and shunt tubing were then pulled out of the femoral vein en bloc. The patient tolerated the procedure well. His recovery was smooth and he was discharged home on Feb. 4, 1978.

Discussion

Catheterization of the right atrium through the femoral vein is a relatively simple procedure, especially in adults. Its use for retrieval of cardiac foreign bodies was first suggested by Tatsumi and Howland.[5] By catheterizing the heart with a Teflon catheter and using a wire snare, a major thoracic operation is averted. It should be possible after a few attempts under fluoroscopic control, to anchor the runaway shunt catheter to the cardiac catheter by trapping it between the wire and cardiac catheter.

The first reported case of recovery of a shunt catheter from the atrium by cardiac catheterization was that of Tatsumi and Howland[5] who used the internal jugular vein from which the shunt had escaped. McCulloch and Cartledge[6] used a flexible rongeur forceps successfully through the same vein. We believe that there is a potential danger in this approach as a thrombus may be dislodged and enter the heart in the process of catheterization or introduction of the rongeur forceps.

Some neurosurgeons prefer to leave the catheter in the heart or internal jugular vein as long as the patient has no symptoms. This may be dangerous since septicemia and thromboembolic complications may develop.[7-9] Cardiac tamponade, erosion and penetration of the cardiac wall and cardiac arrythmia[5] are other well-documented occurrences. In our opinion a free portion of a shunt catheter should not be left in the atrium but should be removed as soon as possible by femoral venous catheterization.

Retrieval of the catheter under fluoroscopic control would have been impossible if the catheter had not been radiopaque. It is, therefore, most important to use radiopaque atrial shunt tubes or tubes with radiopaque markers for all ventriculoatrial shunt procedures.

We thank A. Jean MacGregor, assistant professor of medicine and medical illustrator, for illustrating the retrieval procedure in Fig. 3 and Mrs. M. Faulkner for secretarial assistance.

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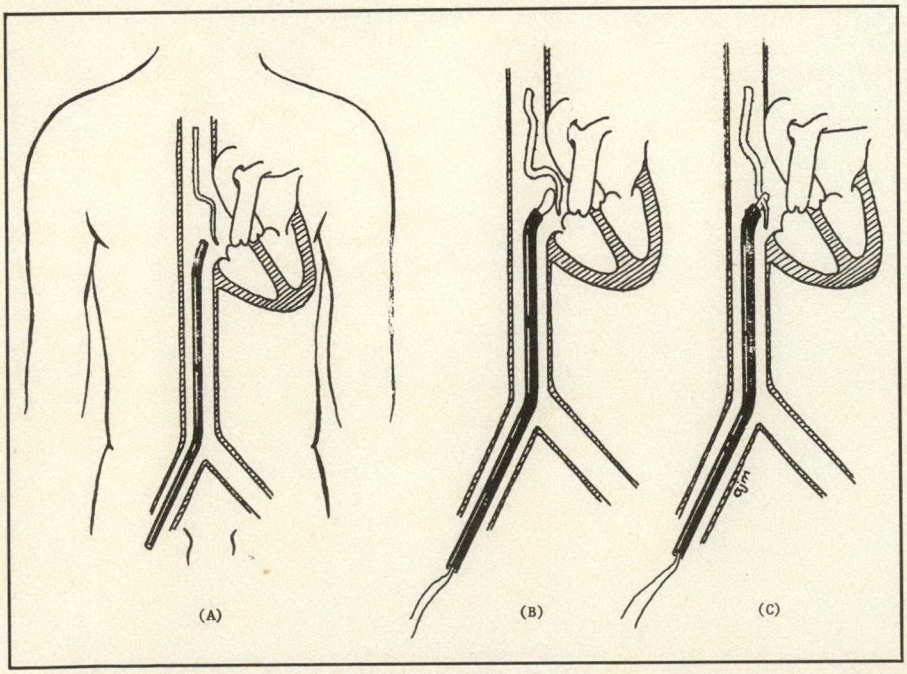

FIG. 3—Procedure for retrieval: (A) Teflon catheter is placed in right atrium. (B) Looped guide wire is placed in right atrium through Teflon catheter. (C) Shunt tubing is trapped between catheter and wire and is pulled out.

BOOKS RECEIVED

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A Major Advance in Controlling Upper Gastrointestinal Bleeding

Tagamet® INJECTION (cimetidine)

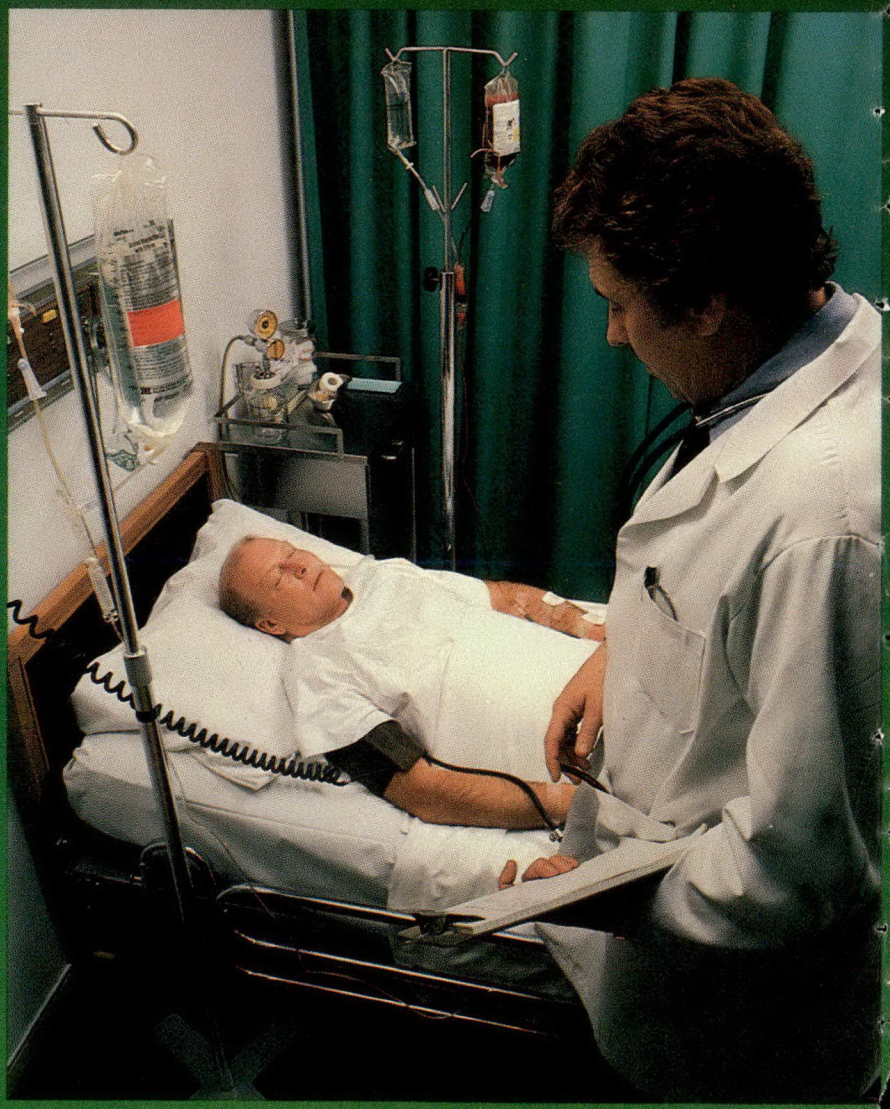
Rapidly Controls Bleeding

In hemorrhage due to stress lesions, bleeding stopped in most patients within 2-6 hours after treatment with 'Tagamet' began, and endoscopic reassessment at 24 hours showed that 57 out of 61 patients (93.4%) had stopped bleeding.[1]

In an additional study with 'Tagamet' it was concluded "that cimetidine is an effective agent for controlling bleeding from hemorrhagic gastritis, even in situations where other medical and surgical measures failed".[2]

Permits Conservative Surgical Decisions

"The histamine H_2-receptor antagonist, cimetidine, was used in 27 patients with erosive gastritis, and bleeding ceased in 24. There is a prospect that such agents will obviate the necessity of total gastrectomy in the occasional resistant cases in favour of conservative surgery."[3]



The H_2 Receptor Antagonist

SK&F
a SmithKline company

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TM:M 69CA

Pr Tagamet®

(cimetidine)

Tablets and Injection

(Product Monograph available to practitioners on request.)

PHARMACOLOGICAL CLASSIFICATION

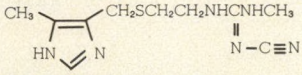
Histamine H_2-Receptor Antagonist

CHEMISTRY

Chemical Name:

Cimetidine is *N'*-cyano-*N*-methyl-*N'*-[2[[(5-methyl-1*H*-imidazol-4-yl) methyl] thio] ethyl] guanidine.

Structural Formula:



Molecular Formula: $C_{10}H_{16}N_6S$

ACTION

Cimetidine competitively inhibits the action of histamine at the histamine H_2 receptor, and thus represents a new class of pharmacological agents, the histamine H_2-receptor antagonists.

Cimetidine is not an anticholinergic agent. Studies have shown that cimetidine inhibits both daytime and nocturnal basal gastric acid secretion. Cimetidine also inhibits gastric acid secretion stimulated by food, histamine, pentagastrin, caffeine and insulin. Its ability to inhibit gastric acid secretion via this unique mechanism of action permits a new approach to the treatment of acid-related gastrointestinal disorders.

Cimetidine is absorbed rapidly after oral administration. The plasma half-life is approximately two hours. The principal route of excretion is the urine. The degree and duration of inhibition of basal and stimulated gastric acid secretion is dose-related; the data suggest that 80% or higher inhibition throughout a 24 hour period can be achieved by a dosage regimen of 300 mg four times daily given with meals and at bedtime.

Cimetidine 300 mg reduced total pepsin output as a result of the decrease in volume of gastric juice. The drug had no effect on the rate of gastric emptying or lower esophageal sphincter (LES) pressure.

INDICATIONS AND CLINICAL USE

'Tagamet' (cimetidine) is primary therapy for conditions where the inhibition of gastric acid secretion is likely to be beneficial, such as:

- —Duodenal ulcer
- —Non-malignant gastric ulcer
- —Gastroesophageal reflux disease
- —Management of upper gastrointestinal hemorrhage
- —Pathological hypersecretion associated with Zollinger-Ellison Syndrome, systemic mastocytosis and multiple endocrine adenomas.

CONTRAINDICATIONS

There are no known contraindications to the use of 'Tagamet' (cimetidine).

PRECAUTIONS

Use in Pregnancy; Nursing Mothers: There has been no experience, to date, with use of 'Tagamet' (cimetidine) in pregnant patients. Reproduction studies performed in rats, mice and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to 'Tagamet'. Studies have demonstrated that 'Tagamet' crosses the placental barrier. It is also secreted in the milk of animals. 'Tagamet' should be used in pregnant or lactating patients or women of childbearing potential only when, in the judgment of the physician, the anticipated benefits outweigh the potential risks.

Use in Children: Clinical experience in children is limited. Therefore, 'Tagamet' (cimetidine) therapy cannot be recommended for children unless, in the judgment of the physician, anticipated benefits outweigh the potential risks. In very limited experience, 20-40 mg/kg per day has been administered in divided doses by mouth or intravenously.

Use in Impaired Renal Function: Because 'Tagamet' (cimetidine) is excreted by the kidney, a reduced dosage should normally be administered to patients with impaired renal function. (See DOSAGE AND ADMINISTRATION)

Drug Interaction: In patients on coumarin-type anticoagulants, further prolongation of the prothrombin time has been observed with concomitant 'Tagamet' administration. For this reason, close monitoring is recommended, and adjustment of the anticoagulant dose may be necessary when these drugs are administered concomitantly.

Use in Gastric Ulcer: Symptomatic response to 'Tagamet' does not preclude the presence of a gastric malignancy.

ADVERSE REACTIONS

Mild and transient diarrhea, muscular pain, dizziness and rash have been reported in a small number of patients during treatment with 'Tagamet' (cimetidine). A few cases of reversible confusional states have been reported usually in elderly, severely ill patients such as those with renal insufficiency or organic brain syndrome. Overdosage may have played a role in some cases. These confusional states generally cleared within 24 hours of drug withdrawal. There have been reports that a few patients have developed mild non-progressive gynecomastia during prolonged treatment. No evidence of induced endocrine dysfunction was found, and the condition remained unchanged with continuing 'Tagamet' treatment. Rare cases of fever and interstitial nephritis which cleared on drug withdrawal, have been reported. Some increases in plasma creatinine and serum transaminase have been reported.

OVERDOSAGE

In cases reported to date, involving oral ingestion of up to 10 grams of 'Tagamet' (cimetidine), no untoward effects have been noted and recovery has been uneventful.

Treatment: The usual measures to remove unabsorbed material from the gastrointestinal tract, clinical monitoring and supportive therapy should be employed. Studies in animals indicate that assisted respiration may be of value and that any tachycardia may be controlled by administration of a beta-blocker.

DOSAGE AND ADMINISTRATION—ADULTS

(Experience with 'Tagamet' in children is limited and it has not been evaluated in clinical studies—see *PRECAUTIONS).*

In clinical studies 'Tagamet' (cimetidine) has been used in divided doses of up to 2400 mg a day.

DUODENAL ULCER

The recommended adult oral dosage for duodenal ulcer is 300 mg four times a day, with meals and at bedtime.

While healing with 'Tagamet' often occurs during the first week or two, treatment should be continued for at least four weeks unless healing has been demonstrated by endoscopic examination.

While some patients may require concomitant antacids initially, 'Tagamet' alone has been shown to promote rapid relief of symptoms.

Daily maintenance therapy may be used for those patients who would benefit from a reduction of gastric acid secretion, as well as those patients who are known to suffer frequent recurrence of duodenal ulcers. Following healing, maintenance therapy for periods of 6 to 12 months may be initiated at a reduced frequency of dosage, with the last daily dose taken at bedtime. After this period of maintenance, patients should be reassessed periodically, preferably by endoscopy.

NON-MALIGNANT GASTRIC ULCER AND GASTROESOPHAGEAL REFLUX DISEASE

The recommended adult oral dosage for non-malignant gastric ulcer and gastroesophageal reflux disease is 300 mg four times a day, with meals and at bedtime. While healing of non-malignant gastric ulcer may occur within the first two weeks, treatment should be continued *for at least six weeks* unless healing has been demonstrated by endoscopic examination.

While some patients may require concomitant antacids initially, 'Tagamet' alone has been shown to promote rapid relief of symptoms.

MANAGEMENT OF UPPER GASTROINTESTINAL HEMORRHAGE

In patients with upper gastrointestinal bleeding of sufficient magnitude as to require blood transfusions, 'Tagamet' should be administered parenterally, preferably by intravenous injection or intermittent infusion until 48 hours after active bleeding has stopped. At this time an oral dosage regimen may be instituted and should be continued for at least 7-10 days.

Recommended dosage for oral administration: 300 mg every 6 hours.

Recommended dosage for intramuscular injection administration: 300 mg every 6 hours. Inject the entire contents of a 2 ml ampul.

Recommended dosage for intravenous injection administration: 300 mg every 6 hours. Dilute 'Tagamet' in Sodium Chloride Injection (0.9%) (or other compatible i.v. solution) to a total volume of 20 ml and inject over 1-2 minutes.

Recommended dosage for intermittent intravenous infusion administration: 300 mg every 6 hours. Dilute 'Tagamet' 300 mg in 100 ml of Dextrose Injection (5%) (or other compatible i.v. solution) and infuse over 15-20 minutes.

In some patients it may be necessary to increase dosage. When this is necessary, the increases should be made by more frequent administration of a 300 mg dose, but total daily dosage should not exceed 2400 mg.

DOSAGE ADJUSTMENT FOR PATIENTS WITH IMPAIRED RENAL FUNCTION

Usage in patients with severely impaired renal function has been very limited. Cimetidine half-life has been determined in patients with varying degrees of renal insufficiency to be:

Creatinine Clearance	Cimetidine Half-life
50-80 ml/min.	2.6 hr.
10-50 ml/min.	2.9 hr.
<10 ml/min.	3.7 hr.

On this basis, the recommended dosage in those patients who have creatinine clearance rates lower than 10 ml/min., including those who are anephric, is 300 mg every 12 hours orally or by intravenous or intramuscular injection. Should the patient's condition require, the frequency of dosing may be increased to every 8 hours or even further with caution.

Hemodialysis: Greater than 80% of a 300 mg intravenous dose is cleared in a single 4 hour period of hemodialysis. It is completely cleared in an 8 hour period.

Peritoneal Dialysis: Peritoneal dialysis does not appear to remove cimetidine to any appreciable extent.

PATHOLOGICAL HYPERSECRETORY CONDITIONS (eg. Zollinger-Ellison Syndrome)

Recommended adult oral dosage: 300 mg four times a day with meals and at bedtime. In some patients, it may be necessary to administer 300 mg doses more frequently to control symptoms. Dosage should be adjusted to individual patient needs, but usually should not exceed 2400 mg per day. If intravenous administration is required, the dosage schedule should be the same as that recommended for control of upper gastrointestinal bleeding.

SPECIAL CASES

In patients in whom control of gastric acid secretion is desirable, the recommended oral dosage of 'Tagamet' is 300 mg four times a day, with meals and at bedtime. If intravenous administration is required, the dosage schedule should be the same as that recommended for control of upper gastrointestinal bleeding.

Stability of injectable form: 'Tagamet' Injection when added to or diluted with most intravenous solutions, such as Sodium Chloride Injection (0.9%) or Dextrose Injection (5% or 10%), is stable for 48 hours at normal room temperature.

'Tagamet' Injection should not be refrigerated.

AVAILABILITY

Tablets: Pale green, circular, biconvex, film coated tablets, each containing cimetidine 300 mg (monogrammed SKF T13). Bottles of 100 tablets.

Injection: Each 2 ml dose contains cimetidine HCl equivalent to 300 mg of cimetidine, in Sterile Water for Injection. Preserved with phenol, 0.5%. Ampuls of 2 ml, packaged in 10's.

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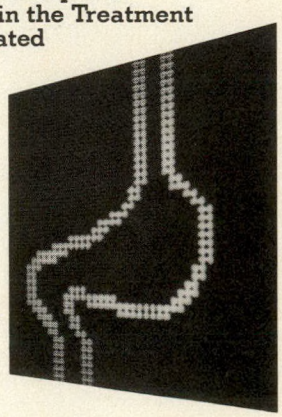
Creating a Therapeutic Revolution in the Treatment of Acid-Related Disorders



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Involvement of Small Intestine in Familial Polyposis Coli

D.A. WARMINGTON, MB, B CH, FF PATH, MRC PATH AND R.B. PASSI, MD, FACS, FRCS[C]

Extracolonic intestinal manifestations of familial polyposis coli have been described in recent years, but the exact frequency is still unknown. To date the more common sites of extracolonic polyposis appear to be stomach and duodenum with true adenomas being somewhat rare in jejunum and ileum. The authors report a further two cases of ileal polyposis in siblings from a family with familial polyposis coli and conclude that this condition cannot be considered as a disease exclusively of the large bowel. They emphasize that examination of the upper gastrointestinal tract and small bowel must be included in the investigation and follow-up of patients with familial polyposis coli.

Les manifestations intestinales extracoliques de la polypose colique familiale ont été décrites au cours des dernières années, mais leur fréquence exacte demeure inconnue. A ce jour, les foyers les plus communs de polypose extracolique semblent être l'estomac et le duodénum, alors que les adénomes véritables sont quelque peu rares dans le jéjunum et l'iléon. Les auteurs signalent deux nouveaux cas de polypose iléale chez des membres d'une famille atteinte de polypose colique familiale, et ils concluent que cette maladie ne peut pas être considérée comme une maladie du gros intestin exclusivement. Ils soulignent que l'examen des voies gastro-intestinales supérieures doit être inclus dans l'investigation et le contrôle ultérieur des patients souffrant de polypose colique familiale.

Familial polyposis coli is a well-known condition inherited through autosomal dominant transmission and characterized by multiple adenomatous polyps of the large intestine. The disease may be associated with Gardner's syndrome (hyperplasia and neoplasia in other tissues) and indeed, it has been suggested that the two conditions are the same disease.[1]

The existence of extracolonic lesions, in the form of stomach and small bowel polyposis, in cases of familial polyposis coli is a notion which, until recently, was not generally accepted. The classic concept of familial polyposis has been one of large bowel involvement with little or no expectation that polyps will be present in the rest of the bowel; at best the occurrence of polyps in the upper gastrointestinal tract of these patients was thought to be extremely rare, if indeed it ever occurred.[2,3]

Hauser was the first, in 1895, to describe the presence of multiple polyps of the stomach and small intestine in a case of familial polyposis coli.[4] Over the next 75 years, sporadic reports of this phenomenon were published as is aptly demonstrated in the analysis of Hoffman and Goligher[5] in 1971. According to the figures they obtained, the commonest sites for extracolonic polyp formation were stomach and duodenum in 11 and 10 instances respectively, followed by jejunum and ileum with 5 reported instances in each. (These figures represented a filtered-down analysis of the literature to that time, with exclusion of cases not clearly examples of familial polyposis.)

More recently, a number of publications, from the Japanese group in particular, have drawn attention to the occurrence of stomach, duodenal and small bowel involvement in cases of familial polyposis coli.[1,6-8]

Whether the generalized polyposis represents a variant of the common form of the disease as we know it,[8] or whether, as the Japanese workers and others have suggested, the apparent dearth of such cases merely represents a failure to detect the condition, are points still to be clarified.

With regard to anatomical distribution of the extracolonic polyps, recent publications support the apparent trend indicated by earlier reports that the stomach and duodenum are the most common sites followed by jejunum and ileum. At present, the ileum in cases of familial polyposis coli appears to be the least common of these extracolonic sites of polyposis. We present a further two cases of ileal involvement. The patients, a man and a woman, were siblings from a family with known familial polyposis.

Case Reports

Case 1.—In 1952 at the age of 26 years, on the basis of existing familial polyposis, a 52-year-old man had under-

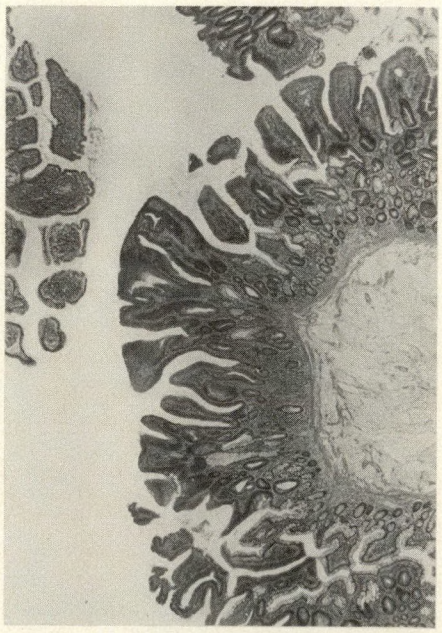

FIG. 1—Ileal villotubular adenoma (hematoxylin and eosin, reduced by 50% from ×100).

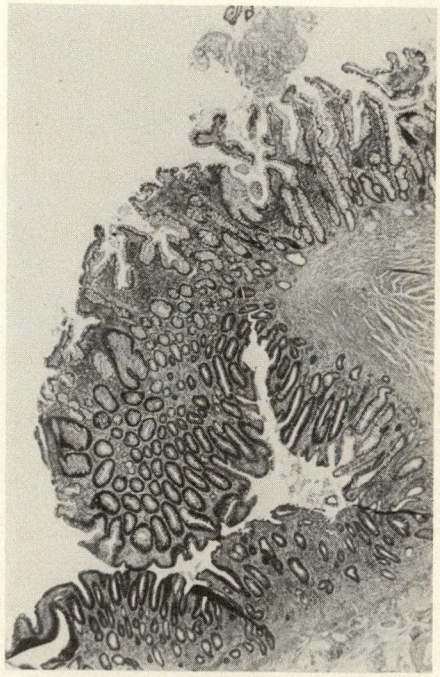

FIG. 2—Ileal adenoma with admixture of normal and abnormal glands (hematoxylin and eosin, reduced by 51% from ×100).

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gone colectomy and ileorectal anastomosis. Following the operation and in the interim period of 26 years, recurring rectal polyps were dealt with by means of electrofulguration and the patient remained clinically well. In February 1978 a segment of bowel including a 2.5-cm ileal cuff was removed because of a carcinoma found at the upper end of the rectal stump. In addition to the carcinoma, the rectal mucosa contained numerous polyps, ranging from 2 to 6 mm in diameter. Close inspection of the ileal cuff disclosed a diffuse nodularity of the mucosal surface; individual nodules did not exceed 1 to 2 mm in size. Histologic examination confirmed the presence of a rectal carcinoma with involvement of paracolic lymph nodes. The rectal polyps were tubular adenomas with no evidence of malignant change. Sections from the ileal cuff (Figs. 1 and 2) clearly demonstrated further adenoma formation, but now unequivocally involving small intestinal mucosa. The polyps were in close proximity to each other, in some instances with only a microscopic segment of normal mucosa intervening. The majority of the lesions were of simple tubular pattern, occasionally with villotubular variation. In each instance Paneth cells were readily identified in adjacent mucosa. Loss of mucosal villi was an early feature in some areas and the surface of these lesions was moderately flat. The overall appearance of the small bowel adenomas was identical to that of their large bowel equivalents. No evidence of malignant change was found in the small bowel polyps. The intervening segments of ileal mucosa were histologically unremarkable.

Case 2.—Following the diagnosis of familial polyposis at the age of 15 years, this 39-year-old woman, the sister of the patient in case 1, had undergone total colectomy with ileorectal anastomosis 24 years previously. As was the case with her brother, follow-up management had been that of frequent observation with fulguration of recurring rectal polyps. In March 1978 on the basis of dysplastic changes found in several polyps recently removed, an abdominoperineal resection was performed. Numerous adenomas were present in the rectal mucosa and a superficial carcinoma was also found on histologic examination. The accompanying ileal cuff (2 cm in length) demonstrated a patch of mucosal granularity measuring 0.3 cm in maximal dimension. Histologic examination of this granular area (Figs. 3 and 4) demonstrated small bowel tubular adenomas. In this instance the ileal lesions were not as numerous as in the case of her brother and some of the polyps contained lymphoid deposits deep to the adenomas. Further histologic study of the lesions revealed that they were identical to the small bowel lesions seen in case 1 and to their large bowel counterparts. The remainder of the ileal mucosa was free of adenomatous change.

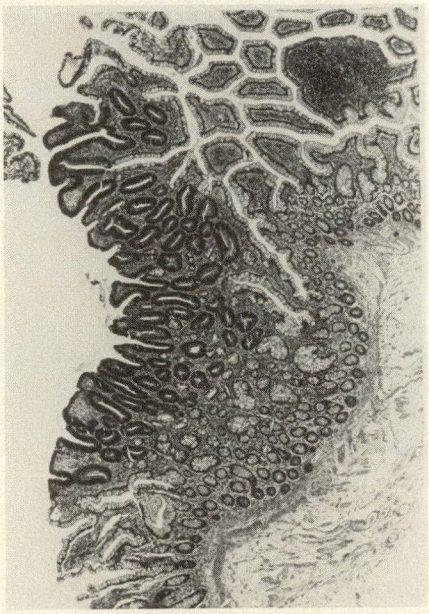

FIG. 3—Ileal microadenoma (hematoxylin and eosin, reduced by 53% from ×100).

Discussion and Conclusions

With regard to the microscopic morphology of ileal polyps in cases of familial polyposis, previously documented cases frequently demonstrated marked lymphoid hyperplasia, either alone or in combination with true adenomas.[6,7,9,10] Of our two patients, the brother had true adenoma formation while the sister had lymphoid hyperplasia in association with adenomas, but this did not account for false polyp formation on its own. (Two other members of this family have marked ileal lymphoid hyperplasia but without true adenoma formation.)

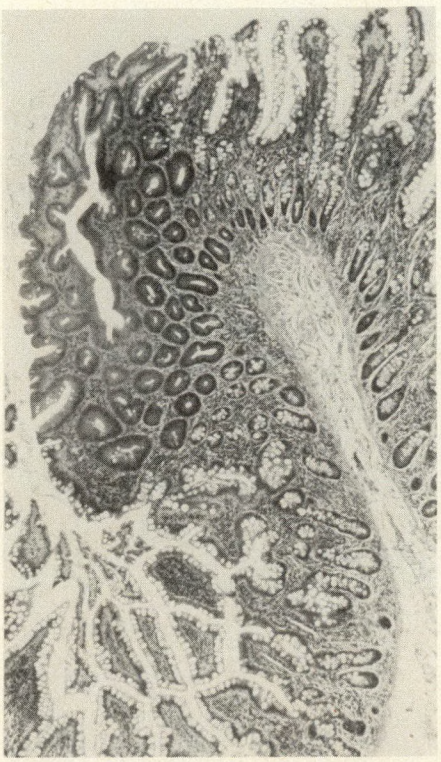

FIG. 4—Ileal adenoma with normal adjacent small intestinal mucosa (hematoxylin and eosin, reduced by 41% from ×100).

The concept that familial polyposis is exclusively a disease of large bowel can no longer be accepted[1,5-8] and we have presented two further cases of ileal adenoma formation in patients with familial polyposis coli. These findings emphasize the need for upper gastrointestinal tract and small bowel examination, both as part of the original work-up and in the follow-up of patients with familial polyposis coli.

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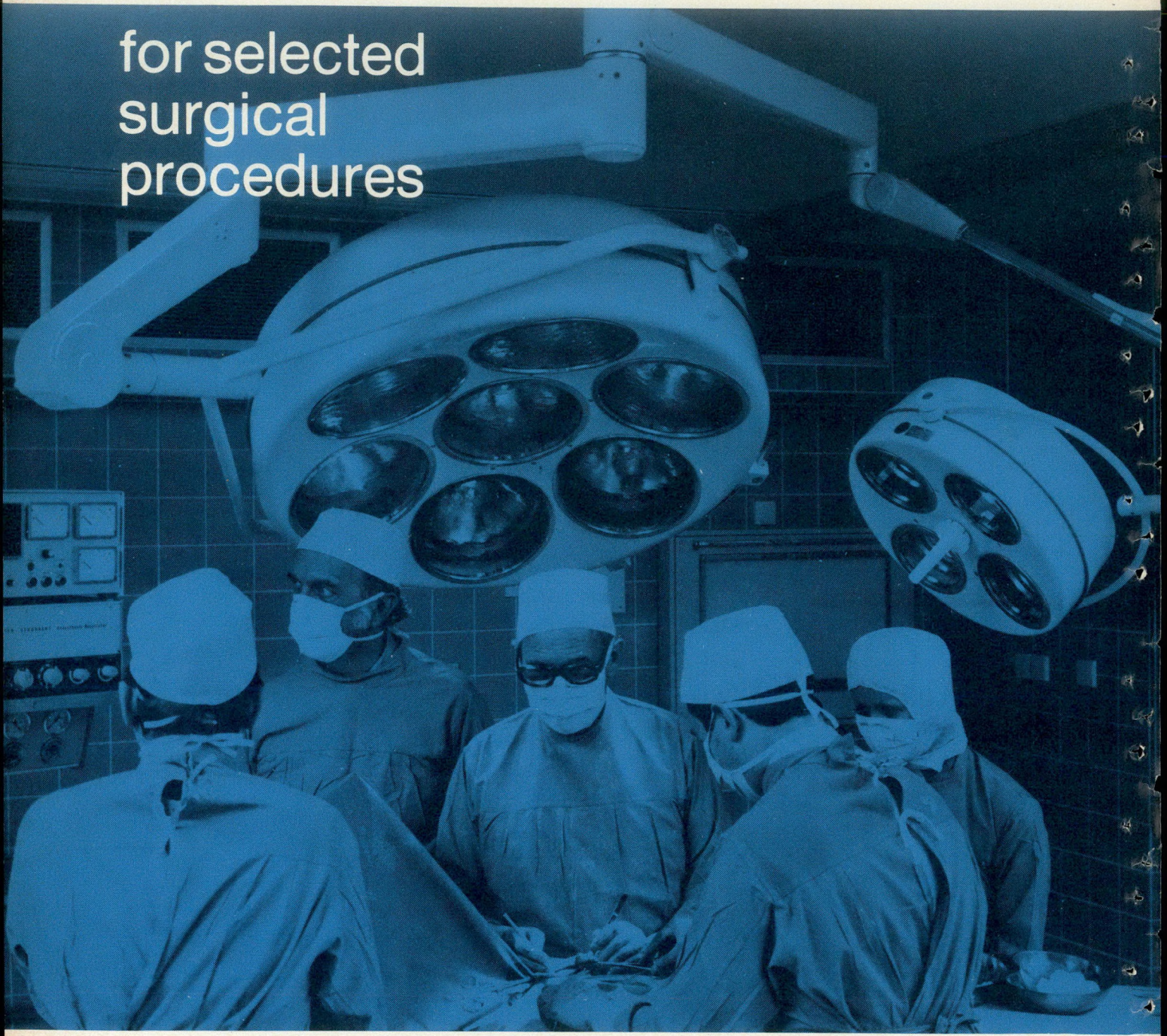
To lower
blood pressure
during
anesthesia

for selected
surgical
procedures



Nipride*

reduces excessive
blood loss

Nipride* (sodium nitroprusside)

for controlled hypotension during anesthesia

Rx Summary

'Nipride' is only to be used as an infusion with sterile 5% dextrose in water without preservatives. Not for direct injection.

Indications

'Nipride' is indicated for producing controlled hypotension during anesthesia to reduce bleeding in surgical procedures where deemed appropriate. Benefit-risk ratio should be carefully considered on an individual basis.

Contraindications

In the treatment of compensatory hypertension, e.g. arteriovenous shunt or coarctation of the aorta. It is also contraindicated in physically poor-risk patients (A.S.A. Risk 5), in patients with uncorrected anemia or hypovolemia or in those with known inadequate cerebral circulation. In patients with liver disease, severe renal disease, Leber's optic atrophy and disease states associated with vitamin B_{12} deficiency.

Warnings

'Nipride' is only to be used as an infusion with sterile 5% dextrose in water without preservatives. Not for direct injection. Infusion rates greater than 8 μg/kg/minute are virtually never required. If at this rate an adequate reduction in blood pressure is not obtained within 10 minutes, administration of 'Nipride' should be stopped.
Fatalities due to cyanide poisoning have occurred following sodium nitroprusside administration. One factor is common to all known cases, namely that large amounts of nitroprusside were infused at high rates. Since detoxification relies upon enzymatic action, the rare possibility of deficient or atypical enzymes occurring in humans should always be considered. Patients most apt to run into difficulties are those who are resistant to the hypotensive effect or those in whom maintenance at the selected blood pressure level is difficult or impossible.
Constant attention to the patient's dose-response characteristics is mandatory. If infusion rates are in excess of 8 μg/kg/minute determine the nature of the response (effective constant response at higher dose; tachyphylactic; resistant – none or less than expected). As soon as either tachyphylaxis or resistance is determined the infusion of 'Nipride' should be discontinued immediately. In abnormal responders it has been noted that metabolic acidosis may occur at higher doses.

Caution should be exercised in using 'Nipride' in patients with hypothyroidism or severe renal impairment.
Blood levels of thiocyanate should be determined if treatment is to be extended especially in patients with severe renal dysfunction. As long as blood thiocyanate levels do not exceed 10 mg/100 ml, it is probably safe to continue with the infusion. Peritoneal dialysis can be helpful if too high levels of thiocyanate are found.
Hypertensive patients are more sensitive to the intravenous effect of sodium nitroprusside than are normotensive subjects. Patients receiving concomitant antihypertensive medications (especially hydralazine or hexamethonium) are more sensitive to the hypotensive effect of sodium nitroprusside and the dosage of 'Nipride' should be adjusted downward accordingly.
The following Warnings apply to the use of 'Nipride' for controlled hypotension during anesthesia:

1. Extreme caution should be exercised in patients who are especially poor surgical risks (A.S.A. class 4 and 4E).
2. Tolerance to blood loss, anemia and hypovolemia may be diminished. If possible, preexisting anemia and hypovolemia should be corrected prior to employing controlled hypotension.
3. Hypotensive anesthetic techniques may alter pulmonary ventilation perfusion ratio. Patients intolerant of additional dead air space at ordinary oxygen partial pressure may benefit from higher oxygen partial pressure.
4. Resistance and tachyphylaxis occur more frequently in normotensive patients infused with sodium nitroprusside. Induction of deliberate hypotension in healthy young individuals may prove to be more difficult than in other segments of the population.
5. Upon discontinuance of the sodium nitroprusside infusion for the purpose of controlled hypotension during anesthesia a rebound hypertension has been observed on rare occasions.

Usage in pregnancy

The safety of 'Nipride' in women who are or who may become pregnant has not been established; hence, it should be given only when the potential benefits have been weighed against possible hazard to mother and fetus.

Usage in children

The safety of 'Nipride' in children has not been established. Clinical experience is limited.

Precautions

Adequate facilities, equipment and personnel should be available for frequent and vigilant monitoring of blood pressure. When the infusion is slowed or stopped, blood pressure usually begins to rise immediately and returns to pretreatment levels within one to ten minutes. It should be used with caution and initially in low doses in elderly patients, since they may be more sensitive to the hypotensive effects of the drug.
If, in the clinical situation, stress induced by pain or manipulation is reduced or eliminated during 'Nipride' infusion, the patient could experience a greater than expected reduction in blood pressure unless the rate of infusion is adjusted downward as required.
'Nipride' tends to deteriorate in the presence of light. Therefore, the infusion bottle should be wrapped with aluminum foil or other opaque material. Solutions of 'Nipride' should not be kept or used longer than four hours. 'Nipride' in aqueous solution yields the nitroprusside ion, which reacts with even minute quantities of a wide variety of organic and inorganic substances to form usually highly coloured reaction products (blue, green or dark red). If this occurs, the infusion should be replaced as quickly as possible.

Adverse reactions

Nausea, retching, emesis, diaphoresis, apprehension, headache, restlessness, agitation, muscle twitching, retrosternal discomfort and chest pain, palpitations, dizziness, faintness, weakness, rash, abdominal pain, confusion and somnolence have been noted with too rapid reduction in blood pressure. These symptoms rapidly disappeared with slowing of the rate of infusion or temporary discontinuation of infusion and did not reappear with continued slower rate of administration.
Irritation of the injection site may occur. Methemoglobinemia and one case of hypothyroidism following prolonged therapy have been reported.

Dosage and administration (for controlled hypotension)

Use of 'Nipride' in anesthetized normotensive patients undergoing deliberate hypotensive surgery must be restricted to carefully selected cases. There is a possibility of an abnormal response occurring in normotensive patients. In this event, the infusion of 'Nipride' should be discontinued immediately. (See Warnings).

The contents of a 50 mg 'Nipride' vial should be dissolved in 3 ml of sterile dextrose in water without preservatives. **No other diluent should be used.** Depending on the desired concentration, all of the prepared stock solution should be diluted in 500 or 1000 ml of 5 percent sterile dextrose in water and promptly wrapped in aluminum foil or other opaque material. Both stock solution and infusion solution should be freshly prepared and any unused portion discarded. The freshly prepared solution for infusion has a very faint brownish tint. If it is highly coloured, it should be discarded. (See Precautions). The solution should not be kept or used longer than four hours from initial reconstitution. The infusion fluid used for the administration of 'Nipride' should not be employed as a vehicle for simultaneous administration of any other drug.
'Nipride' dosage varies considerably from patient to patient, hence the need for individual titration. The infusion should be started at the lower dosage range, 0.5 μg/kg/minute and increased by 0.2 μg/kg/minute every 5 minutes until the desired reduction in blood pressure is obtained. The blood pressure usually starts to drop immediately or at least within a few minutes. Continuous monitoring of the blood pressure is necessary. Blood pressure should not be allowed to drop at too rapid a rate and systolic pressure should not be lowered below 60 mm Hg.
Infusion rates greater than 8 μg/kg/minute should rarely be used. The maximum recommended dose is 800 μg/minute.
'Nipride' should be administered by an infusion pump, micro-drip regulator or any similar device that will allow precise measurement of the flow rate. Avoid extravasation. The rate should be adjusted to maintain the desired hypotensive effect, as determined by frequent blood pressure determinations.
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Early Surgical Management of Acute Cholecystitis

STUART D. ARCHIBALD, MD, FRCS[C], NICHOLAS D. COLAPINTO, MD, FRCS[C] AND PETER FROST, MD, FRCS[C]

Between 1971 and 1977, 361 patients underwent early elective cholecystectomy for acute cholecystitis, and the complications and mortality were studied according to the length of time from admission to operation. A substantially greater proportion of the complications, and the only deaths, occurred in the patients operated upon more than 7 days after admission. The mortality rate was 0.6%. Nine additional high-risk patients underwent cholecystostomy. There were four postoperative deaths in this group, all related to the debilitating underlying conditions. The mortality for the entire series was 1.6%. These results compare favourably with those following delayed elective operations for acute cholecystitis. Early elective operation, using cholecystectomy when possible and cholecystostomy when necessary, is recommended for general use in experienced hands. This practice is safe and sound particularly when the diagnosis is made more certain preoperatively by the use of intravenous cholangiography.

Entre 1971 et 1977, 361 patients ont subi une cholécystectomie non urgente précoce pour cholécystite aiguë, et les complications et la mortalité ont été étudiées en fonction de l'intervalle écoulé entre l'hospitalisation et l'opération. Un nombre significativement plus grand de complications et les seuls décès sont survenus chez les patients opérés plus de 7 jours après l'hospitalisation. La mortalité a été de 0.6%. Neuf autres patients à risque élevé ont subi une cholécystostomie. Il y eut quatre décès postopératoires dans ce groupe, tous reliés aux maladies débilitantes intercurrentes. Pour cette série, la mortalité globale a été de 1.6%. Ces résultats se comparent favorablement à ceux qui suivent des opérations non urgentes retardées pour cholécystite aiguë. Une opération non urgente précoce, recourant à la cholécystectomie si possible et à la cholécystostomie si nécessaire est recommandée pour utilisation générale entre des mains expérimentées. Cette pratique est sûre et valable, surtout lorsque le diagnostic est rendu plus certain, avant l'opération, par l'emploi de la cholangiographie intraveineuse.

There has been continued dispute over the timing of operation in the management of acute cholecystitis. Three approaches have been recognized: emergency operation, delayed elective operation and early elective operation. Operation carried out as an emergency, formerly recommended when it was thought that the treatment of acute cholecystitis ought to parallel that of acute appendicitis,[1] is now usually reserved for salvage of deteriorating patients who initially have been managed expectantly.[2] Delayed elective operation is that performed 6 to 12 weeks after the conservatively managed acute cholecystitis has subsided. Proponents of this approach[3] argue that operations can then be performed after elective investigation, when patients have finally recovered from the acute cholecystitis and at a time when operation is easiest. Early elective operation consists of definitive surgery, performed in the first few days of the acute attack, as soon as the diagnosis is established and the patient optimally prepared.[4]

During the past 9 years at St. Michael's Hospital, Toronto, acute cholecystitis has been managed by early elective operation and now constitutes the most common reason for laparotomy in acute abdominal conditions.

Most cases have been treated by cholecystectomy, with cholecystostomy reserved for the few patients whose general condition was unusually precarious. A review of our experience in the 7-year period 1971 to 1977 is presented to assess the morbidity and mortality associated with this approach.

Patients and Method

A retrospective review was conducted of all patients in whom acute cholecystitis was diagnosed between Jan. 1, 1971 and Dec. 31, 1977, inclusive, and who underwent operation during the acute illness. There were 370 patients; 211 were female and 159 were male, giving a female:male of 1.3:1. Their ages ranged from 17 to 89 years (means 51 years) and 140 (38%) patients were over 60 years of age. The diagnosis was made clinically. In most recent cases, the diagnosis was confirmed preoperatively by 2-hour infusion cholangiography,[5] with tomography at the completion of the infusion and 6 hours later. At operation, the morphologic changes of acute cholecystitis were obvious in all instances. The patients who had cholecystectomy were grouped according to the time at which operation was performed after admission to hospital. The time of admission to hospital rather than of the onset of symptoms was selected as the starting point, because the latter could not be accurately determined from the records in all cases. In the great majority of those for whom this could be ascertained, the duration of symptoms before hospitalization was less than 24 hours. In order to determine whether the timing of early elective operation significantly influenced morbidity or mortality, the 361 patients who underwent cholecystectomy were studied in three groups: group 1, 199 patients who were operated on within 72 hours of admission; group 2, 121 patients who underwent operation between 72 hours and 7 days after admission; and group 3, 41 patients who were subjected to operation more than 7 days after admission.

In the last group, the delay of operation usually occurred in patients admitted to a nonsurgical service with unrecognized cholecystitis, and the longest time interval from admission to operation was 18 days. Thus group 3 does not include any patients who had "delayed elective operation" as defined above.

There were only nine cholecystostomies, too few to allow analysis by groups, and these are considered separately.

Results

Intravenous cholangiography was performed in 192 patients and gave

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"positive" results in 157 (82%), showing lack of filling of the gallbladder but opacification of the extrahepatic biliary tree on tomography. Twenty-eight studies failed to demonstrate either the gallbladder or bile ducts. There were no false-positive results. Only seven examinations gave false-negative results, in which the gallbladder was opacified, but the diagnosis of acute cholecystitis was nevertheless confirmed at operation, which was performed because of clinical findings. Thus in the cases in which the biliary tree was demonstrated, cystic duct obstruction was diagnosed with 96% accuracy. Only one serious allergic reaction occurred and this readily responded to treatment.

Cholecystectomy alone was performed in 282 patients, and both cholecystectomy and exploration of the common bile duct in 79 (21%). All patients had intraoperative assessment of their extrahepatic ducts and an operative cholangiogram was obtained when indicated, using the same criteria as in an elective cholecystectomy.

Postoperative complications (Table I) were most common in group 3 and of similar frequency in groups 1 and 2. Wound infection was the most frequent complication and was minor in all cases. Bile drainage was prolonged in four patients; in one patient it was due to a dislodged T tube and caused peritonitis, requiring reoperation. In none of these cases did retained common bile duct stones coexist. However, three other patients had retained stones. Three patients had either a subhepatic or subphrenic abscess. In two of these the presentation was in the early postoperative period; the third patient presented 3 months postoperatively with obstructive jaundice from extrinsic compression of the common bile duct (no retained stones were found). Rare complications were pneumonia, atelectasis, myocardial infarction, pulmonary embolism, septicemia, rectus sheath hematoma and postoperative urinary retention. The overall complication rate was 11.9%.

The mean hospital stay was 11.1 days.

There were two deaths in the series, both in group 3, giving a mortality within the three groups of 0.6%. One 82-year-old woman died of myocardial infarction as the culmination of a stormy course which included the development of a subphrenic abscess. The other patient was an elderly man who had a prolonged course of sepsis preoperatively, before transfer from another hospital. The operation, which was undertaken shortly after treatment was instituted for septic shock, was followed by multiorgan failure.

Nine cholecystostomies were performed, constituting 2.4% of our operations for acute cholecystitis. The mean age of patients in this group was 69 years. Three of the patients were admitted to hospital for another reason, and acute cholecystitis developed during their hospitalization. The hospital stay for the other six patients averaged 35.8 days. In every case, cholecystostomy was done because of the very poor general condition of the patient. In no instance was cholecystostomy performed because of the technical difficulty of cholecystectomy. Operation was carried out under local anesthesia in three patients. Four (44%) of the nine patients died postoperatively, raising the overall mortality to 1.6% for the entire series of patients.

Discussion

One of the objections to early operation in acute cholecystitis has been the performance of unnecessary procedures because of the inability to make a definitive diagnosis on clinical grounds alone.[3] The intravenous cholangiogram, in our experience, supplies valuable confirmatory evidence of cystic duct obstruction in acute cholecystitis and may reveal stones within the common duct. No inference can be drawn from a cholangiogram that fails to demonstrate either ducts or gallbladder. Using the slow infusion technique, adverse reactions to the contrast media have been minimal.[5] We do not recommend that intravenous cholangiography supplant operative cholangiography when the latter is otherwise indicated. Some authors[6] have reported that ultrasonography is a useful, noninvasive, diagnostic study in acute cholecystitis, which can demonstrate stones within the gallbladder, and sometimes hydrops, perforation and abscess. However, this test does not assess gallbladder function or cystic duct obstruction. Its role in acute cholecystitis remains undetermined.

An important finding in the present series was the absence of damage to the hepatic vessels or bile ducts. Similarly, no such injuries were reported in other series[7,8] when early elective or emergency operation[2] was employed. We found no prohibitive technical difficulties in doing the definitive surgery. This agrees with the findings of others, who have noted the ready plane for dissection provided by the edema of the acute inflammation, in many cases.[9] In the uncommon event that technical difficulties render cholecystectomy or exploration of the common bile duct too hazardous, cholecystostomy, with drainage of the common bile duct when necessary, provides a reasonable temporizing procedure.[10,11] However, our decision to perform a cholecystostomy was made preoperatively in every case, based on the predicted inability of the patient to withstand a more major procedure. The deciding factors were the presence of other serious medical conditions and advanced age. These factors are known to increase morbidity and mortality.[3,11] In none of the patients who died after cholecystostomy was death caused by a biliary complication, such as inadequate drainage in the presence of unrecognized ascending cholangitis, a danger previously reported.[12-14] Some surgeons[15] have recommended more frequent use of cholecystostomy in managing acute cholecystitis. However, with this approach, the surgeon cannot assess the biliary tree thoroughly (particularly when local anesthesia is employed for the procedure) and there is a risk of stones being retained in the

Table I—Postoperative Complications Affecting 361 Patients following Early Elective Cholecystectomy

Complications	Group 1 (n = 199)	Group 2 (n = 121)	Group 3 (n = 41)	Total (N = 361)
Wound infection	11	6	6	23
Prolonged bile drainage	1	1	2	4
Retained common bile duct stones	2	0	1	3
Intraperitoneal abscess	2	0	1	3
Pneumonia or atelectasis	1	1	1	3
Myocardial infarction	0	0	1	1
Pulmonary embolism	0	1	0	1
Septicemia	0	1	1	2
Rectus sheath hematoma	0	0	1	1
Urinary retention	0	1	0	1
Multiorgan failure	0	0	1	1
	17	11	15	43

gallbladder or common bile duct (in 27% of patients according to one report[16]), or both. Also this operation may be attended by specific complications accounting for significant morbidity and mortality,[17] which, in many cases, necessitate a second definitive procedure.[10] For these reasons, the use of cholecystostomy in the early elective operative management of acute cholecystitis should be limited.

Postoperative complications were more common in our series when operations were performed more than 7 days after admission to hospital, an observation also made by others.[9] When operations were delayed up to 7 days after admission there was no significant difference in complication rates. This supports the concept that early elective operations should be done as soon as the patient can be adequately prepared.[8,18] Although Wright and Holden[18] noted an increase in morbidity and mortality if an early elective operation was delayed more than 4 days after the onset of symptoms, and McArthur and associates[8] reported occasional technical difficulties when operating more than 4 days after the onset of the disease, neither Essenhigh[19] nor van der Linden and Sunzel[20] found any optimal time period for early operation. These varied results may simply reflect the differences in criteria used for the timing of operation. Early elective operation and delayed operation have been attended by similar complication rates.[7,21] However, when early elective operation is performed without delay other than that required for proper resuscitation and diagnostic measures, the number of emergency procedures performed while patients are deteriorating will decrease. The frequency of unexpected urgently performed procedures in worsening patients, reported to be as high as 30%,[22] is a recognized shortcoming of conservative management; this may necessitate an increase in the number of cholecystostomies performed, and consequently an increase in morbidity and mortality.[2]

One of the advantages, verified in the present study, of early operative treatment over delayed elective operation in acute cholecystitis, has been the shortened hospital stay[7,8,21,23] with consequent socioeconomic benefit. Furthermore, elective definitive operation carried out early obviates the risk of recurrent attacks of cholecystitis,[7] each with its pain and attendant dangers, such as perforation of the gallbladder, and avoids the problem of patient refusal of a delayed elective operation which has been reported in up to 25% of patients.[7]

Finally, like others, we have shown that early elective operation for acute cholecystitis can be performed with as low a mortality as delayed elective operation.[7,10,18]

For these reasons, we believe that the early elective operative approach to to the treatment of acute cholecystitis is a safe and sound practice and we advocate its general use in experienced hands. It avoids the dangers associated with delay, exposes the patients to no increased morbidity or mortality, and, when patients are adequately prepared, carries a minimal risk of unnecessary operation and shortens the period of hospitalization, thus reducing cost. We believe that cholecystostomy retains a place in patients whose general condition is jeopardized by other serious illness, or in the rare instance in which technical operative difficulties prohibit cholecystectomy.

Summary

Three hundred and sixty-one cases of acute cholecystitis were treated by definitive early surgery. The complication rate was 11.9% and the mortality 0.6%. Complications and mortality were greater when operation was deferred for more than 7 days following admission. Nine high-risk patients were treated with cholecystostomy, with a mortality of 44%. Deaths were due to the associated conditions. Intravenous cholangiography was a useful diagnostic adjunct. Our experience is supported by the recent literature.

We thank Dr. Donald J. Currie for his constructive suggestions in the preparation of the manuscript.

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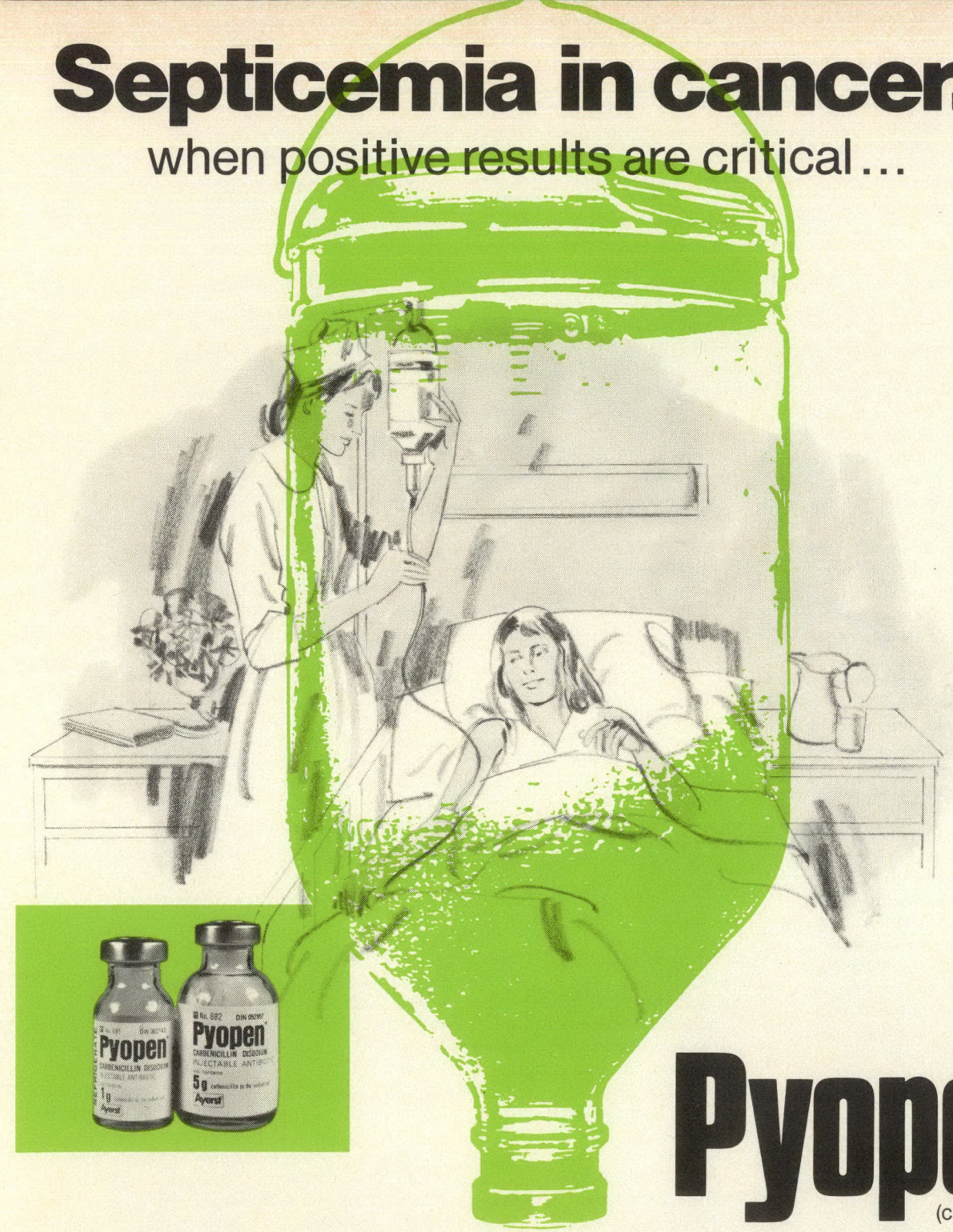
Septicemia in cancer...

when positive results are critical...



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Pseudomonas aeruginosa has long been recognized as a major cause of septicemia in cancer patients.[1] However, the introduction of PYOPEN* (carbenicillin) has had a significant impact on the management of these infections.[1] The true value of PYOPEN can best be appreciated when the survival rate of patients with Pseudomonas septicemia treated with PYOPEN is compared with the survival rate of those treated with gentamicin or polymyxin.

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PYOPEN is a better choice for the treatment of septicemia particularly in immunosuppressed cancer patients.

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Aspirin Prophylaxis of Venous Thromboembolic Disease following Fracture of the Upper Femur

G.M. CHANNON, B SC, MB, CH B, FRCS(EDIN)* AND A.M. WILEY, MB, M CH, FRCS, FRCS[C]†

In a prospective study of 51 patients with fractures of the femoral neck, aspirin was used as a prophylactic measure against thromboembolic disease.

Thrombi were detected by cuff impedence plethysmography, Doppler ultrasonography and ascending venography. Thrombi were identified in 20 (39.2%) of the patients. There was no significant difference between the frequency with which thrombi occurred in men and in women. Blood salicylate values were the same for patients who had and who did not have thrombi. There were no instances of pulmonary embolism. The frequency of deep vein thrombosis was comparable to that in a previous series of untreated patients from the same centre. It appears from this study that in these cases prophylaxis against venous thromboembolism using aspirin in a dosage of 600 mg *bid* is ineffective.

Dans une étude prospective chez 51 patients souffrant d'une fracture du col fémoral, l'aspirine a été utilisée comme mesure prophylactique des accidents thromboemboliques.

Les thrombi ont été décelés par pléthysmographie à impédance, par ultrasonographie de Doppler et par phlébographie ascendante. Des thrombi ont été identifiés chez 20 (39.2%) des patients. Il n'y a eu aucune différence significative entre la fréquence des thrombi observés chez les hommes et chez les femmes. Les salicylémies étaient les mêmes chez les patients qui ont eu des thrombi et chez ceux qui n'en ont pas eu. Il n'y a eu aucun cas d'embolie pulmonaire. La fréquence des thromboses veineuses profondes a été comparable à celle d'une série précédente de patients non traités du même centre. De cette présente étude, il semble que l'aspirine à la dose de 600 mg deux fois par jour soit inefficace comme prophylaxie des thromboembolies veineuses dans ces cas.

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Venous thromboembolism is a frequent complication in current surgical practice, particularly in orthopedic surgery after procedures on the hip joint. The frequency of fatal pulmonary embolism has been reported as approximately 2% after hip arthroplasty[1,2] and at least 5%[3,4] after hip fractures. A frequency of deep vein thrombosis as high as 57% has been reported after knee surgery[5] and 47% after tibial fractures.[6] In hip surgery the high frequency is due to severe predisposing factors including age, obesity, limited mobility, reduced venous flow, extensive trauma and the duration of the surgical procedure.[7]

In recent attempts to prevent this condition, drugs that alter platelet activity received considerable attention. Venous thrombi were thought to be formed by the enmeshment of red blood cells in a fibrin lattice. However, histologic studies have shown platelet aggregates, which suggest that they have a role in the initiation of thrombosis.[8,9] Some platelet studies support this concept.[10,11]

Of the drugs used to alter platelet activity, aspirin has been most often studied, because it is easy to use, is inexpensive and has few side effects. The results, however, have been controversial. After general surgical procedures Clagett and associates[12] showed a beneficial effect of aspirin using phlebography for diagnosis. Loew and associates[13] and Weber, Wolff and Bromig[14] had a similar result in patients who underwent general surgery. In studies on orthopedic patients, Harris and colleagues[15] found aspirin as effective as warfarin (using phlebography for diagnosis), and Jennings, Harris and Sarmiento[16] showed clinically that thromboembolic phenomena were reduced by using aspirin. Hey and associates[17] used ultrasonography and demonstrated a lower rate of thrombosis after giving acetylsalicylic acid, and Zekert, Kohn and Vormittag[18] reported a substantial reduction in the number of patients who had fatal pulmonary embolism. More recently, Harris and associates[19] have reported a protective effect of aspirin after hip surgery in men older than 40 years.

However, some workers[20,21] believe that aspirin does not exert an antithrombotic effect. The Medical Research Council trial[22] showed no beneficial effect and this was supported by the recent study of Stamatakis and associates.[23]

Our study investigated the effect of aspirin prophylaxis on a high-risk group of patients who were admitted to Toronto Western Hospital with fractures of the femoral neck and trochanteric regions. These patients were investigated postoperatively by flow studies and venography. We hoped also to demonstrate any sex variation that might exist in the degree of protection provided by aspirin therapy.

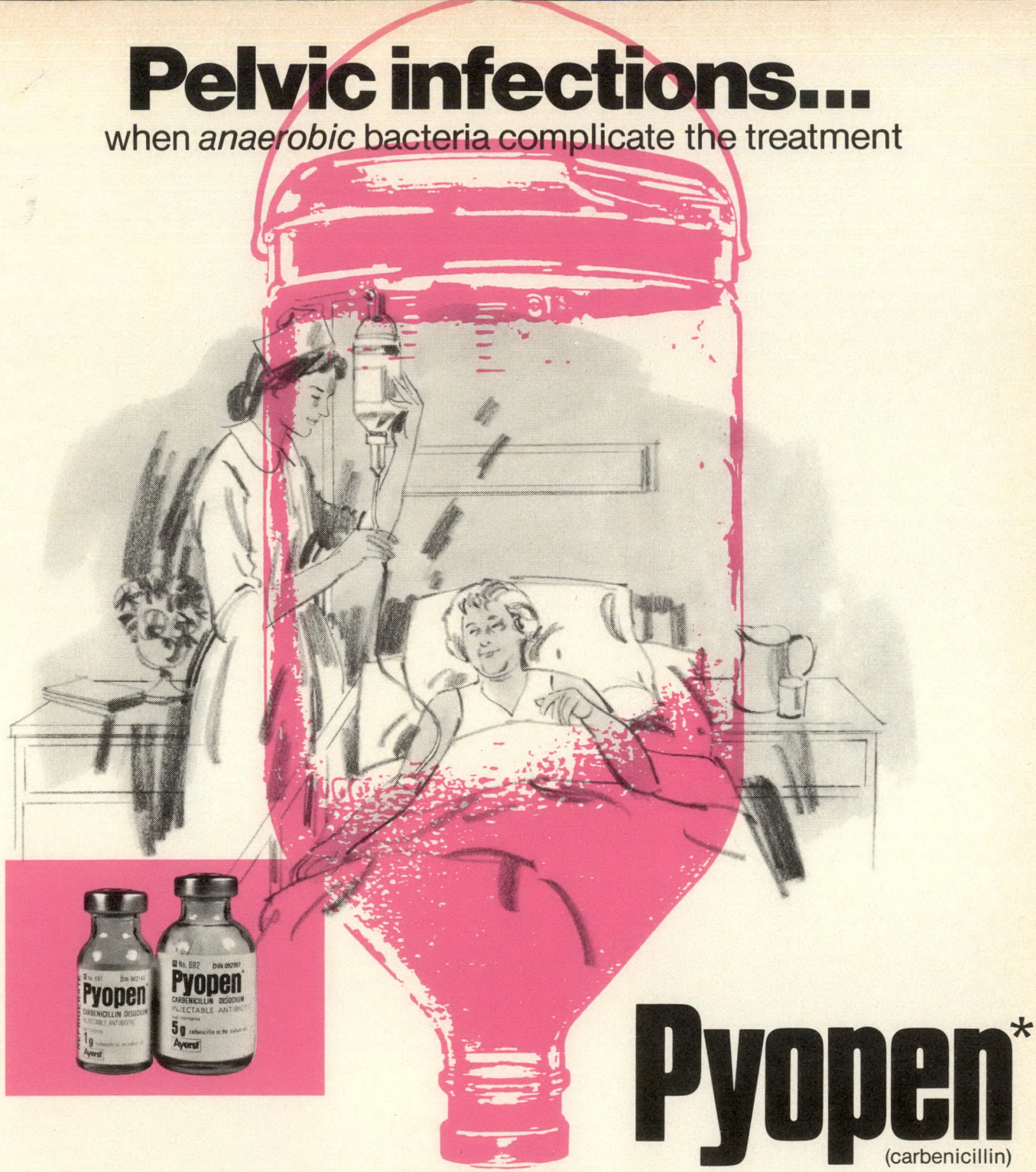
Patients and Methods

All patients admitted to the Toronto Western Hospital between Jan. 1, 1978 and June 30, 1978 with a fracture of the femoral neck or subtrochanteric region were considered for inclusion in the study. Patients excluded were: those with proven peptic ulceration or aspirin sensitivity, those receiving anticoagulants or steroids for intercurrent disease and those receiving a high regular dose of aspirin for any condition, patients known to have blood dyscrasia and those who had undergone surgical treatment of varicose veins of the lower limb which would make subsequent phlebograms difficult to assess. Fifty-seven patients entered the study, but 6 were later dropped (3 died within 10 days of operation from unassociated conditions, venography could not be performed on 2 because of peripheral vascular disease and dye sensitivity and 1 patient was removed from the trial when a history of peptic ulceration was obtained from a relative). Fifty-one patients (11 men, 40 women) were therefore available for study. Their ages ranged from 47 to 99 years (mean 77 years).

On admission, treatment was started

Pelvic infections...

when *anaerobic* bacteria complicate the treatment



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In the past,penicillins were not considered as products of first choiçe in the treatment of anaerobic infections, such as bacteroides, and consequently, other potentially more toxic therapeutic agents were used.

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with aspirin (600 mg of buffered acetylsalicylic acid orally *bid*). If for any reason oral administration was not possible before operation, aspirin suppositories were given using twice the oral dose (1200 mg). Before administering the medication we took blood samples in a search for unsuspected side effects of aspirin and also performed a salicylate assay. The time between injury and operation was noted. The time spent in hospital before operation averaged 2.5 days (including delays of 9 to 14 days in three patients because of general medical conditions).

All but five fractures were sustained within the home. All types of femoral neck fracture were included: subcapital (18 fractures), basal (4 fractures) and trochanteric or subtrochanteric (29 fractures). The method of repair used was dictated by the current treatment practice, so that there were 14 patients who underwent femoral head replacement (Austin Moore prosthesis inserted by the "Southern exposure" with the patient lying on one side) as well as those who had internal fixation by nail plate (30 patients), Enders nails (5 patients) and Knowles pins (2 patients).

At operation, the patient position used, the presence of anesthetic hypotension and duration of surgery were recorded, together with the measured blood loss, amount of fluid replaced and any tendency for increased oozing at the operative site. Hypotensive anesthesia was not employed and no other prophylactic anticoagulant measure was applied intraoperatively.

In the postoperative period the duration of bed rest before mobilization was recorded. Patients were again given aspirin (600 mg *bid*). Each patient underwent a screening test for platelet aggregation with epinephrine to ensure that aspirin had been absorbed and to demonstrate an alteration in platelet activity. Blood was taken for salicylate assay 24 hours and 8 days after operation.

Diagnosis

The diagnosis of deep vein thrombosis was made using a combination of techniques. The patients were assessed clinically on a regular basis. If there was any suspicion of deep vein thrombosis, venography was performed immediately.

If there was no clinical suspicion of the presence of a clot, a combined flow study and ascending venography were done in a 24-hour period 9 days after operation, so that we could compare the diagnostic methods. The flow study comprised Doppler ultrasonography and cuff impedence plethysmography.

Doppler recordings were made from the common femoral vein, popliteal vein and posterior tibial vein at the ankle. Positive results were recorded when there was no signal, suggesting complete occlusion, or an abnormal signal, suggesting obstruction proximal to the recording site.

Impedence plethysmography was carried out using a two-cuff technique. The presence of deep vein thrombosis was diagnosed by variation in the maximum venous outflow, which suggests high resistance collateral flow.

The method of venography was essentially that of DeWeese and Rogoff.[24] To overcome the problems associated with this technique when used in elderly patients, a tilting table with centre prop was used. Renografin-76® in dextrose was infused through an intravenous line in the dorsum of the foot. Films were taken with the table tilted at 30° from the horizontal, and a final film was occasionally used with the patient in a supine position. The criteria for a diagnosis of venous thrombosis were: the recognition of a well-defined defect, and no visualization of popliteal, superficial femoral or common femoral veins with good visualization of the proximal and distal veins, together with the presence of collateral vessels.

The end point of the study was the presence or absence of a deep vein thrombosis as diagnosed by venography. Patients with venographically demonstrated lesions in femoral or pelvic veins were given heparin by constant infusion and subsequently received anticoagulants orally. If the thrombi were confined to calf veins, a program of support and mobilization was instituted. The presence of proven pulmonary emboli (by blood gas measurements and lung scanning) was accepted as presumptive evidence of deep vein thrombosis. Management of these patients was carried out according to current practices.

For several reasons it was impossible to include a control group in this study. Comparable untreated series have been reported from this hospital in which the patients were managed in an identical way under the care of the same surgical teams.[4,25] They vary only in a temporal way from the patients in this study and therefore have been used for comparison.

Invasive and Noninvasive Investigations

Although it was not the purpose of this study to compare the accuracy of noninvasive techniques for studying venous flow with that of venography, certain conclusions were obvious.

Doppler studies and plethysmography were carried out by a trained technician in the flow laboratory associated with the cardiovascular unit. All such studies were followed within 24 hours by venography. The results of the noninvasive techniques corresponded with those of venography in 29 instances, but in 10 others (all above the knee) a positive result of Doppler study or plethysmography, or both, was not confirmed by venography (false positives). On the other hand seven positive results from venography (all below the knee) were obtained when the noninvasive method gave a negative result.

Results

The average operating time for insertion of a Moore prosthesis was 1 hour, 40 minutes and for a pin-and-plate procedure, 2 hours. A number of the patients were treated by residents in training, while for others the staff surgeon performed the operation.

Intraoperative blood loss was calculated by weighing sponges and was similar to that reported in previous studies from this centre when no anticoagulant was used.[25] Excessive oozing was not noted and serious wound hematomas did not develop.

The patients were mobilized early and, on average, were able to sit out of bed 5 days after operation. Walking on the affected leg was encouraged on the 8th day for patients who had had a pin-and-plate operation and on the 14th day for those who had had a Moore prosthesis inserted.

Postoperatively the epinephrine aggregation test showed that aspirin had altered platelet aggregation in each case. Serum salicylate values varied considerably ranging from 15 mg/dl to 0.1 mg/dl (1.0860 mmol/l to 0.0072 mmol/l. In four cases serum concentrations were not measurable on at least one occasion despite a positive result from the platelet aggregation study. The mean salicylate value was 3.5 mg/dl (0.2534 mmol/l); in those who remained free of thrombi the mean value was 3.6 mg/dl (0.2606 mmol/l).

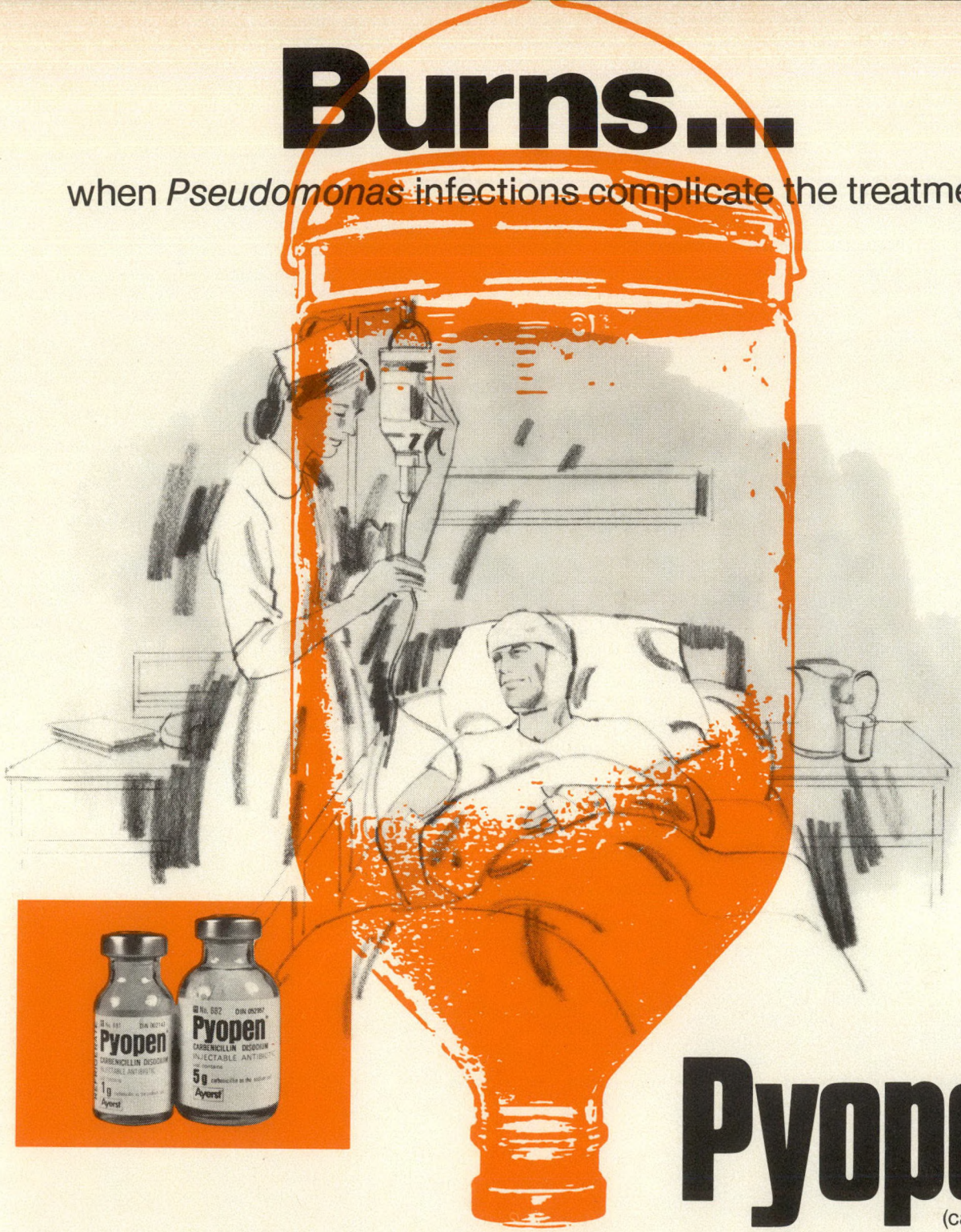
Thrombi were identified venographically in 20 (39.2%) patients. In four patients thrombi formed above the knee; two had numerous thrombi in the common femoral vein, one had a small superficial clot in the superficial femoral vein and a fourth had thrombus in the deep femoral vein.

Seventeen patients had thrombi in the veins below the knee (sural, peroneal, anterior and posterior tibial veins). In two patients thrombi developed in the long saphenous vein.

Heparin was given for femoral vein lesions. No thrombi were identified in the pelvic veins.

Burns...

when *Pseudomonas* infections complicate the treatment



Pyopen*

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Traditional treatments have all involved a significant risk of dose-related toxicities. The introduction of PYOPEN*(carbenicillin) was an important therapeutic advance, providing the safety of penicillin, combined with bactericidal effectiveness against Pseudomonas aeruginosa and other gram-negative organisms.

"...it would appear that carbenicillin is effective in modifying the course of a *Pseudomonas* surface culture in burn patients."[1]

In severe and overwhelming Pseudomonas infections so often found in burn patients, PYOPEN provides a logical choice of therapy—effectiveness without dose-related toxicities and the traditional margin of safety common to all penicillins. So, for the treatment of Pseudomonas infections in burns...consider PYOPEN.

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Sex Ratio

Of the 11 men, thrombi formed in 4 (36.4%); three clots were in calf veins and one in the deep femoral vein. In 16 (40%) of the 40 women venography gave a positive result, 13 had thrombi in calf veins, 3 at higher levels (Table I).

No instance of pulmonary embolism was recorded during the study.

One patient suffered a cerebrovascular accident 8 days postoperatively and a second incident 14 days later. The first incident occurred while the patient was receiving aspirin.

Discussion

The results of this study suggest that aspirin in the dosage that we used has no significant effect on the occurrence of deep vein thrombosis in patients after operation for fracture of the femoral neck. The diagnosis in each case was based on venography, which is generally accepted to be the best diagnostic method available. In almost 40% of our patients thrombi developed while aspirin was being given. In previous studies[4,25] using the same facilities, surgical teams and diagnostic techniques without prophylactic measures, the frequency of thrombosis was 40% and 49%. These figures are similar to those in other reported studies.[26,27]

We could not demonstrate any significant difference in the incidence of thrombi between men and women. Thrombi developed in 4 (36.4%) of 11 men in this study compared with 16 (40%) of 40 women. All the men were about 40 years of age. The discrepancy between our figures and those of other workers[19] cannot be completely accounted for, even allowing for differences in the timing of investigation and the diagnostic methods used.

Attention has been directed to the absence of pulmonary emboli in this series. Under the condition of this trial an expected figure of 2.3% for pulmonary embolism did not materialize although the number of cases is insufficient to allow any firm conclusions based on statistical significance. However, it was possible that the "above average" intensity of investigation of the elderly patients prompted "earlier than average" use of heparin, with its attendant benefits.

This work was financed by a grant from the Ontario Geriatric Research Society to whom we extend our gratitude. We also thank Dr. D. Pantalony, hematological service, Toronto Western Hospital, who provided invaluable guidance, his staff and technical assistance in the platelet studies and aspirin assays.

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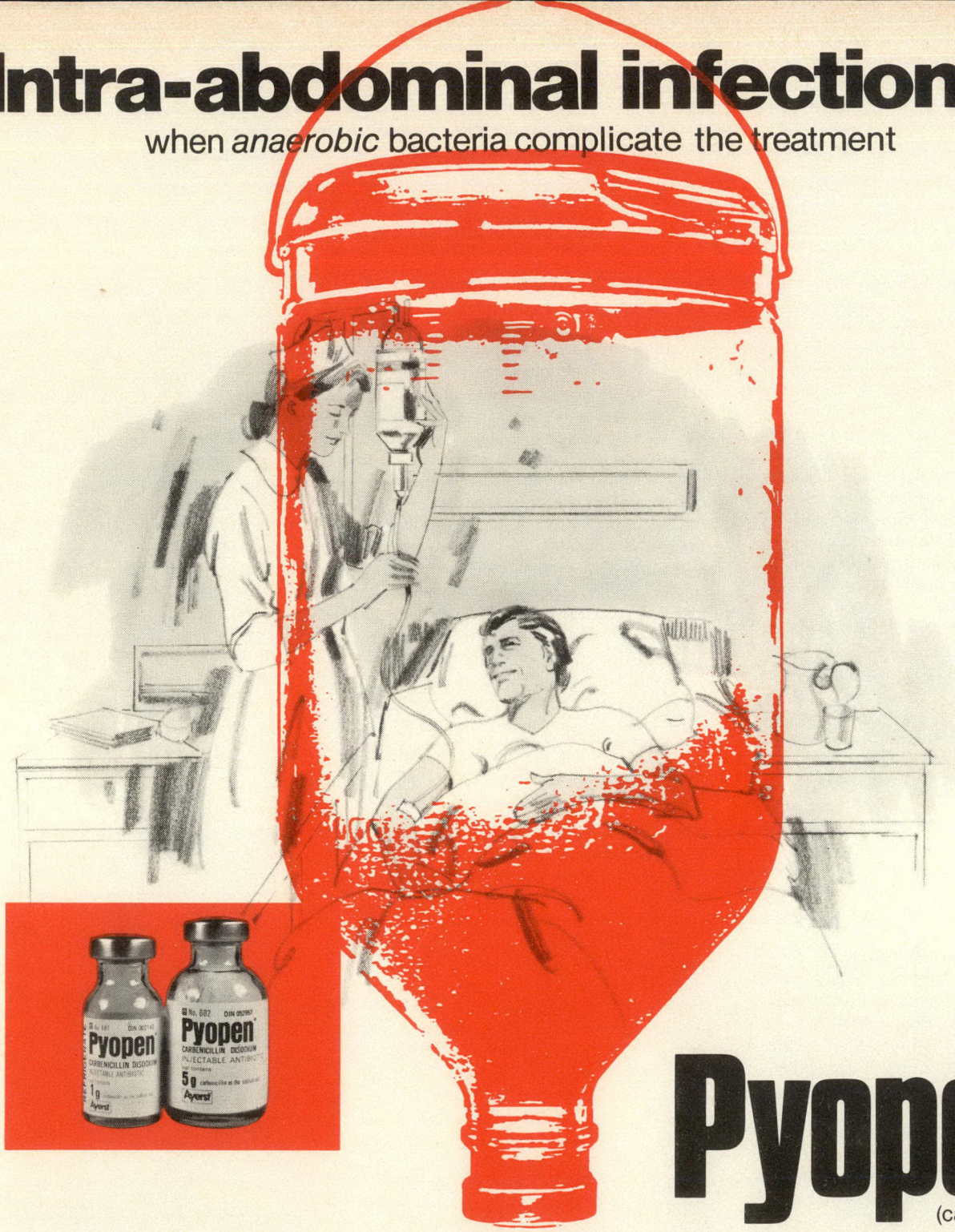
Table I—Distribution of Thrombi according to Sex

Sex	No. of patients	No. with thrombi (and %)	Site	
			Thigh	Calf
Male	11	4 (36.4)	1 deep femoral vein	3
Female	40	16 (40)	2 common femoral vein 1 superficial femoral vein	13

Intra-abdominal infections...

when *anaerobic* bacteria complicate the treatment



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Recent studies[1,2,3] have shown that PYOPEN is effective in 90.3% of cases of intra-abdominal infections due to anaerobic and/or mixed gram-negative infections. PYOPEN is not only effective, it is also free from dose-related toxicities, and provides the traditional margin of safety common to all penicillins.

So, for relatively safe and convenient therapy for both aerobic and anaerobic infections, whether single or mixed... consider PYOPEN.

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Treatment of Unilateral Iliac Artery Disease by Femorofemoral Bypass Grafting

NATHAN M. SHEINER, MD, FRCS[C], DAVID ASHBY, MD, FRCS[C] AND JACK ZELTZER, MD

Between Jan. 1, 1970 and June 30, 1977, 50 men and 23 women underwent femorofemoral bypass grafting. The average age of the group was 64.7 years. The procedure was performed for disabling claudication in 50 patients and for limb threatening ischemia in 23. Knitted Dacron grafts were used in all but two patients. The operative mortality was 4.1% and the late mortality 21.9%. There were six complications related to the prostheses, three infected grafts and three false aneurysms. Thrombosis of the graft occurred in 15 patients; the graft was successfully revised in 2. The cumulative 5-year patency rate determined by life-table methods was 73.4%. The causes of failure appeared to be well defined and unilateral iliac artery disease. The donor iliac artery, poor runoff through a diseased deep femoral artery on the recipient side and infection of the graft. This study indicates that femorofemoral bypass has a definite place in the management of patients with unilateral iliac artery disease. The procedure can be performed on selected patients with a low operative mortality and an acceptable patency rate.

Entre le 1er janvier 1970 et le 30 juin 1977, 50 hommes et 23 femmes ont subi un pontage fémoro-fémoral. L'âge moyen du groupe était de 64.7 ans. L'intervention a été entreprise pour soulager une claudication invalidante chez 50 patients ou pour corriger une ischémie menaçant la survie du membre dans 23 cas. Des greffons de Dacron tricoté ont été utilisés chez tous les patients, sauf deux. La mortalité opératoire a été de 4.1% et la mortalité tardive de 21.9%. Il y a eu six complications reliées à la prothèse, trois infections du greffon et trois faux anévrismes. Une thrombose du greffon est survenue chez 15 patients; le greffon a été réparé avec succès dans deux cas. Le taux de patence à 5 ans déterminé au moyen de tables actuarielles a été de 73.4%. Les causes d'échecs ont semblé être bien définies et comprenaient une maladie non reconnue de l'artère iliaque donneuse, un mauvais écoulement dans une artère fémorale profonde malade du côté receveur et l'infection du greffon. Cette étude indique que le pontage fémoro-fémoral possède une place définie dans le traitement des patients souffrant de maladie unilatérale de l'artère iliaque. Cette intervention peut être pratiquée sur des patients choisis avec une mortalité opératoire faible et un taux de patence acceptable.

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Stenosis or occlusion of one iliac artery is usually managed by iliac endarterectomy or aortofemoral bypass grafting. Either of these operations can be a formidable undertaking in the patient with associated disease of the cardiac, pulmonary, renal or cerebrovascular system. In 1960, McCaughan and Kahn[1] introduced the principle of a crossover graft to treat the patient with unilateral occlusive disease of the iliofemoral artery. They anastomosed a Dacron graft to the left external iliac artery and placed the graft in an extraperitoneal plane superior to the bladder and then through the right femoral canal to the right popliteal artery above the knee where the distal anastomosis was performed. A third anastomosis was then carried out between the graft and the proximal end of the right deep femoral artery. They proposed this crossover procedure as an alternative to aortopopliteal bypass in poor-risk patients. In 1962, Vetto[2] reported the use of a femorofemoral subcutaneous graft in 10 patients with unilateral iliac artery disease. By 1966, he had increased his series to 38 patients and had 32 early successes and no late graft failure.[3] Since these initial reports many others have appeared in the literature and the procedure of femorofemoral bypass has achieved relatively widespread acceptance.[4-15]

We started using this procedure in January 1970 and have used it increasingly since that time. We now report our experience with the procedure over an 8-year period.

Patient Data

Between Jan. 1, 1970 and June 30, 1977, 50 men (average age 68 years) and 23 women (average age 61.8 years) underwent femorofemoral bypass grafting. The average age of the entire goup was 64.7 years. The age distribution is set forth in Table I. Many patients had one or more associated conditions (Table II) that may have increased the morbidity and mortality of conventional intra-abdominal revascularization operations. In the initial years of this study, femorofemoral bypass was restricted to patients with unilateral iliac disease who presented with rest pain, ischemic ulcers or gangrene and who were considered to be poor risks for conventional revascularization procedures because of the presence of associated diseases. In the later years, the indications for femorofemoral bypass were extended to include all patients who were over the age of 65 years. Furthermore, disabling claudication was also considered an indication. Good-risk patients younger than 65 years were still operated on by conventional means. Of the 73 patients, femorofemoral by-

Table I—Age Distribution of 73 Patients Who Had Femorofemoral Bypass Grafting

Age, yr	No. of patients (and %)
40 – 49	5 (6.8)
50 – 59	18 (24.7)
60 – 69	25 (34.3)
70 – 79	23 (31.5)
80	2 (2.7)
	73 (100)

Table II—Associated Diseases in Patients Who Had Femorofemoral Bypass Grafting

Disease	No. of patients (and %)
Diabetes	23 (32)
Hypertension	39 (53)
Coronary artery disease	56 (77)
Cerebrovascular insufficiency	5 (7)
Pulmonary disease	20 (27)
Chronic renal disease	8 (11)
Other	7 (10)

pass was performed in 50 for disabling claudication and in 23 for limb-threatening ischemia. Of the latter group, rest pain was present in 14, ischemic ulcers in 6 and gangrene of one or more toes in 3. Four of the 73 patients had previously undergone unilateral aortofemoral bypass and subsequently disease developed in the opposite iliac artery. Three other patients had occlusion of one limb of a previously inserted aortobifemoral bypass graft.

Angiographic Findings

In all 73 patients translumbar or retrograde femoral arteriograms were obtained. Left iliac artery disease was present in 40 patients and right iliac artery disease in 33 patients. Small abdominal aortic aneurysms were present in two patients. There was associated femoropopliteal disease in 36 patients.

Operative Technique

The technique of femorofemoral bypass has been well described.[3,4,12,15] The procedure can be carried out under local, epidural or light general anesthesia. The graft can be of autogenous saphenous vein or knitted Dacron. In the present series, 71 of the grafts were 8-, 9-, or 10-mm knitted Dacron and autogenous saphenous vein in the other 2. Since approximately 50% of patients with iliac artery disease also have obstruction of the superficial femoral artery, special attention must be paid to the deep femoral artery on the recipient side. If this artery is stenotic at its orifice, the arteriotomy in the common femoral artery should be continued across the stenotic orifice and the bypass graft then tailored to extend onto the deep femoral artery as a patch. If the disease in the deep femoral artery extends distally beyond the first 1.5 cm of the vessel then endarterectomy and autogenous venous patch angioplasty of the deep femoral artery is performed and the graft is anastomosed more proximally to the common femoral artery. Alternatively, the graft can be anastomosed directly to the deep femoral artery.

The tension of the graft when it is in place is important. If the graft is too short, excessive tension will result in traction on both the donor and recipient arteries with resultant turbulence and possible thrombosis. Excessive tension may also cause dehiscence of the anastomosis and false aneurysm formation. If the graft is too long, buckling of the graft may occur and this, too, may lead to thrombosis.

Operative Procedures

In 68 of the 73 patients, the procedure was limited to a femorofemoral or femoral-to-deep femoral artery bypass. In three patients, an extended deep femoral endarterectomy with saphenous vein patch angioplasty was performed on the recipient side. In one patient the femorofemoral bypass was combined with a femoropopliteal vein bypass on the recipient side and in one other patient, the femorofemoral procedure was combined with a femoropopliteal vein graft on the donor side.

Results

Mortality

The early (up to 30 days postoperatively) mortality was 4.1% and the late mortality 21.9% during a follow-up period that averaged 35.1 months. The causes of death are indicated in Table III. Eleven of the 19 deaths were due to myocardial infarction.

Complications

The complications of the operation are listed in Table IV. In six instances the complication involved the graft: three were false aneurysms and three were infected grafts. All three infected grafts were patent; in one case the patient was successfully managed by an iliofemoral bypass through the obturator foramen with removal of the infected graft but in the other two, above-knee amputation was required following removal of the infected graft, and both patients ultimately died as a result of amputation. All three patients with false aneurysms underwent successful repair of the aneurysms.

Graft Thrombosis

Graft thrombosis was the most common complication and occurred in 15 patients—within 30 days in 3, between 30 days and 1 year in 7, 1 and 2 years in 2, 2 and 3 years in 1 and after 3 years in 2 patients. Of these 15 patients, successful revision of the graft was achieved in 2. Three other patients in this group had successful revascularization by another procedure—two by axillofemoral bypass and one by aortofemoral bypass. Of the total group of 73, revascularization ultimately failed in 12 patients (10 patients who could not be revascularized by either revision of the graft or by an alternative procedure and 2 patients in whom a patent graft was removed because of infection). Of this group of 12 patients, 8 underwent major amputation, above the knee in 6 and below the knee in 2.

Relief of Symptoms

All 11 patients with rest pain who underwent successful revascularization had relief of this symptom. Ischemic ulcers healed in all patients who had patent grafts, and local amputations were successful in managing the three patients with gangrenous toes. Of the 50 patients presenting with intermittent

Table IV—The Early and Late Complications of Femorofemoral Bypass

Complication	No. of patients
Early	
Minor wound infection	3
Major wound infection (infected graft)	3
Myocardial infarction	2
Gastrointestinal bleeding	2
Pneumonia	1
Mesenteric thrombosis	1
Thrombosis of graft	3
Late	
False aneurysm	3
Thrombosis of graft	12*

*2 successful revisions.

Table III—The Time and Causes of Death in the 19 Patients Who Died following Femorofemoral Bypass

Time of death	No. of patients	Cause	No. of patients
0 - 30 d	3	Myocardial infarction	1
		Pneumonia	1
		Gastrointestinal bleeding	1
31 d - 1 yr	4	Myocardial infarction	2
		Sepsis	2
1 - 2 yr	3	Myocardial infarction	3
2 - 3 yr	3	Myocardial infarction	2
		Aortoenteric fistula	1
>3 yr	6	Myocardial infarction	3
		Carcinoma	1
		Cerebrovascular accident	1
		Respiratory failure	1

claudication, 33 of the 46 with patent grafts were totally relieved of their claudication or demonstrated marked improvement. The remaining patients improved sufficiently that no further operation was required.

Patency Rate

In this series, the two patients who had grafts that occluded but were successfully revised were considered to have patent grafts. The three patients who had infected grafts that were removed, though patent, were considered to have occluded grafts. The cumulative 5-year patency rate as determined by life-table methods was 73.4% (Fig. 1).

Discussion

A review of several reported series of femorofemoral bypass grafting in the English literature (Table V) reveals a moderate variation in the patency rates of these grafts. The 4-year patency rate of 53% reported by Eugene, Goldstone and Moore[8] is somewhat lower than those reported in other series. Our 5-year cumulative patency rate was 73.4% and included in the group of patients with occluded grafts were three patients whose patent grafts were removed because of infection. If we were to exclude these three patients the 5-year patency rate would exceed 80% and would be comparable to the 80.8% 5-year patency rate reported by Brief and associates.[5]

The causes of failure in our series appear to be well defined and include unrecognized disease in the donor iliac artery, poor runoff through a diseased deep femoral artery on the recipient side and infection of the graft. The problem of unrecognized iliac artery disease on the donor side has been overcome to a large extent by a more careful angiographic assessment of the donor iliac artery with the aid of oblique views, and by measuring the pressure in the donor iliac artery at the time of operation. The problem of poor runoff by way of a diseased deep femoral artery is currently managed by the more frequent use of extended deep femoral endarterectomy and of combined femorofemoral and femoropopliteal or femorotibial bypass on the recipient side. Graft infection in our series occurred in patients with infected ischemic ulcers or gangrenous toes and may be prevented by a longer period of preoperative antibiotic therapy, combined with more intensive local therapy to the infected ischemic ulcer.

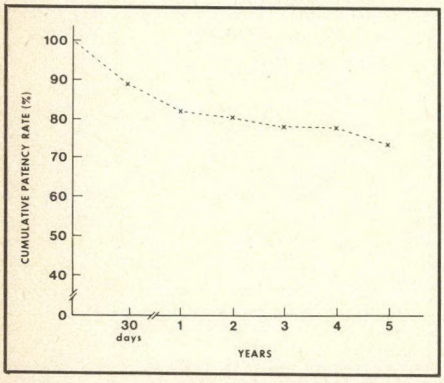

FIG. 1—Cumulative patency of femorofemoral grafts determined by life-table methods.

Conclusion

From our experience we conclude that femorofemoral bypass grafting is a very satisfactory procedure for managing selected patients with unilateral iliac artery disease and can be carried out with a relatively low operative mortality and with acceptable long-term patency rates.

The indications for this procedure have gradually been extended on our service and it is now used for: (a) all patients with unilateral iliac artery disease who require revascularization because of disabling claudication, ischemic rest pain, ischemic ulcers or gangrene and who are over the age of 65 years; (b) for patients who are younger than 65 but who are considered poor-risk candidates for conventional revascularization operations because of severe coronary artery disease, chronic obstructive lung disease, advanced renal disease, cerebrovascular disease, etc.; (c) patients in whom intra-abdominal revascularization is contraindicated because of intra-abdominal sepsis or tumour, numerous intra-abdominal adhesions, infection of the upper abdominal wall or the presence of a colostomy; (d) patients who have occlusion of one limb of an aortobifemoral or bi-iliac graft; and (e) patients who have had unilateral aortofemoral or aortoiliac bypass operation and in whom disease subsequently develops in the opposite iliac artery.

Table V—A Summary of Some Reports of Femorofemoral Bypass

Author	No. of patients	Patency rate, %	Length of follow-up
Vetto, 1966[3]	38	84	27 mo
Sethi and associates, 1975[14]	27	81.5	26.5 mo
Brief and associates, 1975[5]	57	80.8	5 yr
Plecha and Pories, 1976[13]	54	87.4	18 mo
Eugene, Goldstone and Moore, 1977[8]	33	53	4 yr
Sheiner, Ashby and Zeltzer, present series	73	73.4	5 yr

Addendum

Between July 1, 1977 and July 15, 1978, we performed femorofemoral grafting in 16 men and 7 women. There were no operative deaths. Twenty-one of the 23 grafts remained patent in the early postoperative period, giving a 30-day patency rate of 91.3%. In two patients the graft became occluded after the first 30 days and one of the grafts was successfully revised.

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Testicular Scanning: Its Efficacy in Diagnosing Intrascrotal Lesions

WILLIAM L. OROVAN, MD, GORDON A. MCLORIE, MD, FRCS[C]

Radionuclide scanning is a relatively new diagnostic aid for evaluating intrascrotal lesions. The authors present a retrospective analysis of 34 patients who underwent testicular scanning from 1973 to 1978. While the technique may be helpful, misleading results are not uncommon and caution should be exercised in interpreting the results. In this series 22% of scans obtained in cases of testicular torsion and acute epididymitis failed to provide the correct diagnosis. In view of the serious consequence of testicular loss when surgical exploration is delayed, testicular scanning should not be relied upon to the exclusion of other more traditional methods.

La scintigraphie isotopique est un instrument de diagnostic relativement nouveau pour évaluer les lésions intrascrotales. Les auteurs présentent une analyse rétrospective de 34 patients qui subirent une scintigraphie des testicules entre 1973 et 1978. Bien que cette technique puisse être utile, les résultats qui prêtent à erreur ne sont pas rares et ils devraient être interprétés avec circonspection. Dans cette série, 22% des scintigraphies effectuées dans les cas de torsion d'un testicule et d'épididymites aiguës n'ont pas réussi à établir le diagnostic exact. En raison des conséquences sérieuses que peut entraîner la perte d'un testicule, quand l'exploration chirurgicale est retardée, l'on ne devrait pas se fier aux résultats de la scintigraphie des testicules à l'exclusion d'autres méthodes diagnostiques plus traditionelles.

Radioisotopic scanning for evaluating perfusion of the testicles and scrotal contents was first proposed by Nadel and associates[1] in 1973. They used a rectilinear scanner and sodium-99m pertechnetate and were able to differentiate acute testicular torsion, characterized by reduced or absent testicular perfusion, from acute epididymitis in which perfusion to the affected side was markedly increased. Subsequent papers[2-7] have described variations and refinements of the scanning technique and all have suggested that it has a high degree of accuracy in diagnosing intrascrotal lesions including acute testicular torsion, acute epididymitis, torsion of testicular or epididymal appendages, tumours, spermatoceles and abscesses.

Accurate and rapid differentiation of acute testicular torsion, a condition necessitating prompt surgical intervention, from other acute, though nonsurgical, lesions of the scrotum such as acute epididymitis is of great benefit to the patient in avoiding unnecessary exploratory scrotal surgery which is often undertaken to exclude acute testicular torsion in cases that are diagnostically difficult.

Patients and Methods

A retrospective analysis was made of all patients who had scrotal radionuclide examination to help in the diagnosis of intrascrotal lesions at our centre from 1973, when the first such scan was obtained, to 1978. In that 5-year period this examination was performed 34 times. The results of scanning in these 34 patients are summarized in Table I. The diagnosis was confirmed at operation in 22 patients and by clinical follow-up in the remaining 12 patients with acute epididymitis. The patients ranged in age from 5 to 74 years; 10 were children and 24 were adults. In all cases of acute testicular torsion, torsion of an appendix testis and acute epididymitis, radionuclide scanning was performed as part of the initial diagnostic studies. Scanning of suspected testicular tumours found on physical examination was performed as part of the overall preoperative assessment and to evaluate the usefulness of the scanning technique in mass lesions of the testicle.

Table I—Diagnosis in 34 Patients Who Underwent Testicular Radionuclide Scanning of the Scrotum

Final diagnosis	No. of patients	Confirmed at operation, no.(and %)
Acute testicular torsion	8	8 (100)
Torsion of appendix testis	5	5 (100)
Tumour of testis	6	6 (100)
Acute epididymitis	15	3 (20)
Total	34	22 (65)

A standard technique was used in which the patient is positioned supine under the gamma camera and the scrotum isolated and supported from below by a thin lead shield designed to exclude background soft tissue activity of the thigh from the scanning field. The penis is taped to the lower abdomen. Technetium-99m (pertechnetate) (10 mCi) is injected into an antecubital vein; perfusion studies are performed at 2-second intervals for 60 seconds and blood pool images obtained at longer intervals over the next 5 minutes. Frequently markers are placed at the inferior pole of each hemiscrotum to aid in anatomic orientation. Results were interpreted as described by Holder and associates[7] in which the normal pattern of perfusion is characterized by a low-level symmetrical activity in the perfusion phase and an overall intensity similar to the thigh on blood pool image or summation. Acute torsion of the testicle is characterized by decreased or absent perfusion during the dynamic phase of the study and a rounded "cold" area replaces the testicle on the static blood pool image. Acute epididymitis appears as markedly increased perfusion on the involved side with a "hot" spot representing the epididymitis on the blood pool image. Tumour is seen as a slightly altered, usually slightly decreased, area of perfusion in an otherwise normally perfused testicle. Torsion of an appendix testis gives a normal perfusion pattern.

Acute Testicular Torsion

In eight patients the final diagnosis was acute torsion of the testicle. All of these diagnoses were confirmed at operation (Table I). The result of scan-

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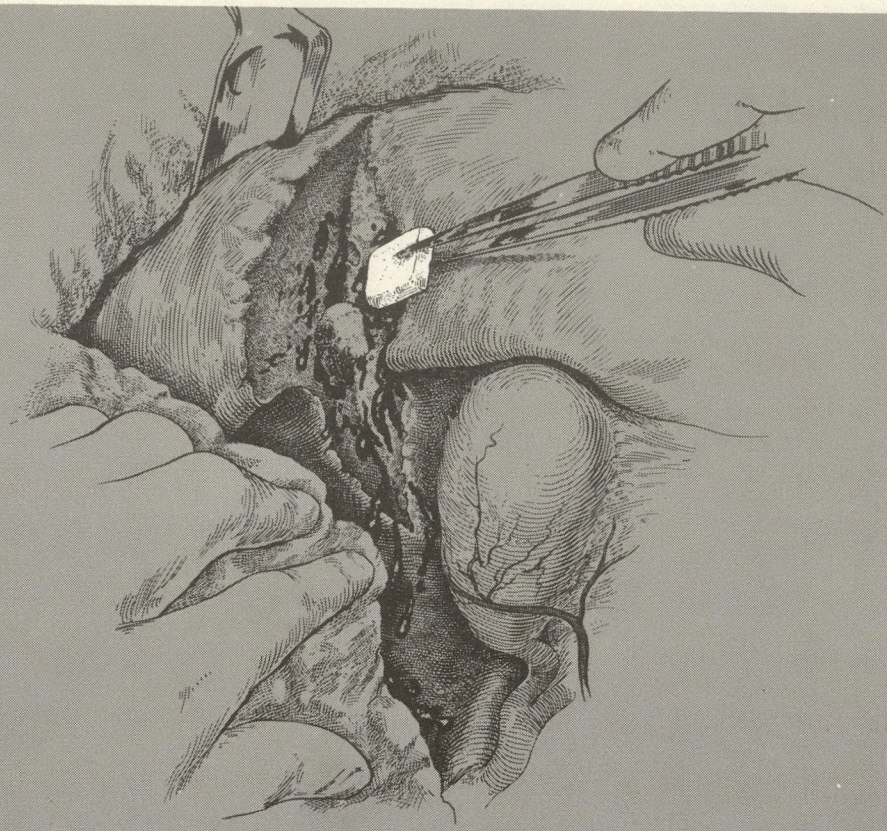

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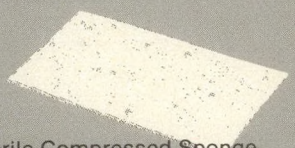

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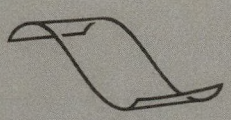

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ning was misleading in three of the eight patients; in two of these three operation was performed immediately on the basis of clinical diagnosis, and in both acute testicular torsion was confirmed. In the other patient the clinical presentation and laboratory findings were equivocal and surgical exploration was deferred on the basis of testicular scanning which indicated the presence of acute epididymitis. The patient was subsequently operated upon when symptoms failed to resolve with conservative therapy; at operation an infarcted, distorted testicle was found which necessitated orchiectomy.

Torsion of Appendix Testis

Five cases of torsion of the appendix testis were diagnosed preoperatively; in all cases the diagnosis was confirmed subsequently at operation. In this group operation was performed either because the diagnosis was in doubt or because of persisting severe pain. In four of six scans obtained in this group, the results (Table II) were at variance with the eventual diagnosis. Secondary inflammatory changes, though not noted clinically, may account in part for the increased perfusion noted in three of the six scans (Table II).

Tumour of Testis

Six patients with tumour were studied. These were all nonacute presentations and testicular scanning was used as an adjuvant investigative procedure. In five patients a mass was delineated within the testicle; in four of these the mass was slightly hypoperfused and in one it was seen as an area of slightly increased perfusion. In the sixth patient no mass could be defined by scanning although subsequent radical orchiectomy did reveal that a 2-cm seminomatous tumour was present.

Acute epididymitis

Fifteen patients with acute epididymitis underwent radionuclide scanning; 13 had a pattern of increased perfusion. Two patients showed normally perfused testicles and hemiscrota (Table II). Three of these 15 patients were subsequently operated upon for unresolved pain or abscesses and the diagnosis of epididymitis was confirmed in all. The remaining 12 were followed clinically and in all the condition resolved with antibiotic therapy. Nine patients have been followed up from 1 to 14 months; in none has there been any indication of atrophic testicles suggestive of missed torsion.

Discussion

The use of testicular radionuclide imaging to aid in the diagnosis of intrascrotal lesions has received widespread attention in the recent surgical and radiologic literature. Several previous reports have attested to its general efficacy as a diagnostic aid. Riley and associates[5] have reported a 6% false-negative scan result in differentiating acute torsion of the testicle from acute epididymitis, while Williamson[8] puts the figure at almost 10%.

While we have found this technique to be generally helpful, misleading results are not uncommon. Our own experience in this admittedly small series shows that in the 23 combined cases of acute testicular torsion and acute epididymitis investigated by radionuclide scanning, the scan failed to suggest the correct diagnosis in 5 (22%). Of the 22 patients in whom the diagnosis was confirmed at operation, the scans were found to be misleading in 7 (32%) (Table III).

In view of our results we would urge that caution be exercised in the use of this diagnostic modality. We would echo the conclusions of Datta and Mishkin[4] that scrotal imaging should be viewed along with all other clinical and laboratory data in the diagnosis of acute intrascrotal lesions. Caution in interpreting the results of these scans is particularly important in view of the serious result of testicular loss which may occur when a diagnosis other than acute torsion is made and surgical exploration is thus deferred until testicular damage is irreversible and salvage impossible. We also stress that no time should be lost in waiting for testicular scanning to be carried out if the clinical impression is that the patient requires an immediate scrotal exploration for salvage of his testicle, as in the case of testicular torsion.

Table II—Scan Result Compared with Trial Diagnosis in 34 Patients Who Underwent Testicular Radionuclide Scanning

	Scan result				
Final diagnosis	Increased perfusion	Decreased perfusion	Normal perfusion	Expected result	Per cent incorrect
Acute testicular torsion	3	5	0	Decreased perfusion	37
Torsion of appendix testis*	3	1	2	Normal perfusion	66
Tumour of testis	1	4	1	Slightly altered	17
Acute epididymitis	13	0	2	Increased perfusion	13

*1 patient underwent scanning on 2 occasions.

Table III—Scanning Results Confirmed at Operation

Final diagnosis	Scan correct	Scan incorrect	Total no. of cases	Scan errors, %
Acute testicular torsion	5	3	8	37
Torsion of appendix testis	2	3	5	60
Tumour of testis	5	1	6	17
Acute epididymitis	3	0	3	0
	15	7	22	32

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Sensory Feedback in a Myoelectric Upper Limb Prosthesis: a Preliminary Report

R.H. BRITTAIN, M SC, P ENG,* W.F. SAUTER, CPO[C]† AND D.A. GIBSON, MD, FRCS[C]†

Upper limb prostheses are often rejected because they do not provide the sensory feedback available from a normal hand. A system for providing sensory feedback has been developed at the University of New Brunswick for use with the three-state myoelectric controls prepared in the Bioengineering Institute there. Strain gauges mounted on the forefinger of an electric hand provide information which is processed electronically to cause a tingling sensation in the patient's stump, proportional in its intensity to the pinch force in the finger.

This system has been used by a patient at the Ontario Crippled Children's Centre in Toronto, since June 1976. She uses it consistently with great satisfaction and enthusiasm. It gives her a sense of competence and confidence she does not have without it.

Les prothèses des membres supérieurs sont souvent rejetées parce qu'elles sont incapables de procurer la rétroaction sensitive offerte par une main normale. Un système capable de procurer une rétroaction sensitive a été mis au point à l'Université du Nouveau-Brunswick pour utilisation avec les contrôles myoélectrique à trois états préparés à leur Institut de Génie Biomédical. Des jauges de tension placées sur l'index d'une main électrique procure l'information qui est transmise électroniquement, causant une sensation de fourmillement dans le moignon du patient, proportionnelle en intensité à la force de compression dans le doigt.

Ce système a été utilisé par une patiente du Ontario Crippled Children's Centre, à Toronto, depuis juin 1976. Elle l'emploie régulièrement avec beaucoup de satisfaction et d'enthousiasme. Cela lui donne un sentiment de compétence et de confiance qu'elle n'a pas sans lui.

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The upper limb is commonly thought of as an organ for grasping and moving things and its sensory function is forgotten. The importance, however, of sensory feedback from the hand becomes obvious when this feedback is impaired by neurologic disease or eliminated by amputation.

Many patients with a good upper limb prosthesis are quite capable of operating it efficiently but prefer not to wear it simply because the effort of monitoring the terminal device visually is too tedious and distracting. The patient may develop a fair sense of where the prosthetic hand is in space from the stump sensation, but firmness of grasp is difficult to appreciate, even visually.

Professionals concerned with prosthetics have long recognized the need to provide sensory feedback, but we have not found any record of successful fittings. The investigator most active in this field is Schmidl[1,2] who has developed experimental feedback systems for strength of grip, position sense and for switching off rapid movements on contact.

A system for providing sensory feedback was developed at the Bio-Engineering Institute of the University of New Brunswick. It provided, in a myoelectric limb, for the delivery of a tingling sensation to an area on the stump. The strength of this stimulus is proportional to the force of the grasp.

Myoelectric Control with Sensory Feedback

The sensory feedback system developed has been made compatible with the University of New Brunswick three-state myoelectric control system. This system allows an amputee to control opening and closing of an electrically driven terminal device by using the myoelectric output from a residual muscle in the stump. The myoelectric signal is sensed by three electrodes mounted in the stump socket and one muscle is used to control both opening and closing. Electrode paste is not required with this system.

The sensory feedback system is designed to generate a stimulus signal in the form of short pulses of current which are delivered to the amputee through an additional electrode placed in the stump socket. The repetition rate or frequency of the pulses is made proportional to the pinch force of the terminal device. The pinch force is sensed by miniature strain gauges mounted on the forefinger of the device under the cosmetic glove. This pinch-force information is processed by the system's electronics and is used to control the frequency of the stimulator. Application of current pulses through the stimulating electrode to the skin produces a tingling sensation which alters with changes in the frequency of the stimulus. The strength of sensation can be adjusted to a comfortable level when the system is fitted. This feedback system works on a time-sharing basis with the myoelectric control unit and, by recognizing structural deflections in the hand skeleton, delivers a proportionate current to the ground reference electrode in the socket.

The control and feedback electronics together with the rechargeable battery are placed in a single package small enough to be enclosed in the forearm of a below-elbow prosthesis. The battery is sufficient for a normal day's use.

The engineering challenges met in the design of this system include miniaturization of the electronics package, reduction of the battery power required to operate it to a minimum and elimination of interference between the feedback electronics and the control system electronics. This last challenge was the most difficult because of the great difference between the extremely small myoelectric signals and the stimulating signals which were both present at the electrodes placed in the stump socket. Special switching and sampling techniques were required to prevent the stimulating signals from being processed by the sensitive myoelectric amplifier. The following case report illustrates the application of the sensory feedback system.

Case Report

In 1967, a 9-year-old girl with a congenital amputation below the left elbow

attended the amputee clinic at the Ontario Crippled Children's Centre in Toronto. Her ulnar stump was 8.9 cm long. She was fitted with a conventional prosthesis and a Dorrance hand operated by a cable harness.

In January 1973, she was supplied with a new myoelectrically controlled prosthesis having a rigid polyester resin Munster-type socket and a three-state University of New Brunswick control system. Within a month, the patient became an excellent user of the prosthesis in spite of some initial problems.

In June 1974, a duplicate prosthesis was fitted, but with a feedback system added by the Bio-Engineering Institute at the University of New Brunswick (Figs. 1 and 2). Initially, there was some interference in the feedback system caused by the inner glove pulling on the leads to the strain gauges. Stretching of the index finger of the inner glove seemed to overcome this. The leads also were rerouted in the hand frame and fixed to it with epoxy. Proper calibration of the feedback system seemed a rather delicate procedure but, eventually, the patient could tell precisely how hard she was gripping.

FIG. 1—Patient showing natural appearance of prosthesis. Proximal part of prosthesis is normally covered by clothing.

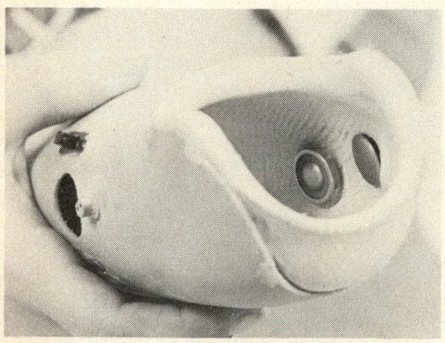

FIG. 2—Laterally in socket of prosthesis is pair of active electrodes; distal one is of bipolar construction. Outer ring of bipolar electrode transmits sensory stimulus. Reference electrode situated medially is not shown.

By September 1974, the patient's stump was covered with a severe rash. She had become allergic to the Beckman silver-chloride electrodes. The electrolytic environment created by the feedback current and the ever-present saline electrode paste tended to aggravate the situation. This problem persisted in spite of various medical treatments and replacement of the silver electrodes with gold-plated ones. Various makes of electrocardiographic pastes were tried unsuccessfully. It seemed essential to let the skin irritation subside before any further attempt at fitting was made and, therefore, in June 1975, she was supplied with a passive cosmetic prosthesis with a socket made of silicone rubber. By February 1976, the skin of her stump had healed well and she was fitted with a new myoelectric prosthesis with a three-state dry control system (without feedback). The socket comfort and suspension, which was by a suction valve, were excellent and the patient obtained good control over this myoelectric hand.

In June 1976, a three-state dry control system with feedback was added to this satisfactory limb. Again, adjustments to the sensitivity of the feedback system had to be made over a period of about 2 days.

Since that time, the patient has used this hand with great satisfaction.

Discussion

Although the sensory feedback system provides the patient with information about the force of grasp only and does not match a normal hand's ability to distinguish shapes, texture and temperature, it provided our patient with a sense of competence and confidence she never had without it. Her enthusiasm for it more than justified the trouble taken to overcome the problem of skin sensitivity and her continued use of this prosthesis demonstrates that sensory feedback in an upper limb prosthesis is both practical and valuable.

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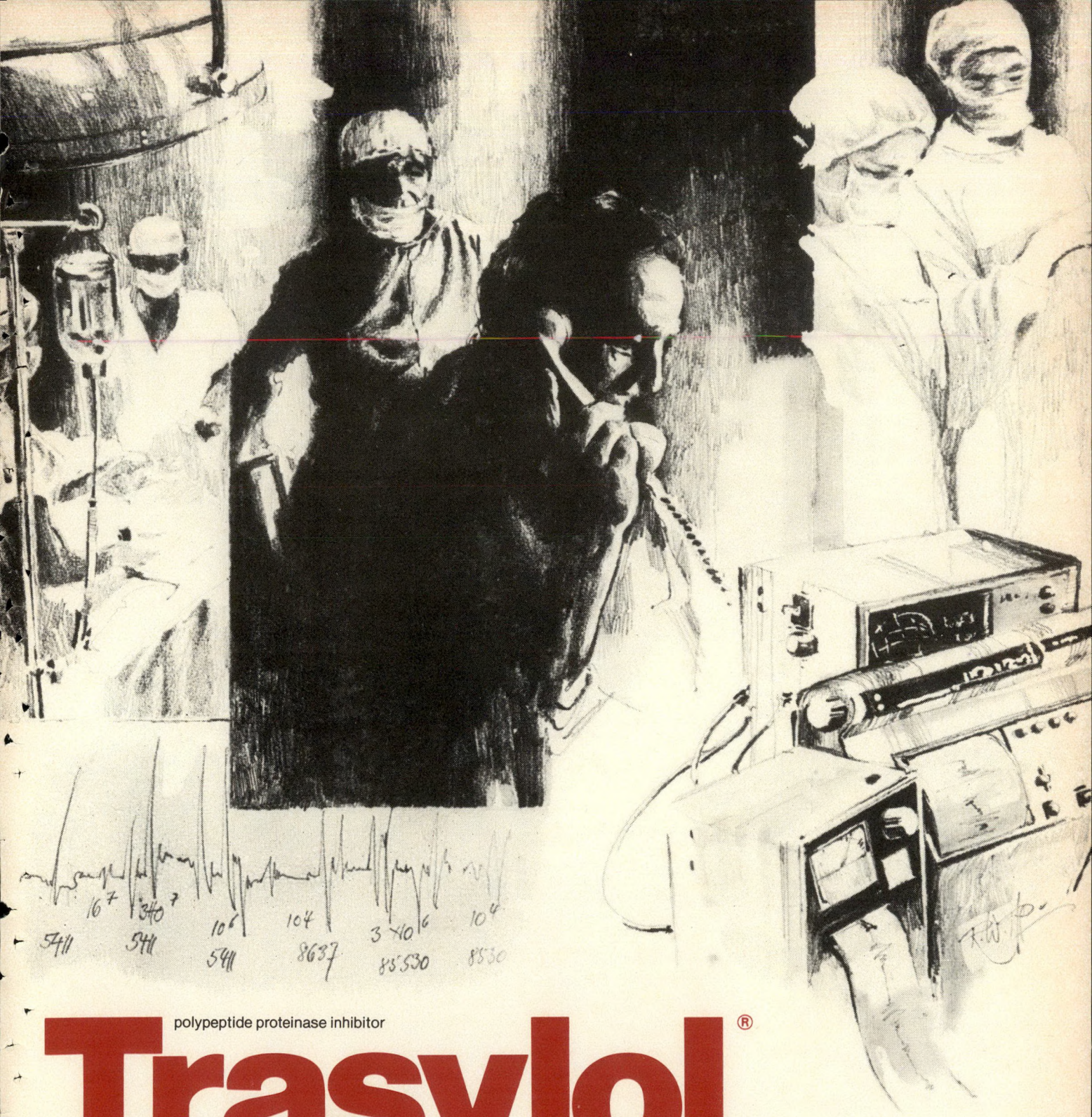
November issue

In addition to a group of urology papers, the next issue of this journal will contain a symposium on portal hypertension. The symposium comprises four papers (including a guest lecture on the emergency treatment of variceal hemorrhage by M.J. Orloff) and a panel discussion.



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Colorectal Neoplasm: a Rare Complication of Ureterosigmoidostomy

SERGE DUBÉ, MD,* JEAN-PAUL PERREAULT, MD, FRCS[C],* ANDRÉ DUMONT, MD† AND DENIS BERNARD, MD, FRCS[C]*

A 24-year-old woman had a rectal neoplasm which occurred 20 years after she had undergone ureterosigmoidostomy for exstrophy of the bladder. Only 41 cases of benign or malignant tumours of the large bowel developing after ureterosigmoidostomy have previously been reported in the literature. Adenocarcinoma of the colon is most frequently found and can develop even after urine has been diverted away from the colon. The presenting symptoms are either those of ureteral obstruction or of colorectal neoplasm. This rare complication remains intriguing and the possible pathogenetic mechanisms are discussed.

Les auteurs rapportent un cas de néoplasie rectale survenu 20 ans après urétéro-sigmoïdostomie pour extrophie vésicale. La revue de la littérature fait état de 41 cas de tumeurs bénignes ou malignes. La tumeur la plus fréquente dans ces cas est l'adéno-carcinome du côlon et elle peut se développer même après l'interruption de l'urétéro-sigmoïdostomie. Les manifestations cliniques peuvent être celles de l'obstruction urétérale ou des tumeurs du côlon. Cette complication, tout en état rare, demeure problématique et les principaux facteurs pathogénétiques sont présentés.

Ureterosigmoidostomy as a procedure of urinary diversion is associated with several complications, namely hyperchloremic acidosis, hydronephrosis and renal damage from reflux and infection. Tumour originating at the site of ureterocolonic anastomosis is a rare, well-recognized but not well-understood phenomenon. Benign and malignant colorectal tumours have been reported previously.[1-25] We report a case of rectal tumour occurring after ureterosigmoidostomy and review the literature to emphasize that a tumour may appear even after urine no longer flows into the colon. We also discuss the possible pathogenesis of this phenomenon.

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Case Report

A 24-year-old white woman was admitted to hospital in February 1972, complaining of intermittent rectal bleeding for the previous 2 years. She had also noted changes in her bowel habits. At the age of 4 years, she had undergone bilateral ureterosigmoidostomy for exstrophy of the bladder, which was subsequently resected. At 11 years of age, because of deteriorating renal function secondary to infection and reflux, her ureterosigmoidostomy had been converted to an ileal conduit. Both ureters were transected at the ureterosigmoid junction and the sigmoid colon was closed. For the next 12 years she had no problems except for the rectal bleeding mentioned above.

Upon admission her hemoglobin value was 10.4 mg/dl; results of all other laboratory tests were normal. Sigmoidoscopy revealed a sessile, ulcerated lesion (diameter 3 cm) situated 12 cm from the anal margin and a large polypoid lesion with a broad pedicle (diameter 1 cm) 18 cm from the anal margin. Biopsy of the distal lesion suggested that it was a villous tumour. The patient underwent anterior resection of the rectum. Her postoperative course was smooth.

Gross examination of the resected specimen showed two polypoid growths, measuring 1.5 and 3.5 cm, at the proximal end; 6 cm distal to these lesions there was a 3-cm ulcerated growth, which on macroscopic sectioning was seen to invade the muscularis of the rectum. Microscopic examination of the 1.5-cm polypoid lesion (Fig. 1) showed a non-neoplastic polyp covered by hyperplastic colonic mucosa; there was underlying edematous inflammatory tissue with round cell infiltration and numerous blood vessels around a fragment of sectioned ureter. The larger polypoid lesion (Fig. 2) was covered by hyperplastic mucosa; there were tubular adenomatous changes (adenomatous polyp), basophilic cytoplasm, loss of mucous secretion, areas of pseudostratification of the nuclei and numerous mitoses consistent with intraepithelial malignant proliferation. The pedicle was not affected. The pedicle itself contained some fragments of sectioned ureter. The ulcerated lesion (Fig. 3), found 6 cm distal to the ureteral stumps, appeared to be a moderately differentiated adenocarcinoma invading the superficial layers of the muscularis propria of the rectum, a true Dukes A lesion.[26]

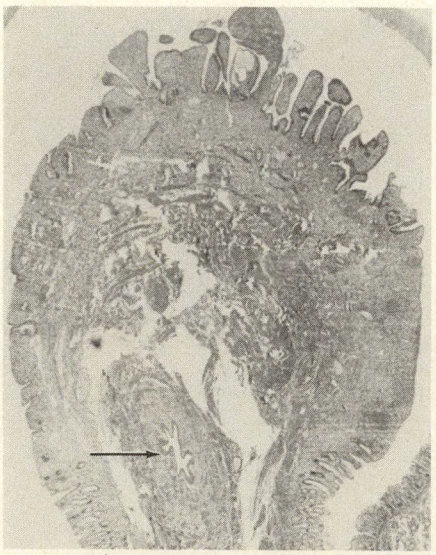

FIG. 1—Detail of polypoid growth measuring 1.5 cm in diameter. Inflammatory polyp is covered by hyperplastic colonic mucosa. Lamina propria and submucosa show edema and chronic inflammatory reaction. At base of lesion, segment of sectioned ureter is present (arrow). (hematoxylin and eosin, reduced by 27% from ×7.15).

FIG. 2—Larger polypoid growth. Hyperplastic colonic mucosa (arrow 1) covers this broad-based polypoid lesion. Adenomatous changes are present with focal cellular atypia consistent with superficial intramucosal malignant proliferation (arrow 2). Fragment of sectioned ureter is present at base of polypoid growth (arrow 3) (hematoxylin and eosin, reduced by 43% from ×3.8).

This patient, now 31 years old, is alive and well 7 years after operation. At her regular follow-up examinations, the anastomotic area has been pliable and sigmoidoscopic examinations have shown no evidence of tumour recurrence in the remaining rectum or sigmoid colon. As an interesting corollary, exactly 5 years after this patient's operation we operated on her mother for a polypoid adenocarcinoma of the sigmoid colon, with a good result.

Review of the Literature

Hammer,[1] in 1929, reported the first case of a neoplasm developing at the site of ureterosigmoidostomy 10 years after implantation, in a patient with exstrophy of the bladder. Forty more cases have since been reported in the literature.[2-25] The sex distribution (Table I) shows that males are predominantly affected. One of the reasons for this distribution is the greater frequency of exstrophy of the bladder in boys. Of the 42 patients 26 (62%) required ureterosigmoidostomy diversion for this condition. Other clinical conditions which have been treated by surgical diversion are shown in Table II. Of the 42 lesions 32 were malignant. Of the malignant tumours, 20 (62%) were adenocarcinomas of the colon, 5 were undifferentiated carcinomas, 4 mucinous adenocarcinomas and 3 were transitional cell carcinomas. The 10 benign lesions were almost all adenomatous polyps. The high frequency of adenocarcinoma in the colon of younger patients is statistically significant.[25] Urdaneta and associates[25] have calculated the frequency to be 500 times greater than expected in this age group. It is interesting that in 62% of the reported cases the patient was younger than 40 (Fig. 4) (mean 38 years), whereas only 7.5% of the colonic carcinomas in the general population occur before the age of 40 years (mean 58 years).[27] However, the frequency of malignant tumours does not seem to be related to the period of time after the ureterosigmoidostomy (Fig. 5).

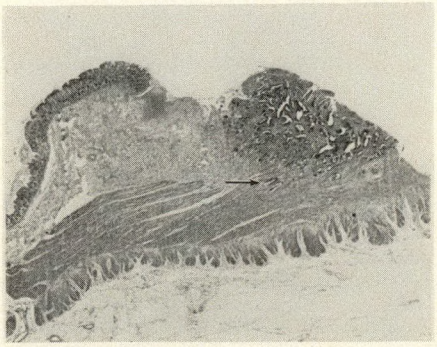

FIG. 3—Ulcerated lesion that was situated 3 cm distal to ureteral stumps is moderately differentiated adenocarcinoma which invaded wall of rectum as far as superficial portion of muscularis propria (arrow) (hematoxylin and eosin, reduced by 43% from ×9.28).

Discussion

Among the etiologic factors involved in the formation of tumour at the site of ureterosigmoidostomy, two particularly have been implicated: the presence of urine in the colon and mechanical irritation of the ureteral stoma.

Possible carcinogens and irritants in the urine have been suggested as important factors. Although Scott and Boyd[28] in relatively long-term experiments were unable to demonstrate that B-naphthylamine, well recognized as a carcinogen, caused malignant degeneration in dogs with ureterosigmoidostomy, we could not rule out the role played by the urine as a carcinogenic factor even though our patient had undergone ileal conduit diversion 13 years earlier. The study of Sommo and Traverso[29] appears to provide some evidence to confirm the importance of urine in the histologic modification of the colonic mucosa. They studied histologic and histochemical changes in the bowel mucosa of patients from 2 to 48 months after ureterosigmoidostomy. They first noted a period of proliferation during which the glandular epithelium showed marked cellular hyperplasia and overproduction of mucus. This was followed by atrophic changes. Undifferentiated cellular elements, which produced little mucus, formed solid cords replacing the normal glandular cells.

Some patients may lack repair enzymes or possess enzymes that consistently lead to miscoding and perpetuation of an error in DNA production and its transcription. As Weisburger[30] stressed in discussing the role of the diet in colonic neoplasm, urine could also modulate the effects of carcinogens on the gut by its influence on the microflora. Activation of the microflora provokes the formation of split products that may be carcinogenic.

When there are mechanical factors causing chronic inflammation, there is a need for continuous repair of the mucosa which increases the risk of an abnormal healing process.

Although urine is diverted from the colon, once the cellular changes have been initiated their progression can-

Table I—Sex Distribution of Benign and Malignant Tumours of the Colon and Rectum Occurring after Ureterosigmoidostomy

Sex	Benign	Malignant	Total (and %)
Male	8	21	29 (69)
Female	2	11	13 (31)
	10	32	42 (100)

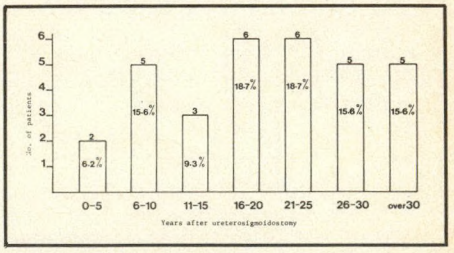

FIG. 4—Age distribution of malignant ureterocolonic tumours compared to that of colonic cancers in general population (n = number of patients).

Table II—Distribution according to Primary Urologic Condition and Differentiation into Benign or Malignant Lesions

Primary conditions	Benign	Malignant	Total (and %)
Bladder exstrophy[1,2,4–6,9,10,12–15,17,18,20,21,24,25]*	6	20	26 (62%)
Transitional cell carcinoma[3,10,11,19,25]	2	5	7
Epispadias[8]	1	1	2
Nonbacterial cystitis[10]	1	0	1
Interstitial cystitis[25]	0	1	1
Squamous cell carcinoma of bladder[25]	0	1	1
Persistent urinary fistula[7,20]	0	2	2
Congenital incontinence[22]	0	1	1
Trauma to bladder[15]	0	1	1
	10	32	42

*Includes present study.

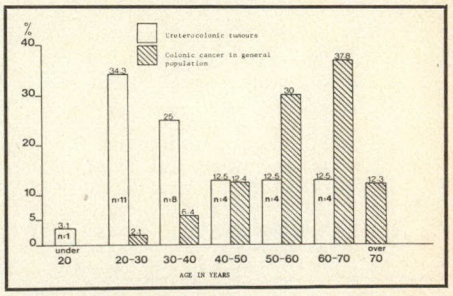

FIG. 5—Distribution of malignant tumours in relation to time elapsed after uterosigmoidostomy.

not be limited. In the present case, we can witness the progressive response of the mucosa to the different stresses. At the ureterosigmoidostomy junction we found two hyperplastic lesions, and in one there were both adenomatous and carcinomatous proliferations. The third tumour, found 3 cm distal to the ureteral stumps, was a well-differentiated adenocarcinoma.

There is another possible explanation. In some cases there may be predisposing factors; the mother of our patient also had an adenocarcinoma of the sigmoid colon. Thus the role of the urine, in this case, seems to have been an adjuvant in manifesting a pre-existing propensity for tumour formation.

A number of factors are most likely implicated in the pathogenesis of this condition and their interrelationships lead to a great deal of speculation.

Conclusion

Although ureterosigmoidostomy has been replaced to a large extent by other methods of urinary diversion, those patients who have had the procedure should be followed up very carefully. In the presence of rectal bleeding or deteriorating renal function, patients should be examined by intravenous pyelography, roentgenography after a barium enema and sigmoidoscopy. Moreover, if conversion to an ileal conduit is indicated, resection of the colonic segment into which the ureters had been implanted should be done to prevent tumour forming at the site of the ureteral stomas. It will be interesting to see if this complication develops more frequently with the increasing use of a colonic conduit. The colonic mucosa is perhaps more sensitive to malignant degeneration than the ileum but with the colonic conduit, mechanical trauma and stagnation of urine are less marked. However, one must be aware that these tumours exist and that they should be sought when indicated.

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Critique of Item 606 (SESAP II)

In a young man a painless testicular mass which does not transilluminate is a neoplasm until proved otherwise. A hydrocele or spermatocele, and possibly a hernia, would transilluminate. Preliminary studies should include a roentgenogram of the chest, an intravenous pyelogram, and an assay for gonadotropins. The preferred response is orchiectomy through an inguinal incision. Needle aspiration of fluid or needle biopsy is contraindicated because a testicular tumor is usually well contained by the tunica albuginea, but once it is entered, the tumor spreads rapidly to the scrotum and to the lymph nodes in the groin. For the same reason, the incision should not be made through the scrotum. The mass as described is very unlikely to be an epididymitis, and administration of antibiotics, and observation for two to four feeks, are therefore not justified.

C

Reference

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Intraoperative Transmural Myocardial Biopsy: a Simple Technique

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S.M. WASAN, MD, M SC, FCAP, FRCP[C]† AND E.J.P. CHARRETTE, MD, FRCS[C]*

A Tru-cut disposable biopsy needle was used in 10 pigs, 3 cadavers and 63 humans to obtain transmural ventricular myocardium for diagnostic and research purposes. The technique proved simple and safe. In every case an adequate amount of full-thickness myocardium was obtained which was examined by light and electron microscopy and used for enzyme studies and glycogen measurement.

Une aiguille à biopsie jetable Tru-cut a été utilisée chez 10 porcs, 3 cadavres et 63 humains pour obtenir un prélèvement du myocarde à travers la paroi du ventricule pour fins de diagnostic et de recherche. La technique s'est avérée simple et sûre. Dans tous les cas, une quantité suffisante du myocarde entier a été obtenue et ensuite a été examinée aux microscopes optique et électronique et utilisée pour des études enzymatiques et des mesures du glycogène.

Although endomyocardial biopsy can be performed by the percutaneous route,[1-3] transmural myocardial samples are more difficult to obtain. Search for a simple method led us to use a disposable needle which gave uniformly successful results.

Material and Methods

Ten Poland-China pigs were anesthetized. The heart was exposed and separate biopsy specimens were obtained from left ventricular myocardium using a Tru-cut biopsy needle (Travenol Laboratories, Inc., Deerfield, IL) (Figs. 1 and 2). The full-thickness specimens (0.1 × 1.7 cm) weighing 8 mg each (Fig. 3) were examined by light and electron microscopy, and were used for glycogen measurement and enzyme studies.

The need for transmural myocardial biopsy specimens for clinical investigation and diagnostic purposes prompted us to try the same needle in three cadaver hearts. The technique was equally successful. This was followed by use of the needle in a series of 63 patients of whom 55 had elective coronary artery bypass surgery, 5 had valve replacement, 2 underwent elective closed mitral commissurotomy and 1 had emergency pericardiectomy. Two separate biopsies were done at the apex of the left ventricle, at the start of cardiopulmonary bypass and again following completion of the proximal anastomoses just before unclamping of the aorta. The puncture site produced by the needle was closed with a simple superficial figure-of-eight suture of 4-0 Prolene (Ethicon Sutures Ltd., Peterborough, Ont.).

In the patients who underwent valve replacement, the left ventricular biopsy was done at the site where the vent is usually inserted.

There were no complications associated with the biopsy procedure. An adequate amount of tissue was obtained in every patient and was used for clinical research in 60 patients and for diagnostic purposes in 3 patients.

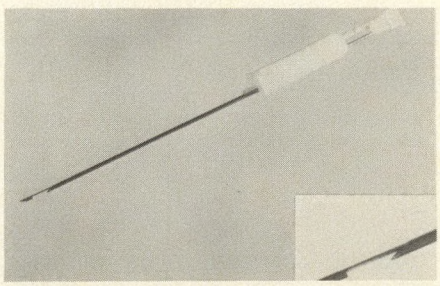

FIG. 1—Disposable biopsy needle. Insert shows cutting edge.

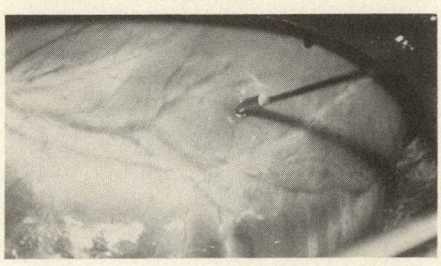

FIG. 2—Biopsy needle being positioned before transmural myocardial biopsy.

Discussion

Endomyocardial biopsy specimens can be easily obtained by the percutaneous route. The sample, however, may not be representative of the ongoing processes in the other layers of the heart. Other techniques including the use of the Silverman needle,[4] the Menghini needle[5] and the Dobell biopsy gun (Dobell ARC: unpublished data, 1971) have been used to obtain a specimen that includes all layers of myocardium. The method we describe is easy and reproducible. No complications have occurred. In every case adequate full-thickness tissue cores were obtained. Specimens of this sort may be of great value in elucidating the nature of ongoing processes in the different layers of the heart. We think we have solved a major problem for the cardiac surgeon involved in clinical research, namely, that of obtaining a full-thickness biopsy of the myocardium.

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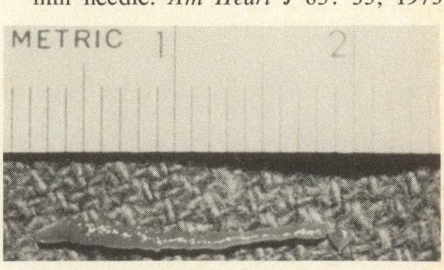

FIG. 3—Core of myocardium obtained with Tru-cut biopsy needle.

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continued from page 451

DIE UNTERSUCHUNG DER BAUCHSPEICHELDRUSE. I. Hamberger Medizinisches Symposium 12. und 13. Dezember 1975. Edited by Heinrich Bartelheimer, Meinhard Classen, Friedrich-Wilhelm Ossenberg. 172 pp. Illust. Georg Thieme Verlag, Stuttgart, 1976. DM 50, paperbound. ISBN 3-13-5446-01-8.

This well-prepared monograph presents the proceedings of a conference devoted to the diagnostic aspects of pancreatic disease. The majority of the papers are written in German, but some are in English. Various diagnostic tests and procedures introduced recently are reviewed competently by different experts reporting their own experiences. Tests for enzymes and fetal antigen, ultrasonography, biopsy, angiography and cannulation of the pancreatic duct through a fiberoptic endoscope are some of the diagnostic aids described and discussed. With the use of these new procedures pancreatic disease can be diagnosed accurately.

This text is an excellent, concise state of the art review which can be recommended to all interested in pancreatic disease.

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GENERAL SURGICAL OPERATIONS. Edited by R.M. Kirk. 412 pp. Illust. Churchill Livingstone, Edinburgh; Longman Canada Limited, Don Mills, Ont. 1978. Price not stated. ISBN 0-443-01597-X.

This book is essentially a technique text but has a unique style. The format of each chapter is identical. The author provides all data under the headings of preoperative care, operative techniques, operative considerations, problems, safeguards and access. Most major procedures are covered in one to two pages, yet the information is complete and readable. There are only two or three references for each section but all are important and provide good direction for further reading.

The first 12 of the 27 chapters are devoted to abdominal surgery and 9 of these are by Kirk himself so that there is good continuity. The chapter on anorectal diseases is written by Lord who is a well-recognized expert in that field. While there were many technical points with which I would raise mild objections, only in Lord's chapter did I find two worth pointing out. On page 148, there is considerable confusion as to whether the patient is actually in the Sims or the lithotomy position. The statement that "patients remain in hospital for six to ten days after hemorrhoidectomy" would certainly raise some eyebrows. Also, Lord states that anal dilatation should be undertaken with "caution in the elderly". This point is not emphasized enough since the text indicates that anal dilatation is quite acceptable and the author does not define what is meant by "with caution". The frequency of incontinence is unacceptably high when rectal dilatation is performed in patients over 55 years of age.

Chapters 13 to 27 cover every other sphere of surgery and, with one exception, each chapter has been written by a separate author. Included in this block are three chapters specifically related to general surgery dealing with the breast, endocrine system and the head and neck respectively. I found the chapter on the endocrine system quite brief (three pages). Also, in view of the increasing incidence of hyperparathyroidism, I thought that a half page dealing with this topic and providing no illustration was inadequate coverage. On the other hand, there are ample articles in the literature dealing with this sphere of endocrine surgery.

Orthopedic surgery is rather heavily weighted receiving in this text three chapters for a total of 75 pages. Peripheral vascular surgery, on the other hand, is dealt with in 16 pages; although this chapter is brief it is quite well done. Similarly, cardiothoracic surgery received only 20 pages. Perhaps, the editor could justifiably argue that he wished to provide only the bare essentials in these two areas since the book is oriented towards the general surgeon who might possibly have to deal with all situations. However, the intricate procedures described in the three orthopedic chapters indicate that editing was poor in these areas. My impression was that the chapters on peripheral vascular, cardiothoracic and orthopedic surgery were solicited and then simply inserted into the text as received. This is, of course, a common problem with multiple-authored texts. To give Kirk the benefit of the doubt, it is possible that general surgeons perform more orthopedic surgery than peripheral vascular or cardiothoracic surgery in Great Britain. Also, the format of these chapters is identical to that used in the other chapters suggesting that some editing was carried out.

In summary, this textbook of surgical techniques is brief but very complete and to the point. Every aspect of surgery from ingrown toenails to foreign bodies in the eye is covered in cookbook style. This renders the text excellent for rapid preoperative review of the subject material. I particularly like the appropriate check lists provided with most of the procedures. This text does not replace the standard surgical technique books such as those of Cooper or Maingot but it apparently was not intended to compete with them. For the intern, the first- or second-year surgical resident, "General Surgical Operations" is an excellent and highly recommended book. It might be useful to the surgeon located in a small community who must perform many types of surgery. Advanced surgical residents or completely trained surgeons would find this text beneficial only for teaching more junior colleagues.

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GENITOURINARY PROBLEMS IN WOMEN. Jack R. Robertson. 149 pp. Illust. Charles C Thomas, Publisher, Springfield, IL, 1978. $16.75. ISBN 0-398-03668-3.

This book consists of an introduction and chapters on the history of gynecologic urology, anatomy and physiology, methods of evaluating urinary incontinence, the Robertson method, the neglected female urethra, vesicovaginal fistula, bladder drainage, urinary tract infections, the dysfunctional bladder and urethra, and pelvic surgery with endoscopic control. It is devoted chiefly to the evaluation and treatment of urinary incontinence in women, the female urethra and vesicovaginal fistula. The author presents his views on the etiology, pathogenesis and treatment of these conditions, often in great detail.

The most interesting features of the book are the sections devoted to the investigation and management of urinary incontinence in the female. However, it is difficult to recognize that stress incontinence is seen within the larger framework of functional and etiologic classifications of urinary incontinence.

Most urologists believe that the classic paper by Marshall, Marchetti and Krantz (The correction of stress incontinence by simple vesicourethral suspension. *Surg Gynecol Obstet* 88: 509, 1949) remains the standard by which other methods for investigating and treating stress incontinence are judged. They put forward the exceedingly simple etiologic concept which formed the basis of treatment. As different methods of investigation have appeared since 1949, each has developed with its own jargon. The result is that many different terms are now used to explain the basic concept of Marshall, Marchetti and Krantz, but these terms are related to the different methods of investigation and not to the underlying pathology, thus causing much unnecessary confusion. This book is one example of many.

There are numerous examples in this book of its parochial approach. There is no mention of Victor Bonney's paper of 1923 in the history chapter, a surprising omission. No mention is made of attempts at surgical treatment of stress incontinence before that of Kelly in 1893. In the foreword, it is stated, "urologists have concentrated their efforts on the male, and most of them know very little about the female urethra and bladder". The lack of knowledge of urologic interest in these conditions in the past 30 years is again surprising. There seems to be little recognition that many of these problems are now managed by multidisciplinary treatment teams. The methods presented are undoubtedly successful in

the hands of the author and are interesting in this context.

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A MANUAL OF THORACIC SURGERY. Arndt von Hippel. 247 pp. Illust. Charles C Thomas, Publisher, Springfield, IL, 1978. $13.75, clothbound; $8.75, paperbound. ISBN 0-398-03689-6, clothbound; ISBN 0-398-03690-X, paperbound.

This book is an expanded version of a previous publication, "Chest Tubes and Chest Bottles", by the same author. The format is the same, chapters being divided into short sections for easy reading. The book is written in a flowing narrative style and points are illustrated using simple diagrams and anecdotal "case reports".

"Chest Tubes and Chest Bottles" has been enlarged by adding new chapters on the diaphragm, the lung, the *blood pump* (my italics), and pleural effusions; previous topics have been discussed more fully with extra emphasis on diagnosis and methods of treatment of thoracic surgical disorders. No attempt has been made to cover the technical aspects of surgery, although detailed methodology for pleural aspiration and insertion of chest tubes is given. The technique of closed needle biopsy of the pleura is not mentioned.

This expanded text attempts to deal with thoracic physiology and surgery as they relate to closed chest drainage. However, to describe the diaphragm as a muscle sandwich, the respiratory system as the air pump, or the heart as the blood pump seems rather simplistic. Physiologic misconceptions in the text may be the result of this oversimplification, detractisg from the book's quality as do some errors of omission.

The chapters on chest tubes and bottles, almost unchanged from the previous publication, are very good. Included are indications for insertion of tubes, detailed technique for introduction and an excellent diagram illustrating an easy way to secure the tube—always, I think, one of the most difficult parts of the procedure. There is also a useful section on "trouble shooting" problems that may occur while the chest tube is in place.

The book is aimed at "less experienced, or more highly specialized thoracic surgeons". Although the author relates his personal experience rather than giving a didactic review of the literature, I think most thoracic surgeons will find it oversimplified. It would, however, make excellent reading for practitioners who only occasionally deal with chest tubes and bottles, and for all nurses who care for patients who have undergone thoracic surgery.

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PLASTIC AND RECONSTRUCTIVE SURGERY OF THE FACE AND NECK. Proceedings of the Second International Symposium. Volume 1: Aesthetic Surgery. Edited by George A. Sisson and M. Eugene Tardy, Jr. 236 pp. Illust. Grune & Stratton, Inc., New York; Longman Canada Limited, Don Mills, Ont., 1977. $45.65. ISBN 0-8089-0941-X.

PLASTIC AND RECONSTRUCTIVE SURGERY OF THE FACE AND NECK. Proceedings of the Second International Symposium. Volume 2: Rehabilitative Surgery. Edited by George A. Sisson and M. Eugene Tardy, Jr. 348 pp. Illust. Grune & Stratton, Inc., New York; Longman Canada Limited, Don Mills, Ont., 1977. $59.40, ISBN 0-8089-0956-8.

In 1975 the American Academy of Facial Plastic and Reconstructive Surgery hosted the second international symposium on the subject for which this Academy was named. Inevitably these two volumes are a summary of the proceedings, containing some papers in full and others greatly shortened. The panel discussions have also been included. The books are thus neither detailed enough to explain the latest techniques nor broad enough to be used as general reference works.

The illustrations are the greatest drawback to these two books. Preoperative and postoperative pictures have been taken from different angles, different distances and under different lighting, so that a true comparison is impossible. Indeed the majority of comparative pictures are useless.

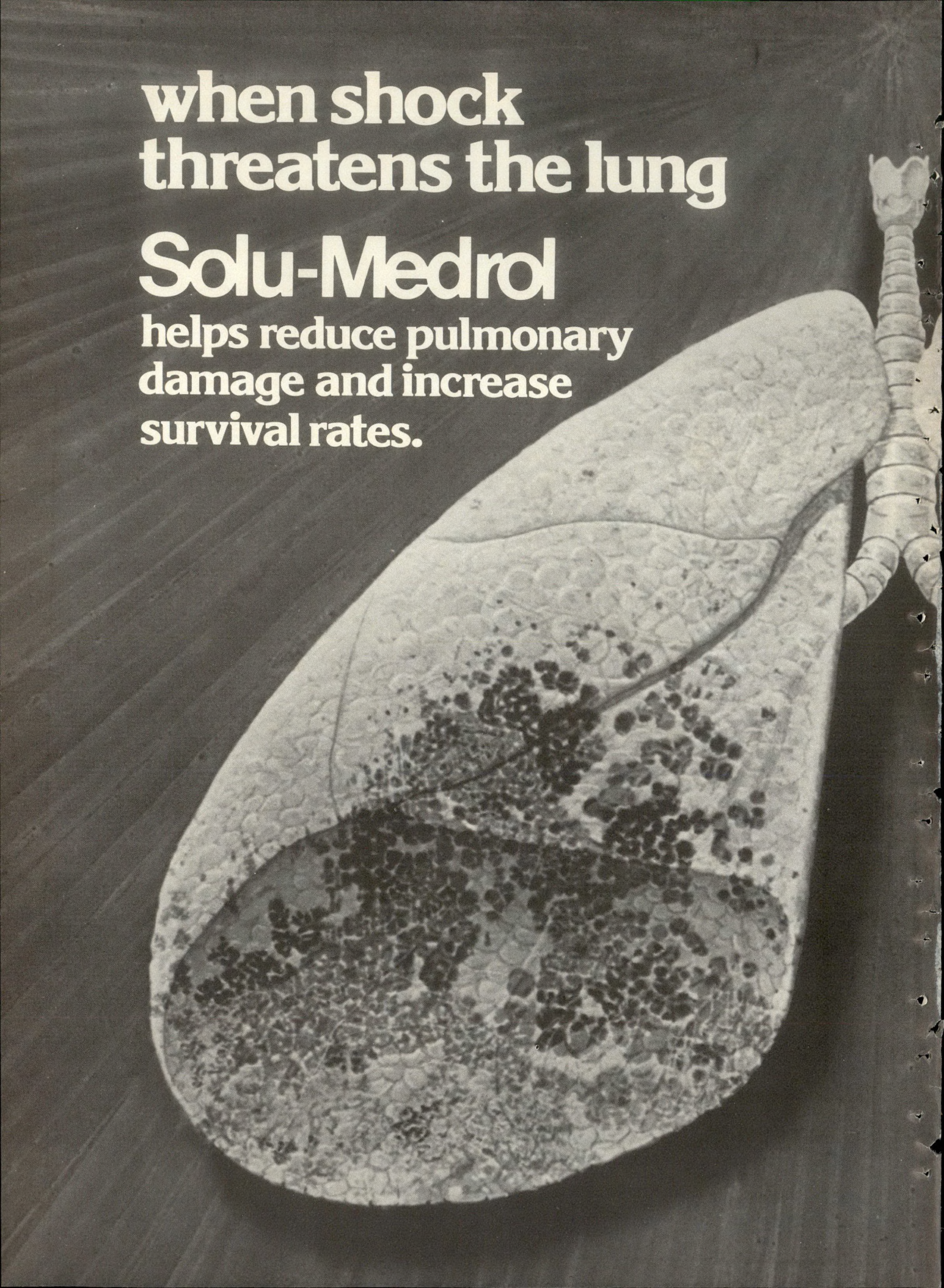
Half the first volume on aesthetic surgery is devoted to rhinoplasty. An experienced rhinoplastic surgeon may gain a few tips but no basic techniques are discussed. A very short section is devoted to rhytidectomy and most postoperative photographs were taken at such a short interval after operation that they are of no use. The segment on the orbit discusses blepharoplasty and devotes a substantial chapter to supraorbital ridge reduction. Again it is difficult to tell the difference between preoperative and postoperative appearances. Otoplasty is limited to three pages on one technique.

The second volume on rehabilitative surgery covers many subjects from the head and cancer to laryngeal prominence reduction for trans-sexual patients. As in the first volume the photographs are poor and distorted. Often they show change but no improvement for the patient. Many chapters consist of case reports only. Indeed one chapter is a case report of one patient and an old technique for reconstruction of the temporomandibular joint. A new superior pharyngeal flap technique (which is not new) is described based on five patients! Many of the best and most modern techniques such as in microtia correction, traumatic ear reconstruction or electrical burns of the mouth seem to

when shock threatens the lung

Solu-Medrol

helps reduce pulmonary damage and increase survival rates.



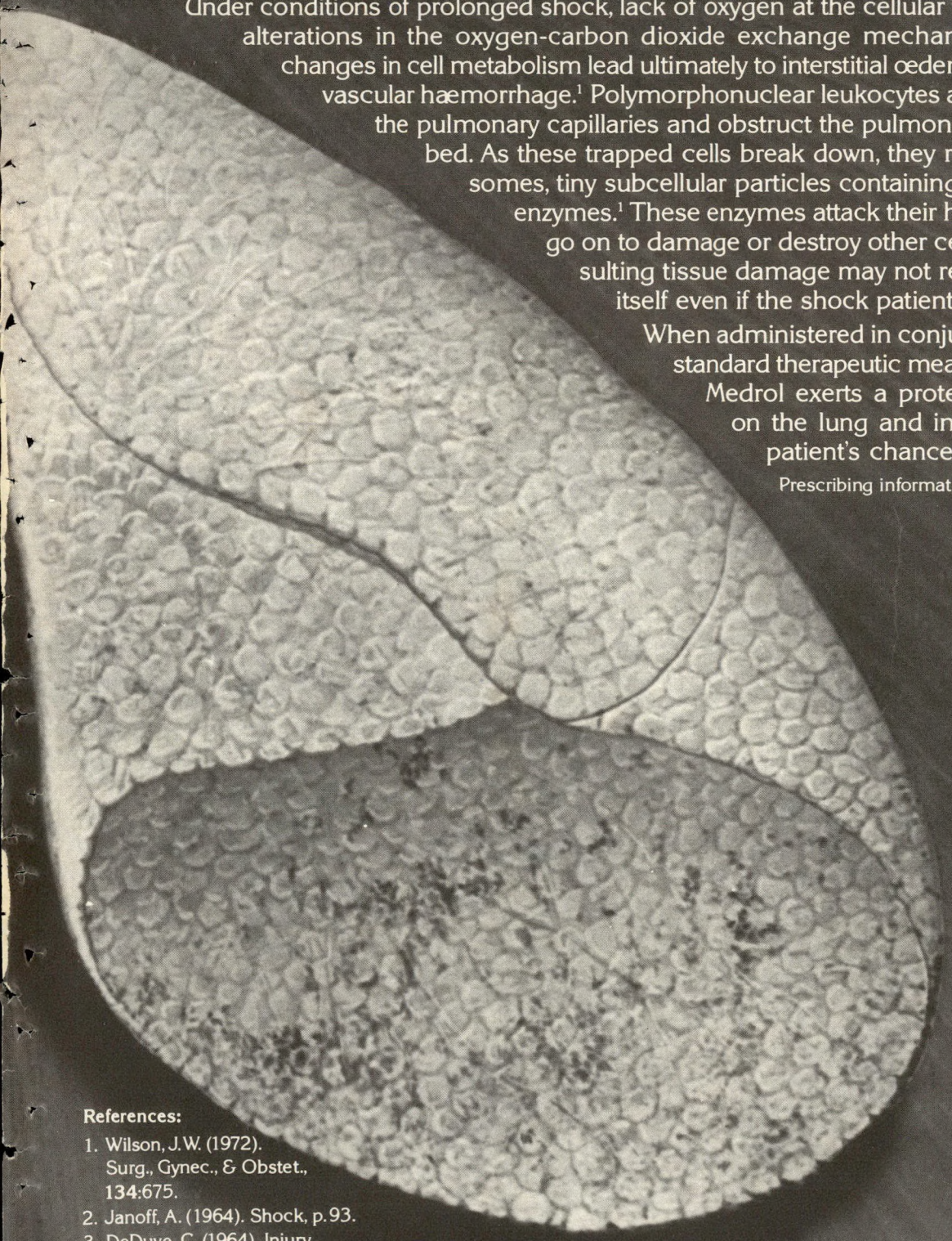
- preserves lysosome and cell membranes, thereby preventing the release of destructive lysosomal enzymes[3]
- preserves platelets thereby reducing the risk of intravascular coagulation[1]
- preserves leukocyte integrity thereby helping to maintain the pulmonary architecture[1]

The recovery of patients in shock is often complicated by a pattern of deteriorating pulmonary function, commonly described as shock lung. This pulmonary insufficiency progresses despite restoration of hæmodynamic balance and apparent stabilization of the acute episode.

Under conditions of prolonged shock, lack of oxygen at the cellular level causes alterations in the oxygen-carbon dioxide exchange mechanism. These changes in cell metabolism lead ultimately to interstitial œdema and perivascular hæmorrhage.[1] Polymorphonuclear leukocytes aggregate in the pulmonary capillaries and obstruct the pulmonary vascular bed. As these trapped cells break down, they release lysosomes, tiny subcellular particles containing proteolytic enzymes.[1] These enzymes attack their host cell and go on to damage or destroy other cells.[2] The resulting tissue damage may not readily repair itself even if the shock patient survives.

When administered in conjunction with standard therapeutic measures, Solu-Medrol exerts a protective effect on the lung and improves the patient's chance of survival.

Prescribing information on page 492



References:

1. Wilson, J.W. (1972). Surg., Gynec., & Obstet., **134**:675.
2. Janoff, A. (1964). Shock, p. 93.
3. DeDuve, C. (1964). Injury, Inflammation, and Immunity, p. 283.

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be omitted and possibly are unknown to the authors.

In summary there is little value in these two volumes apart from historical interest for those who attended this symposium.

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THE SECOND INTERNATIONAL SYMPOSIUM ON MALIGNANT HYPERTHEMIA. Proceedings of a Symposium Held in Denver, Colorado, April 1-3, 1977. Edited by J. Antonio Aldrete and Beverley A. Britt. 560 pp. Illust. Grune & Stratton, Inc., New York, 1978. $25.50. ISBN 0-8089-1073-6.

Malignant hypermia has become recognized as one of the principal causes of death in patients who are anesthetized for surgical procedures. The syndrome is rare with prevalence ranging from 1 in 14 000 to 1 in 110 000 but is inherited as an autosomal dominant characteristic. Therefore, every surgeon and anesthetist should be acquainted with the recent advances in etiology, detection, prevention and management of this condition.

The first international symposium was held in Toronto in May 1971. Since then, much new knowledge has accumulated on the subject. We can be proud that some of the most fruitful research in this field has been performed in Canada.

This text is divided into sections on muscle physiology and biochemistry, diagnostic and predictive tests, clinical observations, studies in pigs exhibiting the porcine stress syndrome (a condition similar to malignant hyperthermia in humans) and the current treatment of this affliction.

The main site of the disease is in skeletal muscle where the regulation of calcium ion distribution is abnormal. Muscle samples from susceptible individuals show increased contraction in response to a wide variety of stimuli including anesthetic agents and various forms of stress. The exposure of malignant hyperthermic muscle to halothane, succinylcholine and some other anesthetic agents in vivo leads to a sudden release of calcium ions into the myoplasm which produces all of the clinical features of the syndrome. Recent studies suggest that the "membrane disorder" responsible for the disease may be present elsewhere in the human body including cardiac muscle.

All individuals susceptible to malignant hyperthermia have an underlying muscle disease and two predisposing myopathies have been defined; the commoner myopathy affects young boys whose physical abnormalities include short stature, cryptorchidism, pectus carinatum, antimongoloid slant of the palpebral fissures, ptosis, webbed neck, low set ears, kyphosis, lordosis and weakness of the serrati muscles. Malignant hyperthermia is also known to be associated with osteogenesis imperfecta.

Clinically, the syndrome develops during the administration of anesthesia usually in response to such potent agents as halothane or succinylcholine. However, many different types of drugs have been shown to precipitate the condition. Even the use of regional anesthesia does not always ensure protection. The usual symptoms are tachypnea, tachycardia, hypertension, cardiac arrhythmias, hypotension and a rapid increase in body temperature of approximately 2°C/h; muscle rigidity may or may not be present. Laboratory studies show severe metabolic and respiratory acidosis, hyperkalemia, hyperglycemia and hypercalcemia followed by hypocalemia, myoglobinurea and a marked increase in the metabolic rate and in oxygen consumption. The patient may become comatose, convulse, experience cardiac arrhythmias or sudden cardiac arrest. The condition may be further complicated by disseminated intravascular coagulation, renal failure or sepsis.

Proper management depends on the detection of susceptible persons so that steps can be taken to prevent the use of agents which may trigger the syndrome. Immediate appropriate therapy at the first signs of the syndrome will often abort an attack and thus reduce mortality.

This text reviews and evaluates various tests that have been used to screen individuals for the condition when a family history of death during or following anesthesia alerts the anesthetist or surgeon to the possibility that other family members may be afflicted. Creatinine phosphokinase values will generally be higher in susceptible persons. However, false-positive and false-negative results can occur.

Once suspected, muscle biopsy will generally confirm the diagnosis. A positive result from the caffeine or halothane contracture test indicates susceptibility to the syndrome. After additional trial studies have been completed measurement of serum inorganic pyrophosphate concentrations may be valuable.

Anesthesia can be administered to susceptible patients providing that agents known to trigger the condition are avoided. Once the clinical signs have been recognized during anesthesia, the use of the responsible agents should be discontinued immediately and cooling procedures instituted. The lactic acidosis, electrolyte imbalance, disseminated intravascular coagulation and anuria should be treated vigorously.

The main message delivered by this excellent collection of papers is that by the utilization of current knowledge this rare syndrome can be detected and effectively treated or prevented with a consequent reduction in perioperative mortality.

A new drug, dantrolene sodium, which lowers the myoplasmic calcium concentration, promises to be a most effective agent in treating malignant hyperthermia.

The impressive papers, featuring graphic illustrations on the anatomy, biochemistry and pathophysiology of skeletal muscle deserve special commendation and should be of interest to those concerned with muscle related diseases.

This book is recommended to all physicians as a source of information on the complex subject of malignant hyperthermia. However, this book is not easy to read. Assimilation of the information requires time and concentration.

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SHAW'S TEXTBOOK OF OPERATIVE GYNECOLOGY. 4th ed. Revised by John Hawkins and Christopher N. Hudson. 547 pp. Illust. Churchill Livingstone, Edinburgh; Longman Canada Limited, Don Mills, Ont., 1977. $98. ISBN 0-443-01394-2.

Henry Gage, writing in "The Science of Political Economy" in 1898, said: "The value of a thing is the amount of labouring or work that its possession will save the possessor." Using this criterion, Shaw's book is not a good purchase for the practising gynecologist. However, it can be recommended for medical libraries catering to students and prospective specialists.

To dispense with its main liability: the publisher's brochure states that in recent years there has been greater emphasis on the medical and endocrinologic aspects of modern gynecology, yet gynecologists still require the traditional skills of surgery. I agree with that statement, but neither this book nor any other I've seen will ensure this heritage. Why do authors and publishers of surgical texts continue to fantasize on this point? No one can ever learn surgical technique from a book. The techniques the surgeon uses are those taught during the residency period.

The artist's drawings in this book are typical of those seen in surgical texts. They are grossly inadequate. One would need the genius of Michelangelo, the innovative spirit of Leonardo da Vinci and a touch of Picasso to illustrate the flowing dynamics of a surgical operation. Authors of surgical texts should stop deceiving themselves that it can be done.

This book does have some merits. Students and residents will benefit from the chapters on anatomy, preoperative preparation and postoperative complications. There are also sound discussions on the basic gynecologic diseases. Moreover, since this is an operative textbook, it provides the nonspecialist reader with a general idea of the surgical approach to these problems.

There is an adequate section on laparoscopy. I heartily concur with the author that one eye in the pelvis is often better than two fingers in the vagina. But I disagree on one technical point. The author advises surgeons to make an incision at the inferior margin of the umbilicus. This is a potentially hazardous location. The umbilicus is not the entrance to the pelvis. The aorta lies directly beneath it and several reports in the medical literature discuss injuries to this vessel resulting from laparoscopy. More injuries will occur in future if surgeons continue to use this site. Why not use the true entrance to the pelvis? This is three fingers' width below the umbilicus. And the short transverse incision in this location can hardly be seen a few weeks later.

I found a glaring example of British conservatism in the chapter dealing with hysterectomy for benign conditions, in which the author suggests the preservation of healthy ovaries for any woman under 50 years of age. I cannot see much sense in this approach in Canada. Most ovaries have lost their usefulness several years before this age. I can understand why this advice is offered in England—estrogen therapy for menopause is not as well accepted in Britain as it is in North America. There must be tens of thousands of women needlessly suffering from senile vaginitis in that country. But such advice for Canadian readers is questionable.

To end on a positive note, practising gynecologists have a good track record in avoiding bladder, ureter and bowel injuries, but should they experience trouble in this area, the chapters in this text dealing with these problems give good advice. Similarly the sections on diagnostic radiology and chemotherapy also help to refresh the memory.

Texts such as this obviously have some merit, but whether the book is worth $98 to the practising gynecologist is debatable.

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TRAUMA OF THE CHEST. The Coventry Conference 1977. Edited by W.G. Williams and R.E. Smith. 266 pp. Illust. John Wright & Sons Ltd., Bristol; Year Book Medical Publishers, Inc., Chicago, 1977. $22.10, paperbound. ISBN 0-7236-0484-3.

At a time when the frequency of chest trauma associated with motor vehicle accidents is diminishing, due to the use of seat belts and lower speed limits, there has been a resurgence of interest in the topic, as evidenced by new books dealing exclusively with chest trauma.

The fourth Coventry Conference was devoted to trauma of the chest, and this book is the proceedings of that conference.

The three previous conferences covered surgery of the esophagus, of the lung and of the heart. At the fourth conference authorities from Europe, Great Britain, and United States and Canada discussed in detail their experiences with various aspects of chest trauma. The book is not intended to be a reference nor a review of all facets of thoracic injuries, but comprises papers and discussions of selected topics. The topics include flail chest, injuries to the aorta and great vessels, rupture of the bronchus, post-traumatic pulmonary insufficiency, penetrat-

ing chest wounds and physical and chemical injuries to the lung.

Particularly interesting are the divergent views on the management of flail chest, with renewed interest being shown in open reduction and fixation as exemplified in a well-documented paper by Dr. F. Paris from Valencia, Spain. Trinkle's remarks on the pathophysiology of flail chest are cogent and reflect the experimental and clinical work he has carried out in San Antonio emphasizing the underlying pulmonary pathology rather than the unstable chest wall.

Also included is an extremely complete, somewhat tedious, review of traumatic diaphragmatic hernias. This review contains a well-researched bibliography.

The section on penetrating wounds of the chest, discussed by Platt from Dallas and Trinkle, reflects their extensive experience with this type of injury in Texas. While their methods of approach, particularly in the management of cardiac injuries, differ slightly, their views are valuable to anyone who may be required to manage such injuries.

It is hoped that the excellent papers on post-traumatic pulmonary insufficiency will finally lay to rest the slick, but inappropriate, term "shock lung". The relative roles of excessive crystalloid fluid replacement and sepsis in the development of this condition are thoroughly detailed.

The print used and the layout of this soft cover book do not make for particularly easy reading, but there is a wealth of information to be gleaned from some of the papers, and, as such, the book should be of interest to anyone dealing with chest trauma.

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URINARY SYSTEM MALFORMATIONS IN CHILDREN. Proceedings of the International Pediatric Urological Seminar, Philadelphia, 1976. The National Foundation—March of Dimes. Birth Defects: Original Articles Series, Volume XIII, Number 5, 1977. Edited by Daniel Bergsma and John W. Duckett. 481 pp. Illust. Alan R. Liss, Inc., New York, 1977. $50. ISBN 0-8451-1014-4.

This book is a compilation of papers and comments, most of which were presented at a seminar on malformations of the urinary system in children. Many of the book's contributors are well known for their work on congenital anomalies and surgery of the urinary tract.

The book is divided into nine logical sections, ranging from megaureters to urethral valves, prune-belly syndrome, neuropathic bladder, exstrophy, hypospadias, reflux and cryptorchidism. It offers a clear, concise summary in many cases of the authors' views on these subjects. At the end of each section is a discussion by some of the eminent contributors to the field.

The physical appearance of the text does not compare with the glossy, slick texts recently published on pediatric surgery or reconstructive surgery of the urinary tract. However, on close reading, the roentgenograms are well reproduced and the charts and tables are accurate and well presented. The index, although accurate, is only six pages long and could be expanded.

As with the publication of any proceedings, the text bespeaks a familiarity with the topics presented. A surgeon with limited experience in urinary malformations in children and their management might be confused by some of the articles. However, for any surgeon familiar with these malformations, this publication will be of immense interest and use. It should be present in the hospital library of any institution where pediatric surgery is performed.

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THE YEAR BOOK OF ORTHOPEDICS AND TRAUMATIC SURGERY. 1977. Edited by Mark B. Coventry. 429 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1977. $25.25. ISBN 0-8151-1876-7.

This year book follows the routine format of previous editions, updated to reflect the current interests in orthopedic and traumatic surgery. One is always impressed by the progressive improvement in quality of the abstract selections in succeeding years, a particularly difficult assignment for the editor.

The major attractions of the year book series are the reader's enjoyment in the rapid scanning of a choice selection of abstracts from a multitude of journals and the inherent satisfaction of having a glimpse at the world-wide orthopedic scene in "Reader's Digest" form. Such abstracts are easily perused, demand minimal concentration and readily arouse the curiosity of the practising physician, the academician or the trainee. As anticipated, specific interest in a certain title invariably prompts the reader to search out the full article from the given reference.

The editorial comments on each article are especially worth while, the remarks of Coventry, the editor, being particularly relevant and appropriately critical.

The changing emphasis in orthopedic surgery is again reflected in this edition. More space is now devoted to orthopedic research, the popular trend of the 1970s. Less space is allocated to such subjects as prosthetics.

For relaxed reading in the field of orthopedic surgery, this book is good value. For the academic pursuit of a detailed subject, it has very limited use.

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