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- Mortality and Morbidity of Open Cholecystectomy
- Use of Blood in Resuscitation After Trauma
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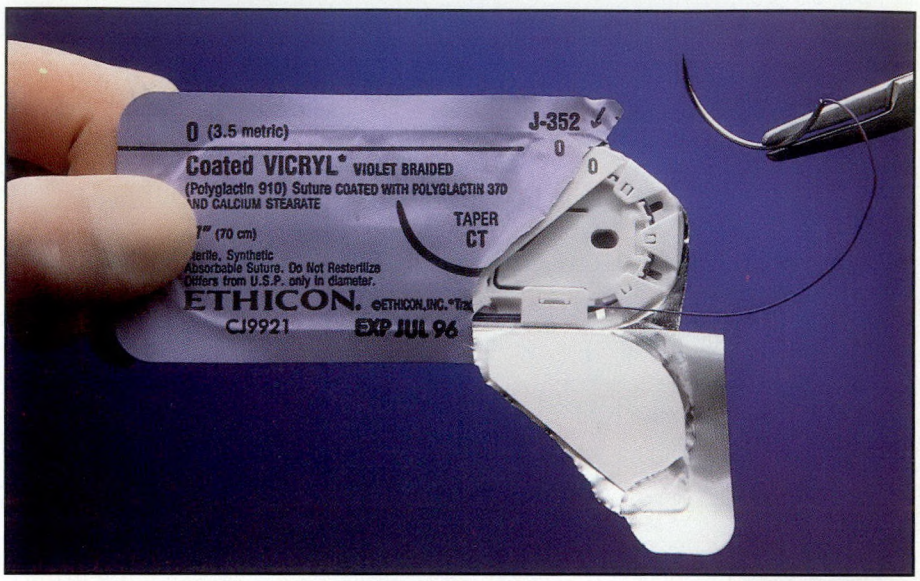

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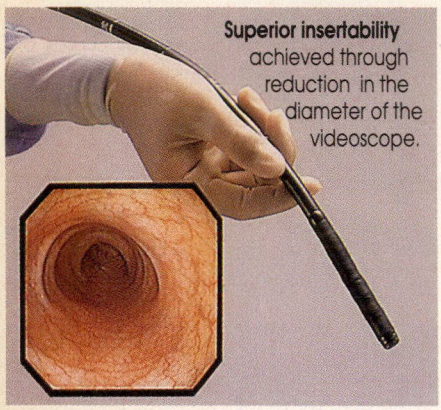

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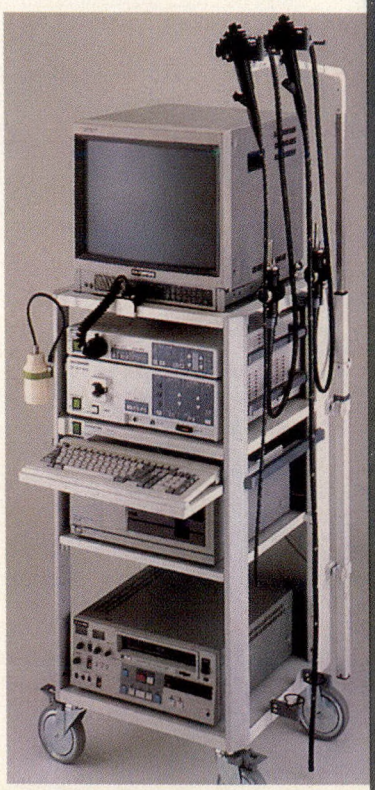

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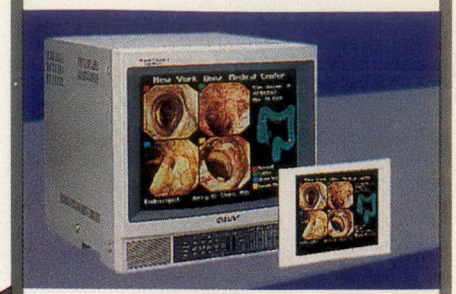

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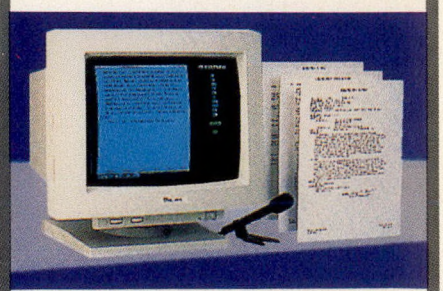

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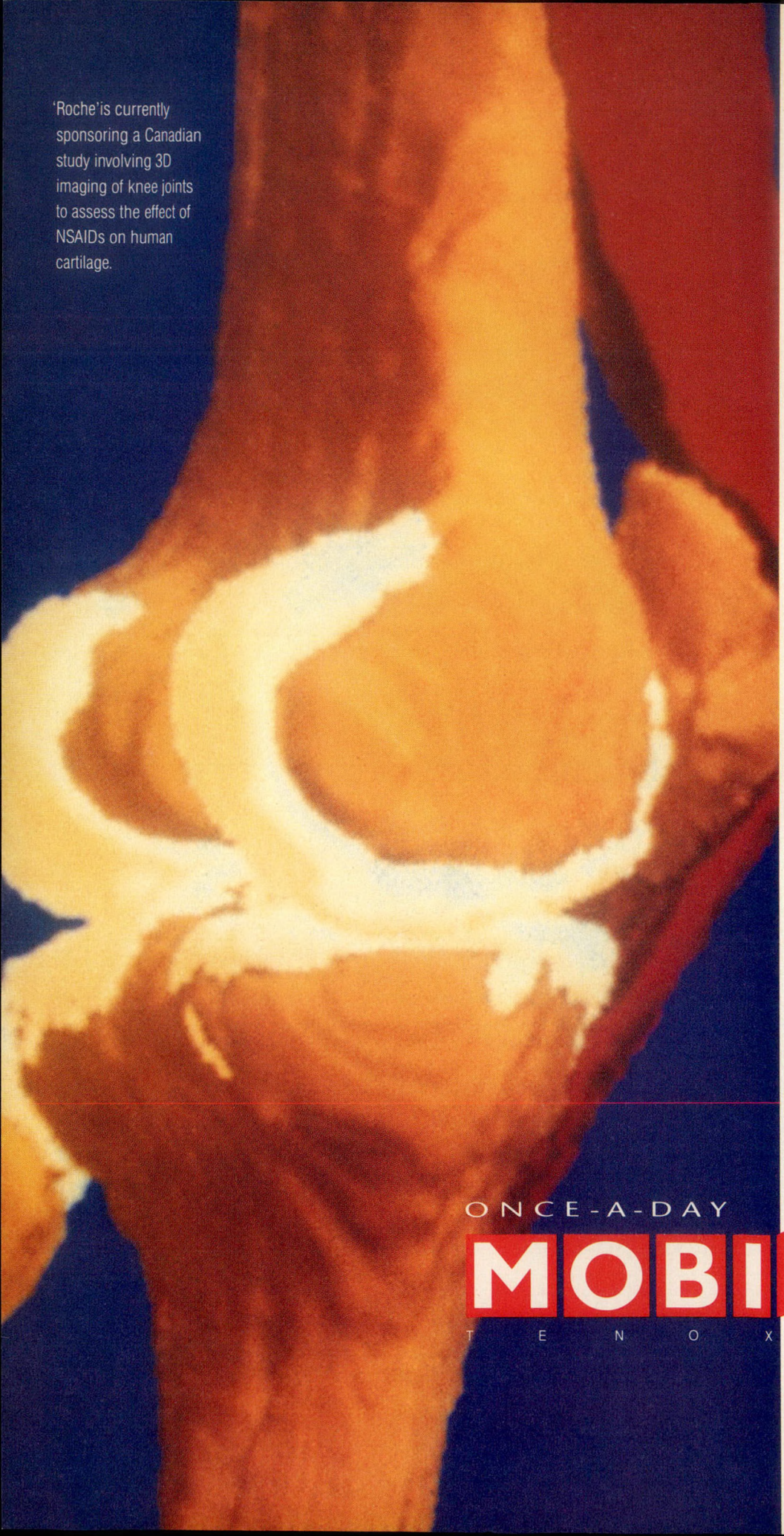
Surgery in Ethiopia (see article on pages 91 to 95). This Ethiopian woman presents two benign surgical problems: a cleft lip and a characteristic endemic goitre. The cleft lip could have been repaired and the goitre prevented. In Ethiopia patients with goitres seek treatment only when the goitres reach the size seen here or when difficulties with respiration and swallowing become intolerable.



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Current Management of Choledocholithiasis

Roger G. Keith, MD, FACS, FRCSC, FRCS

Chairman, Department of Surgery, Royal University Hospital, Saskatoon, Sask. Coeditor, Canadian Journal of Surgery

Abdominal surgeons have been the recognized experts in management of disease of the biliary tract, but technologic advances have now opened a welcome door for radiologists and gastroenterologists to participate in the management of stone disease. Currently, interventional endoscopists see far more bile duct disease than a surgeon would have seen during a comparable period of the "operative era." In Europe and especially in the United States, the interventional endoscopist is rarely a surgeon. Such is not the case in Canada. A substantial number of general surgeons in Canadian medical centres have expertise in endoscopic biliary intervention. The working relationship between surgeons, gastroenterologists and interventional radiologists has developed favourably in most teaching centres in this country.

During the decades before the advent of laparoscopic cholecystectomy, exploration of the common bile duct was frequently performed in association with cholecystectomy. This was standard treatment for common bile duct stones. With the introduction of endoscopic retrograde cholangiopancreatography (ERCP) in the early 1970s and the subsequent development of interventional techniques, preoperative endoscopic stone removal became popular. Experienced surgical and medical endoscopists were able to remove the majority of common duct stones with ever-decreasing morbidity and mortality. Nevertheless, during the early 1980s, the majority of general surgeons still favoured open exploration of the common bile duct, and this became the accepted choice for patients with the gallbladder in situ and with documented common bile duct calculi. In the mid-1980s, authoritative "ERCPists"[1,2] recommended clearance of the common bile duct by endoscopic sphincterotomy (ES) before cholecystectomy and limiting the open operation to cholecystectomy with operative cholangiography to confirm a stone-free biliary tract. In the hands of such experts, this protocol reduced overall morbidity and mortality compared with those reported in surgical series.[3–5] Endoscopists noted that the common bile duct remained cleared of stones after ES, and occasionally stones cleared from the gallbladder as well. Inconsistency of gallbladder clearance, disturbance of function and stasis all preclude ES as total treatment for cholelithiasis and choledocholithiasis.[6]

Interventional endoscopy for the management of retained common bile duct stones after cholecystectomy had the same effect on reoperative biliary surgery as H2 receptor blockers have had on peptic ulcer surgery. Residents training in general surgery have limited exposure to reoperative biliary procedures. Trainees will require increasing experience with endoscopic interventional procedures.

In this issue (pages 75 to 80), Girard and Morin from the Université de Montréal report a Canadian experience with open cholecystectomy, which will serve as a cited publication by virtue of case numbers and the excellence of outcome immediately predating the shift to laparoscopic cholecystectomy. Pursuant to management strategy for choledocholithiasis, Girard and Morin documented a death rate for open duct exploration of 1.6%. This is superior to the rate reported in most other large surgical series and is comparable to the 1% death rate recognized for ERCP with ES. Similarly, the death rate of 0.3% for open cholecystectomy alone in Girard and Morin's series will likely be comparable to that from laparoscopic cholecystectomy after accrual of data from single centres to more than 9000 cases. In Girard and Morin's series, only 24 bile duct injuries were reported in the cholecystectomy group, of which 7 were considered major — an incidence of 0.07%. This represents a high-water mark for safe open cholecystectomy.

Except for the incidence of bile duct injury, laparoscopic cholecystectomy dramatically reduces perioperative morbidity, shortens hospital stay and hastens return to work. Early reports of bile duct injury during laparoscopic cholecystectomy by well-trained surgeons was 0.2%.[7] Recent data and longer term follow-up suggest that the incidence may be 10- to 20-fold greater. The time of recognition and the site of injury associated with laparoscopic cholecystectomy render the consequences more threatening than injuries associated with open cholecystectomy.

Additional manipulations of the bile duct for stone extraction during laparoscopic cholecystectomy include transcystic duct retrieval or lithotripsy, cystic duct or direct laparoscopic choledochoscopy, and laparoscopic choledochotomy and exploration. As biliary surgical techniques, these are not new methods; however, recent advances are through the minimal access approach. These methods are in the development stage and must be critically evaluated over the longer term for the incidence of retained common duct stones and increase in the frequency of bile duct injury.

Roy, McAlister and Passi (pages 81 to 84) from London, Ont., present their preliminary experience with perioperative ERCP in association with laparoscopic cholecystectomy. Endoscopists have achieved ERCP success rates of 85% to 95%. Therefore, the London group favours selective laparoscopic cholangiography. This approach demands that the following be recognized: (a) liberal use preoperatively of ERCP and possible ES, based on indications outlined by Roy, McAlister and Passi in their Table II; (b) safe and effective laparoscopic clearance of common duct stones after positive laparoscopic cholangiography; and (c) effective postoperative clearance of common duct stones by ERCP and ES. Postoperative diagnostic ERCP will be indicated for all suspected biliary complications of laparoscopic cholecystectomy.

Deaths recorded after ERCP have been due to pancreatitis or sepsis. There is virtually no evidence of iatrogenic bile duct stricture or transection after ERCP. Clearance rates of common duct stones approaching 100% will be achieved by experienced endoscopists through ERCP and ES. Recently, Carr-Locke[8] reported a 1.5% incidence of residual stones utilizing selective preoperative ERCP and intraoperative cholangiography in 600 consecutive cases. None of these patients had indications for preoperative ERCP or intraoperative cholangiography. All presented within 6 months of laparoscopic cholecystectomy with non-life-threatening symptoms.

Laparoscopic cholecystectomy is now accepted as the treatment of choice for cholelithiasis. To preclude a moratorium on this technique, surgeons must reduce the incidence of bile duct injury close to that reported for open cholecystectomy by Girard and Morin. Choledocholithiasis suspected preoperatively should be diagnosed and treated by ERCP before laparoscopic cholecystectomy is carried out. Current data indicate that this combination would achieve the lowest mortality, morbidity, length of hospital stay and "sick time." Common bile duct stones that are demonstrated by selective laparoscopic cholangiography should be considered for postoperative ERCP and stone extraction, until laparoscopic bile duct surgery proves to be as effective as postoperative ERCP and to create no iatrogenic bile duct injury. The natural history of residual common duct stones will select postcholecystectomy patients for efficacious stone extraction by ERCP with morbidity and mortality far lower than those reported for primary or secondary open exploration of the common bile duct.

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Transurethral Resection of the Prostate: Still the Gold Standard?

Ernest W. Ramsey, MB, ChB, FRCS, FRCSC

Member, Editorial Board, Canadian Journal of Surgery. *Professor, University of Manitoba, Section of Urology, Health Sciences Centre, Winnipeg, Man.*

In this issue of the Journal (pages 37 to 40), Estey, Mador and McPhee report on a 3-year experience with transurethral resection of the prostate (TURP) in a teaching hospital where 75% of the primary resectionists were senior residents. Their results confirm those of other reports that TURP for most patients is a fairly safe procedure with a low death rate and a relatively low complication rate.[1] Mortality was related to age, impaired renal function and higher American Society of Anaesthesiologists class. The article does not address the success of the procedure in relation to improvement in symptoms or long-term complications such as urethral strictures and the reoperation rate. TURP has been used to treat benign prostatic hyperplasia (BPH) for over 50 years and has largely replaced open prostatectomy, which is reserved for large glands. Microscopic BPH seems to be an inevitable consequence of aging.[2] It is more difficult to determine the incidence of clinical BPH because not all men with symptoms seek or undergo treatment. The incidence of clinical BPH appears to range from about 10% of men in the 40- to 50-year age group to about 40% of men over 70 years of age.[3] The probability of a 40-year-old man undergoing TURP in the United States during his lifetime is 29%. This translates into over 400 000 such procedures each year.[4] In Canada in 1991, over 38 000 such resections were performed.

Despite the frequency with which TURP is performed, it is only recently that efforts have been made to assess the short- and long-term outcomes.[5] At the same time, the management of patients with BPH has been thrown into turmoil by recent advances, which have seen the successful use of medication to treat this disease as well as the introduction of a variety of new techniques that may permit treatment with less morbidity. A recent editorial in the *New England Journal of Medicine* was entitled "Is the prostate pill finally here?"[6] This editorial was in reaction to publication of the results of a study of finasteride, a 5α-reductase inhibitor. Finasteride prevents the conversion of testosterone to dihydrotestosterone, the active androgen in the prostate, causing a decrease in the size of the prostate and improving symptoms and urine flow rates. This drug is now approved for use in Canada. Alpha-adrenergic blocking agents have also been studied in BPH. These do not decrease prostate size but cause relaxation of the smooth muscle in the gland, again improving symptoms and voiding. Terazosin, an α-1-adrenergic blocking agent currently approved in Canada for the treatment of hypertension, is undergoing investigation for use in BPH, as are a variety of other treatment options. These include transurethral incision of the prostate, balloon dilatation, prostatic stenting, transurethral microwave thermotherapy and the use of lasers to perform transurethral prostatectomy.

Although the morbidity associated with these treatments appears lower than that for TURP, the effectiveness of some of them, such as thermotherapy, requires further evaluation before they are offered as an alternative treatment. It has become obvious that there is a major placebo effect in the treatment of this disease. This effect must be considered in the assessment of new treatments. Also, not all patients with symptoms require treatment, and observation (watchful waiting) is an option even with the advent of less morbid treatments. Although TURP remains the most effective way to relieve obstruction, the decreased morbidity associated with newer options may make them attractive. The relative costs of the new treatments also need to be assessed.

How is the urologist and the patient to choose from this plethora of treatments? The decision will relate partly to the severity of the problem. Medical treatment for example, has been assessed for patients with symptoms of BPH and is not currently indicated for the treatment of patients with acute or chronic urinary retention. An interesting and possibly helpful approach is that taken by the Foundation for Informed Medical Decision Making, in New Hampshire. This group has produced an interactive videodisc program that allows the patient to review treatment options

along with their harms and benefits and to watch interviews with patients who have chosen particular options. In this way the patient can play an active role in decision making. However, to be effective, the information supplied to the patient must be comprehensive and accurate. This will require prospective, controlled studies of all new treatment options.

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Blood Use in Resuscitation After Trauma

James P. Waddell, MD, FRCSC

Department of Surgery, St. Michael's Hospital, Toronto, Ont. Member, Editorial Board, Canadian Journal of Surgery

In this issue (pages 21 to 27), Hamilton lucidly outlines the use and abuse of blood transfusion in the trauma patient.

In a comprehensive review of the current literature he describes clearly the indications for blood transfusion, the risks associated with such transfusion and the alternatives to banked blood.

Of particular interest is the emphasis on the initial priorities in resuscitating the trauma patient, the different categories of transfusion (emergency versus urgent) and a comprehensive discussion of the complications of blood transfusion.

Surgeons involved in the care of trauma patients know how essential rapid access to a reliable source of banked blood is — both in resuscitation and during surgical treatment of the patient. Too often blood is given at inappropriate times, for inappropriate reasons and in inappropriate amounts. Careful reading of Hamilton's article will help the surgeon rationalize the use of blood and blood products in the trauma patient, ensuring that safe transfusion practice complements safe surgical practice during resuscitation and surgical control of ongoing hemorrhage.

All surgeons and residents involved in the care of trauma patients should be familiar with the principles outlined by Hamilton and should modify their treatment priorities if necessary to reflect current practice in the use of blood in resuscitating the trauma patient.■

The Journal Expands Its Role

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The crisis imposed on the *Canadian Journal of Surgery (CJS)* and the previous coeditors by the staged withdrawal of financial support of the Royal College of Physicians and Surgeons of Canada has given the Journal an opportunity to expand its role and better serve its surgical community, now made up of the Canadian Society for Vascular Surgery, the Canadian Orthopaedic Association, the Canadian Association of General Surgeons, the Canadian Society of Cardiovascular and Thoracic Surgeons and the Canadian Society of Surgical Oncology, with support from the Royal College. These sponsoring societies have begun to publish abstracts and representative portions of their annual meetings in the *CJS*. It is the intention of the coeditors that the involvement of these societies shall expand to include many of their innovative and key manuscripts. It is planned that within the next year the journal will carry a review article solicited from each society, starting in this issue (pages 29 to 32) with an overview of the Royal College's Maintenance of Competence Program.

With this issue a new section "Sponsors' News" (pages 96 to 99) is being initiated. Its purpose is to provide a forum of communication on a bimonthly basis for the Canadian surgical community. This issue carries the initial offering, which, in time, we expect to expand significantly. Although each society's input is focussed on its members, there is much information that with diffusion will benefit the entire Canadian surgical community. The participating societies incorporate Canadian cardiac, general, orthopedic, thoracic and vascular surgeons together with surgical oncologists. Although this represents the majority of Canadian surgery, we look forward to the other surgical specialties participating and publishing their work in the *CJS*.■

SESAP VII Question / Question SESAP VII

Item 360

Which of the following statements about pulmonary function after nonthoracic operation is TRUE?

(A) The site of incision has only a minor effect on postoperative pulmonary function.

(B) Patients with significant chronic obstructive pulmonary disease (COPD) have a 60% incidence of pulmonary complications despite preoperative treatment with bronchodilation, antibiotics, and physiotherapy.

(C) The lower limit of FEV_1 below which a patient should not be given general anesthesia has not been clearly defined.

(D) The changes in lung volume seen after an upper abdominal midline incision can be reversed by intercostal nerve blockade.

(E) The decrease in vital capacity is directly related to the anesthetic agent used.

For the critique of Item 360 see page 52.

IS THERE A BETTER WAY TO CONTROL POST-OPERATIVE PAIN THAN USING NARCOTICS?

NON-NARCOTIC

TORADOL

NARCOTIC EFFICACY WITHOUT NARCOTIC DRAWBACKS

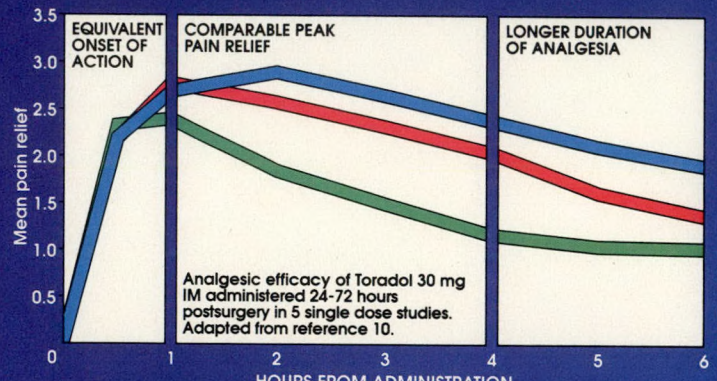
Now, Toradol offers a real alternative to narcotics for the management of pain - an analgesic that provides the strength of narcotics without the associated drawbacks.

CLASSIFICATION

Toradol belongs to the non-steroidal anti-inflammatory drug (NSAID) family. However, unlike conventional NSAIDs, it is a potent analgesic agent with minimal anti-inflammatory and antipyretic activity. And it's the only non-narcotic analgesic available in both IM injection and tablet form.[1,2]

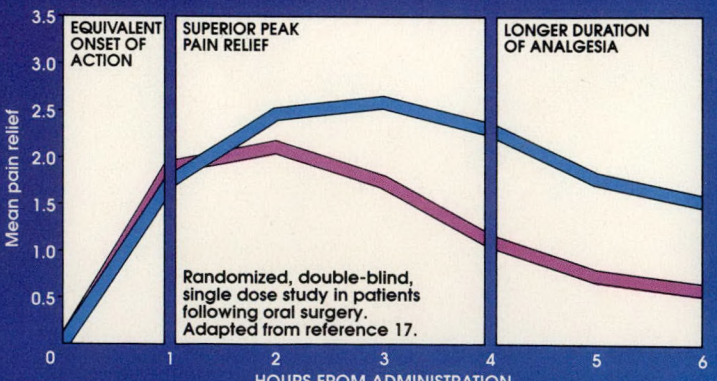
EFFICACY

One Toradol 30 mg IM injection has been proven to be as effective as morphine 12 mg IM and meperidine 100 mg IM,[4-10] while one Toradol 10 mg tablet has been shown to be more effective than 2 tablets of acetaminophen + codeine #3*:[17,18,22]



Analgesic efficacy of TORADOL 30 mg IM vs. morphine 12 mg IM and meperidine 100 mg IM.[10]

Measure of pain relief: 0 = none, 1 = poor, 2 = fair, 3 = good, 4 = very good.



Analgesic efficacy of TORADOL 10 mg Tablet vs. 2 Tablets of acetaminophen + codeine #3[17]

Measure of pain relief: 0 = none, 1 = poor, 2 = fair, 3 = good, 4 = very good.

A STEP AHEAD OF NARCOTICS[30,44]

TOLERABILITY

Because Toradol is peripherally-acting, its tolerability profile is superior to morphine, meperidine, and codeine-containing analgesics, producing less nausea, vomiting, drowsiness[17,18,21] and constipation.[2] Furthermore, Toradol has no reported incidence of respiratory depression,[11,12] and no potential for narcotic addiction or abuse.[3]

COST-EFFECTIVE

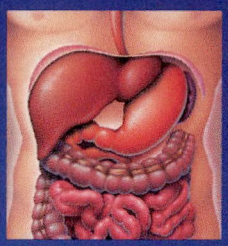
Importantly, Toradol's proven efficacy and tolerability help make it cost-effective for Canadian hospitals.[13] Earlier hospital discharge and a lower incidence of complications result in considerable cost savings - in one well-controlled study, Toradol IM and tablets saved an average of approximately $75.00 per patient compared to meperidine IM followed by acetaminophen + codeine #3.[13]

This study also demonstrated that patients on Toradol were easier to care for and had greater independence, requiring significantly less nursing time and effort.[13]

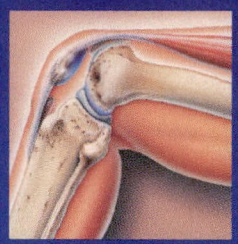
CLINICAL APPLICATIONS

Toradol has been proven effective in managing a wide range of pain following general, orthopedic, gynecological[4-9] and oral surgery[17,18] as well as pain in the Emergency Room setting.[2,9,22-27]

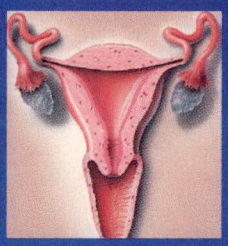
And Toradol is well-suited for the post-operative pain of day-stay surgery, with faster patient recovery,[13] and no need for monitoring of narcotic-related side-effects which can delay discharge.[32]



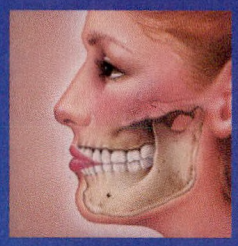
General Surgery[4-9]



Orthopedic Surgery[4-9]

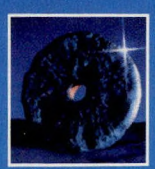


Gynecological Surgery[4-9]



Oral Surgery[17,18]

For a better alternative to narcotics in pain management, consider Toradol IM and tablets. The non-narcotic analgesic that is a step ahead of narcotics.



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For prescribing information see page 71

CORRESPONDENCE
CORRESPONDANCE

Forearm-Plate Removal

To the editors. I am an orthopedic surgeon and practise in a community hospital. I read with interest the article "Complications of forearm-plate removal" by Bednar and Grandwilewski in the August 1992 issue (pages 428 to 431) of the Journal. The authors state that an incidence of infectious and neurologic complications of approximately 10% each may be expected with elective forearm implant removal. Personally, I think that a 10% infection rate with elective upper extremity surgery is unacceptable, and I would suggest the authors review their aseptic technique.

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Dr. Bednar Responds

To the editors. I am happy to review Dr. Aitken's letter and concur with his comment on the surprisingly high infection rate we noted in our review of elective forearm-plate removal.

Frankly, we were surprised and appalled at the finding, much as we would expect any surgeon to be on discovering such a high complication rate in his own case review. Nevertheless, we stand by the importance of the review and encourage all practising orthopedic surgeons to pay thorough attention to aseptic techniques in all of the surgeries they undertake.

The clinical review of this series was most aggressively directed to the definition of complications and probably identified minor, early postoperative cellulitis that might otherwise go unreported. To my knowledge, in the 5 years I have been practising on the Orthopedic and Trauma Service of the Hamilton General Hospital there has been no problem with infection rates generally reported on the service; this close attention to infectious complications may define part of our elevated incidence. Although these minor acute cellulitides are generally not a major clinical problem, their appearance does increase the reported frequency of complications, although perhaps they do not carry any great clinical significance.

Drew A. Bednar, MD, FRCSC, FAAOS
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Retroperitoneal Lymphadenectomy

To the editors. I read with interest the report by Morin and colleagues regarding vascular injury and repair associated with retroperitoneal lymph node dissection (RPLND) in patients with testicular cancer (*Can J Surg* 1992; 35: 253–256). In 78 patients who underwent RPLND, 17 (22%) required vascular repair intraoperatively. Of particular interest were five renal artery injuries, three of which resulted in nephrectomy. The 6.4% renal injury rate and 3.8% nephrectomy rate are noteworthy.

In a review of complications of testicular cancer therapy, we noted six lost renal units in 148 patients who underwent RPLND, for a renal loss rate of 4.1%.[1] In our series, only one nephrectomy was performed at the time of RPLND because of inadvertent injury. However, three patients required nephrectomy within 1 year of operation because of nonfunction or hydronephrosis, and two patients required nephrectomy because of renovascular hypertension. We have now documented five cases of renovascular hypertension after RPLND (unpublished data). Hypertension in three of the cases was due to renal artery injury, in one to cortical necrosis and in one to hydronephrosis from utereral injury. Interestingly, in three of the five cases, hypertension did not develop until more than 10 years after the testicular cancer surgery.

We emphasize the importance of monitoring these patients on a long-term basis for the possibility of delayed renovascular hypertension, which could have resulted from unrecognized surgical insult. In addition, because of the possibility of hypertension as a result of vascular toxicity from cisplatin-based chemotherapy also commonly used to treat this patient population, blood pressure screening takes on added importance.[2] The two patients reported by Morin and colleagues who had renovascular repair and did not require immediate nephrectomy would be interesting to study in the long term for the possibility of renovascular hypertension. Long-term follow-up of their entire cohort with respect to hypertension may also lead to delayed morbidity as our experience has shown.[1,2] We agree with Morin and colleagues

that surgery for the patient with advanced retroperitoneal testicular cancer should encompass a multispecialty approach.

Despite these precautions, morbidity does occur, and the patients require long-term follow-up.

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Bethesda, Md

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1. Moul JW, Robertson JE, George SL et al: Complications of therapy for testicular cancer. *J Urol* 1989; 142: 1491–1496
2. Bosl GL, Letiner SP, Atlas SA et al: Increased plasma renin and aldosterone in patients treated with cisplatin-based chemotherapy for metastatic germ cell tumors. *J Clin Oncol* 1986; 4: 1684–1689

The Need for General Surgeons

To the editors. The article by Blanchard (*Can J Surg* 1992; 35: 531–535) and the editorials by Duff (page 466) and Taylor (pages 467 and 468) are of interest to me and to all rural general surgeons, active or retired.

Time, the Golden Hour — is it forgotten? Weather and its complexities — are they not a factor? Economics — are the patient and his or her loved ones considered? It appears that the tertiary centres supported by the surgeon-scientist will be valid by the 21st century.

Is this the way to go? Personally I, and active and retired rural surgeons, disagree that all patients should go to a tertiary centre and be supervised by surgeon-scientists. Each rural medical centre has its own particular problems. For this reason, regionalization is not the answer.

The seaport of Prince Rupert, BC, is an excellent example, yet there are active surgeons who feel that Terrace, BC, should be a regional centre. Personally, I do not agree. Each year half a million people use the "Inside Passage" or are off shore, whether they are on cruise ships, American or Canadian ferries, commercial fishing or pleasure boats and local or off-shore freighters. Medically and surgically the Prince Rupert Regional Hospital supports five native villages, Oona River and the Queen Charlotte Islands.

In the second paragraph I mentioned time, weather and economics. It takes time to bring a patient to hospital whether for trauma, abdominal surgery, heart attack or pregnancy. The weather and its complexities at times make it difficult to get the patient to a tertiary hospital. Economically it is cheaper for the British Columbia government, since an air ambulance is costly, for a patient to be looked after in his or her own area whenever possible. The loved ones cannot afford the air fare, $600 to go to Vancouver, the nearest tertiary facility.

Trainee surgeons should have an opportunity early in their training to practise under the supervision of a general surgeon in a rural community hospital. The provincial government should provide an adequate allowance for new surgeons until they can support themselves financially. All physicians should take the Advanced Trauma Life Support course. General surgeons will have to make decisions, whether to operate now or later, or to transfer. If they can read, there are books. If they are in doubt, they can phone the resident on call at the tertiary hospital for the specific specialty.

There is an absolute need for true general surgeons now and into the 21st century.

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Training the General Surgeon

To the editors. The recent article by Blanchard in the October 1992 issue (pages 531 to 535) and the editorials from Drs. Duff (page 466), Taylor (pages 467 and 468) and Deschênes (page 469) point out the need for general surgical training programs to be responsive to the changing needs of society.

However, we must also recognize the present constraints on our programs and the resources available for training and be realistic as to what newly trained general surgeons may be willing to undertake. Above all, we must not compromise the quality of our programs or the care of patients in the interests of cost containment, ease of access or short-term political gains.

General surgery training currently takes 5 years. The increase from 4 years was introduced for two reasons. The first reason was to add flexibility to training to allow for the production of community surgeons, academic teachers or surgical scientists and to form a basis for the training of subspecialists in vascular, thoracic and colorectal surgery and in critical care. The second reason was to recognize the increasing scope of general surgery, which has grown to include the technical skills of endoscopy, head and neck surgery and laparoscopic surgery, the cognitive areas of criti-

cal appraisal, research methodology and medical ethics and jurisprudence, and the treatment of the old, the sick and immune deficient. Programs also need to inculcate attitudes of humanity, communication skills, cost consciousness and the need for maintenance of competence.

All of these added requirements make for a very crowded 5-year program. If we are proposing to add extra exposure to plastics, urology, obstetrics and gynecology and orthopedics, what should we drop from the present training?

My nonsurgical colleagues in community hospitals claim that any "well-trained general surgeon" should be able to repair an extensor tendon, do a cesarean section or pin a hip. Will newly trained general surgeons be willing to offer these services, mainly at night and on weekends? Will they still wish to offer them if "capping" dictates that such services are offered without pay? What will lawyers and judges have to say if things go wrong? Finally, and most importantly, would it not be wise to seek the views of the relevant specialty committees on what areas general surgeons could undertake safely without 6 or 7 years of training?

The old-fashioned surgeon who did everything is a popular cult-figure. However, the scope and complexity of modern surgery has made him (few, if any, were women) a virtual anachronism. Let us be careful not to turn the clock back 30 years in the name of progress.

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BOOK REVIEWS
CRITIQUES DE LIVRES

The following books are also reviewed in this issue: **Sabiston Review of Surgery** (page 32); **Surgical Revascularization of the Heart: the Internal Thoracic Arteries** (page 71); **The Principles of Trauma Surgery** (page 71).

HISTORY OF ORTHOPAEDICS. David LeVay. 693 pp. Illust. The Parthenon Publishing Group, Park Ridge, NJ. 1990. $125. ISBN 0-85070-145-8

The hard, mineral nature of bone has preserved evidence of human bone and joint disease since the New Stone Age. Dinosaur fossils have also shown how long vertebrates have suffered from degenerative arthritis.

In this book, David LeVay reviews the history of human musculoskeletal disorders and their treatment from the time of the building of the Pyramids of Giza in the 5th dynasty to the present. The great antiquity of what is now orthopedic surgery was established by a drawing on the wall of the 12th century BC Tomb of Ipuy. In that drawing, a dislocated shoulder is seen being reduced using a method exactly like Kocher's, 3000 years before he described it. The Egyptian Orthopaedic Association, with understandable pride, uses the same drawing as its logo.

LeVay presents a massive amount of historical information in a clever and readable way. He reviews first the period from the Stone Age to the end of the 16th century, ranging with an eclectic pen through the lore of ancient Egypt, India, China, Japan and the well-recorded Hellenic and Roman periods. The section ends in early medieval Europe. It is a fascinating story of pragmatism and of intelligent innovation. The text is both well illustrated and well referenced.

The second and largest section of the book concerns development of the arts and science used in the management of musculoskeletal disorders. A good account is given of finding the term under which the many aspects of this field of interest could be collected. Nicolas Andry (1658–1747), Dean of the Faculty of Physics at the University of Paris, combined the Greek words "orthos" (straight) and "paidion" (a child) into "orthopédie." Other, current and older terms, like Andry's, were used originally as book titles. The *Paedotrophia* of Scévole de Sainte-Marthe and *Callipaedia* of the Abbé Claude Quillet were soon dropped. Nineteenth century efforts — "orthomorphy", "orthosomatics" and "orthopraxy" thankfully also lost out to "orthopaedic surgery."

Major developments in orthopedic surgery and traumatology are described in 18 separate chapters, each devoted to the contributions of a nation. To create a text that is a pleasure to read and not a catalogue, the author has described the work of great surgical pioneers in the form of brief biographical sketches and the diseases, such as poliomyelitis that have had a significant effect on orthopedic practice. Landmark papers are referred to and in some instances, their face pages are reproduced. Indeed, the whole of this section is a treasure-

continued on page 32

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P3AA3

The Use of Blood in Resuscitation of the Trauma Patient

Stewart M. Hamilton, MD, FRCSC, FACS

The ability to transfuse blood (a form of tissue transplantation) with relatively few immediate and long-term complications has led to increased survival in victims of injury who require massive amounts of blood. The primary deficit in hypovolemic shock secondary to trauma is in oxygen transport to the hypoperfused tissues; therefore, blood transfusion has an essential role in therapy during resuscitation and definitive treatment. The major immediate complications to be avoided are hypothermia and acidosis, which are the main causes of the coagulopathy associated with massive transfusion. The most worrisome long-term complication is the transmission of disease, of which hepatitis C is the most frequent. With improved screening techniques and heightened donor awareness, the risk of disease transmission is less than 2%. Until synthetic oxygen-carrying solutions are available, the transfusion of red blood cells, when appropriately indicated, will remain an important component in the resuscitation of the trauma patient.

La capacité à transfuser du sang (une forme de greffe tissulaire) avec relativement peu de complications immédiates ou retardées, a contribué à l'augmentation de la survie des blessés qui nécessitent des quantités massives de sang. Le déficit primaire en cas de choc hypovolémique consécutif à un traumatisme, est relié au transport d'oxygène vers les tissus hypoperfusés; en conséquence, la transfusion sanguine joue un rôle thérapeutique essentiel durant la réanimation et au cours du traitement définitif. Les complications majeures immédiates qui doivent être évitées sont l'hypothermie et l'acidose, les principales causes de la coagulopathie reliée aux transfusions massives. La complication tardive la plus inquiétante est la transmission de maladies, l'hépatite C étant la plus fréquente. Avec les techniques de dépistages améliorées et des donneurs mieux informés, le risque de transmission est inférieur à 2 %. En attendant la venue des solutions de transporteurs d'oxygène de synthèse, la transfusion d'hématies pour les indications appropriées va demeurer une composante importante de la réanimation des patients traumatisés.

Throughout history blood has been synonymous with life. In ancient times it was considered to be the basis of the soul and to carry with it the physical and mental qualities of its owner. The Romans drank the blood of recently slain gladiators to acquire their strength. These attitudes toward blood continued well into the Renaissance, when in 1492, Pope Innocent VIII received blood from three young boys in an unsuccessful attempt to rejuvenate him. Following Harvey's description of the circulation, others, among them Sir Christopher Wren, began to work on the intravenous injection of fluids into the circulation. In 1667, the first recorded transfusion of an animal's blood into a human was made by Jean Baptiste Denis. His work met with some success and led to the first description of a transfusion reaction, including diaphoresis, tachycardia, pain at the injection site and black urine. The patient survived but 2 months later received another transfusion and died the next day. This led to a charge of murder against Denis, of which he was acquitted, and to a ban on all transfusions by the Faculty of Medicine in Paris.[1,2]

It was not until early in the 19th century that man-to-man transfusion was initiated by an obstetrician, James Blundell, for acute hemorrhage. He performed 10 such transfusions, of which 4 were successful.[1] The success rate of transfusion therapy did not improve significantly until the major blood groups (ABO) were described in 1901 by Landsteiner. During the late 1930s progress was made to develop blood banking, and during the Spanish Civil War, mobile transfusion services came into being largely because of work by Bethune. The Barcelona Blood Transfusion Service used more than 9000 L of blood during its existence. In

From the Department of Surgery, University of Alberta, Edmonton, Alta.

Presented at a symposium on trauma, 7th Annual World Congress on Emergency and Disaster Medicine, Montreal, Que., May 1991

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1939 the Rhesus factor system was described, further facilitating blood transfusion and lowering the incidence of transfusion reactions.[2,3]

Blood transfusion is a form of tissue transplantation, with attendant risks that must be weighed against the perceived benefits. Our ability to store blood in large quantities for immediate use has permitted tremendous advances in the fields of surgery and critical care, particularly cardiac, transplant and trauma surgery.

Twenty years ago, survival after transfusion of more than 20 units of blood was reported to be 7%.[4] With improved triage, retrieval, resuscitation techniques, surgical care, anesthetic care and postoperative intensive care, the survival in one series today is over 50%. Additionally, the majority of these survivors returned to gainful employment.[5] Clearly, the ability to transfuse blood, a solution that for the most part remains in the vascular compartment as a volume expander, that carries oxygen and has some buffering capacity, is an important weapon in the management of the injury victim. In fact, if we could be certain that there were no risks of disease transmission, allergic reactions or transfusion reactions, it would be the ideal fluid.

Initial Priorities

The initial treatment of the traumatized patient is challenging and in most cases rewarding. Primary objectives are to ensure an adequate airway, oxygenation and ventilation, with spinal control. Assessment of the circulatory status requires an estimate of the blood-volume deficit and of ongoing losses. This will determine the rapidity with which blood will be used. The response or lack of it, to the initial fluid bolus of 2000 mL of crystalloid, aids in this assessment. Immediate surgical control of ongoing losses must be considered in all hypotensive patients. It is essential to remember that most complications of hemostasis are related to the length of time that the patient is in hypovolemic shock and to the degree of hypothermia present.[6-8] Reversing hypotension and hypothermia are the top priorities of management once oxygenation and ventilation are assured.

In the trauma patient with hypovolemia who does not require immediate surgical control, the options for the type of fluid to be administered are many. That the initial fluid resuscitation should be a balanced electrolyte solution is not controversial, although the administration of hypertonic saline solutions, particularly in the prehospital setting, has its proponents. Intravenous access should be through two large-bore (12 to 14 gauge) short catheters inserted into an uninjured upper extremity. A second option is to access the femoral vein percutaneously using a large-bore line (8.5 French). A third option would be by a saphenous vein cutdown at the medial malleolus. Resistance to flow is proportional to diameter and to length; therefore, for rapid large-volume resuscitation, short, large lines must be placed.

Hemorrhagic shock can be classified into four categories. Loss of up to 1000 mL (15% of blood volume) (class 1) results in minimal clinical symptoms. In uncomplicated cases tachycardia develops, but blood pressure, respiratory rate, capillary refill and pulse pressure are unchanged. In class 2 hemorrhagic shock (a loss of 15% to 30% of blood volume [1001 to 1500 mL]), symptoms include tachycardia (more than 100 beats/min), tachypnea, a decrease in pulse pressure (mainly due to a rise in the diastolic pressure secondary to catecholamine stimulation), anxiety and delayed capillary refill. In class 3 hemorrhagic shock (a loss of 30% to 40% of blood volume [1501 to 2000 mL]), the signs are more dramatic and consist of cold clammy skin, diaphoresis, marked tachycardia and tachypnea, significant changes in mental status and a measurable fall in systolic blood pressure. With this degree of blood loss transfusion is required. In class 4 shock (loss of more than 40% of blood volume [more than 2000 mL]), there is an immediate threat to life. Marked tachypnea and tachycardia and a very narrow pulse pressure, or unrecordable diastolic pressure, indicate this magnitude of bleeding. End-organ function is markedly impaired as manifested mainly by oliguria progressing to anuria. Patients in this situation require immediate blood therapy and surgical intervention.[3]

Oxygen Transport

By definition a patient who is in shock suffers from a generalized state of circulatory inadequacy. Specifically, in hemorrhagic shock, cellular hypoperfusion exists because of a primary deficit in circulating blood volume resulting in inadequate oxygen delivery. It follows that the major objective of treatment is to restore cellular perfusion. This requires the restoration of oxygen delivery which can be defined by the equation: oxygen delivery = oxygen content × cardiac output, which equals percent oxygen saturation × (hemoglobin × 1.34) × cardiac output.

Oxygen saturation can be optimized by ensuring that an adequate airway and an adequate minute ventilation exist, either spontaneously or with intervention. Cardiac output is determined by preload, contractility and afterload. It is unusual for

intrinsic cardiac disease to exist in the majority of injury victims. However, with increasing numbers of elderly people involved in motor vehicle accidents, intrinsic cardiac disease must be considered. In the younger patient population, the component most commonly involved in causing a decrease in cardiac output is inadequate preload. This is corrected by the administration of fluids or blood, or both. Obstructive causes of shock in the form of pericardial tamponade or tension pneumothorax, must be diagnosed and treated. It is rare for increased afterload to be of concern, and if it is, it can be rectified by volume infusion and augmented cardiac performance.

The ability of the blood to oxygenate tissues is determined by the intrinsic ability of the hemoglobin molecule to carry oxygen. This relationship between oxygen and hemoglobin is further defined by the hemoglobin-oxygen dissociation curve. The association of hemoglobin and oxygen is influenced by many factors, but with respect to the quantity of oxygen carried and in a young patient without intrinsic lung or cardiac disease, the hemoglobin concentration is the major determinant of oxygen delivery.

Hemoglobin-Oxygen Dissociation

The primary function of the red cell is to carry oxygen to the tissues and to carry carbon dioxide away from them, both functions being performed by the hemoglobin molecule. In the terminal vascular bed, the ability of the hemoglobin to unload oxygen is modified by three intracellular factors: the hydrogen ion concentration, the carbon dioxide tension and the level of 2,3-diphosphoglycerate (2,3-DPG). An increase in concentration of each or any of these substances allows oxygen to dissociate more easily from hemoglobin, a "shift to the right" of the hemoglobin-oxygen dissociation curve, resulting in improved oxygen delivery. Other conditions that assist oxygen delivery are not commonly found in the acute situation of hemorrhagic shock associated with trauma.[9]

Manipulation of the hemoglobin-oxygen dissociation curve can be valuable in assisting oxygen delivery when resuscitating a patient with extensive blood loss (Fig. 1). Most importantly, a "shift to the left," in which an increased affinity of hemoglobin for oxygen occurs, must be prevented. All stored red cells become depleted in 2,3-DPG, although functionally this reverses with transfusion. In the traumatized patient it is treatment of the associated hypothermia and avoidance of an alkalotic state, by overadministration of sodium bicarbonate, that can prevent this leftward shift. Mild elevation of temperature is preferable to hypothermia, and a moderate acidosis with pH ranging between 7.25 and 7.35 is preferable to alkalosis.[3] In summary, although adequate preload to maximize cardiac output and restoration of hemoglobin to maintain oxygen-carrying capacity are the first goals of resuscitation, attention to the effects on the hemoglobin-oxygen dissociation curve, particularly with respect to hypothermia, will assist in achieving the overall objective: restoring cellular perfusion.

Indications for Blood Transfusion

Emergency Transfusion

In certain situations, consideration must be given to immediate transfusion. This decision is made on clinical grounds after a rapid initial assessment reveals a patient in a state of profound hypoperfusion, unresponsive to volume loading. As venous access is being established, blood must be sent for

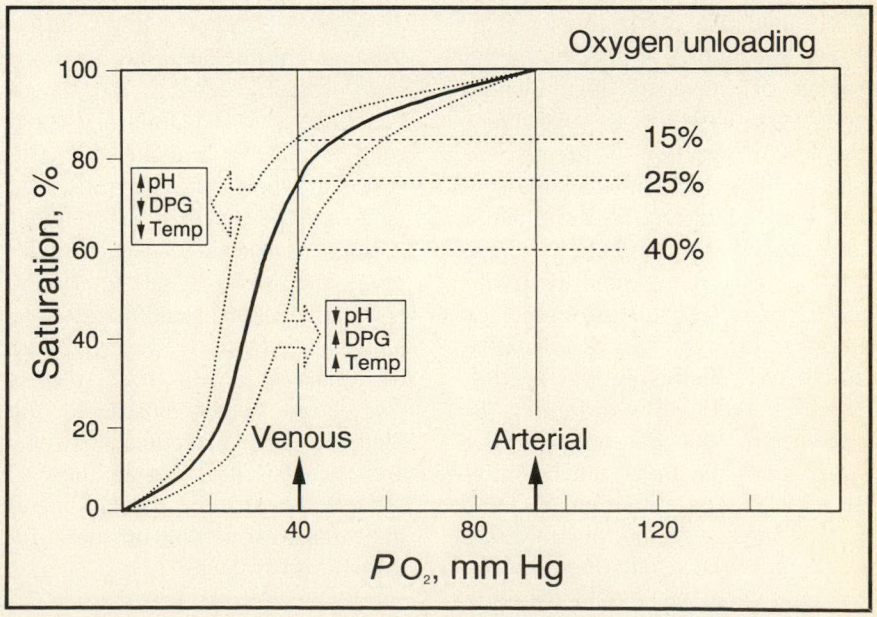

FIG. 1. Hemoglobin-oxygen dissociation curve. Relationship of hemoglobin to oxygen as function of saturation versus partial pressure of oxygen. Increased acidosis, decreased 2,3-diphosphoglycerate (DPG) and decreased temperature all shift curve to left, interfering with the unloading of oxygen in terminal vascular bed.

typing and crossmatching. It is imperative that this be done before the administration of blood products. After the blood has been typed and crossmatched, the trauma team has three options: (a) use of type-specific blood, (b) use of type O, Rh-negative blood and (c) autotransfusion.

In most situations, the time taken to establish lines and infuse a 2000-mL bolus of crystalloid is long enough for type-specific blood to be made available. It is axiomatic that the typing of the patient be done by the blood bank giving the blood. This process should take no longer than 5 minutes, so the need for "universal donor" blood is minimal, and if it is used, it should be used only until type-specific blood is available.[10] That this is possible is borne out by military experience: even in situations of mass casualties, the number of units of type O, Rh-negative blood transfused is less than 5%.[11]

If type O, Rh-negative blood is to be transfused, it should be as packed cells and not as whole blood. Because of the presence of anti-A and anti-B antibodies in the plasma of universal donor whole blood, the risk of a subsequent transfusion reaction is greatly enhanced. The lack of available low titre anti-A and anti-B whole blood precludes it as a solution whose supply can be relied upon. It should be necessary to transfuse only 1 or 2 units of type O, Rh-negative packed red cells before type-specific blood is ready. By switching to type-specific blood early in the transfusion, reactions can be minimized.[10] If the situation dictates that a large volume of universal donor blood be used, then type O, Rh-negative blood should continue to be given, to prevent a reaction, until the patient is stable and can manufacture red blood cells.

Potentially, autologous blood transfusion is the safest alternative to type-specific blood in emergency situations. There is no risk of a transfusion reaction or of the transmission of disease. The ability to predict the potential benefit of using an autotransfusion device is difficult and very subjective. Age, presence of shock and mechanism of injury are not predictors of autotransfusion efficacy. Some very general indicators that may assist in determining that autotransfusion could be beneficial are an initial hematocrit of less than 35% and the requirement for more than 2000 mL of crystalloid solution for resuscitation.[12]

Blood that is confined to the thorax is usually clean, as is blood from the abdominal cavity, provided the gastrointestinal tract is not open. Devices for collection and subsequent administration of blood from the chest are readily available and are not expensive. Red blood cell-saver techniques used intraoperatively for retrieval of intraperitoneal blood require more set-up in equipment, personnel and disposal costs. They require a larger priming volume and have slower, less powerful suction. To be of benefit at least 3.5 units of packed cells should be transfused.[13] The major drawbacks to autotransfused blood are the potential for contamination, microemboli from platelet plugs and fractured red blood cells, and anticoagulant administration to a bleeding patient. However, it must be remembered that the patient's own blood comes closest to the "ideal fluid" in all trauma situations and therefore it is perhaps best to err on the side of having liberal indications for setting up the autotransfusion system.

Urgent Blood Transfusion

The decision to transfuse a patient who is responding to resuscitation must be based on a complete assessment of the clinical situation. Blood is a scarce resource, and its administration is not without complications. Young adults without cardiac disease can tolerate hematocrit levels of 25%, and it is appropriate in many situations to allow the patient's own bone marrow to resolve the anemia. However, the decision to withold blood must be based on which organ systems are injured and the trend in the patient's hemodynamic status. If there are signs of circulatory inadequacy such as a persistent tachycardia, ongoing lactic acidosis, a fall in blood pressure of more than 20% that is refractory to crystalloid therapy and an estimated blood loss of greater than 20% with some ongoing losses, blood should be transfused to correct the primary problem or to stabilize the situation until surgical control is obtained. Associated injury to the brain demands close attention to maintaining oxygen delivery and an adequate cerebral perfusion pressure. In acute lung injury, the management of ventilation to minimize barotrauma may necessitate lower oxygen saturations. In these situations oxygen transport must be maintained by optimizing the hemoglobin concentration.[14]

Complications of Blood Transfusion

The complications of blood transfusion can be broadly classified into the general complications of all fluid resuscitation and complications that are specific to blood transfusion. The most important of the general complications are hypothermia and coagulopathy. The specific complications pertaining to blood transfusion that can occur immediately include an allergic reaction (4% of recipients), a febrile reaction (2% of recipients), bacterial sepsis (0.01% of recipients) and he-

molytic transfusion reaction (0.03% of recipients).[3] The long-term risks of transfusion are most often associated with the complications of transmissible disease and immunosuppression.

Hypothermia

Hypothermia is defined as a core body temperature of less than 35°C. With progression to moderate hypothermia (32°C to 28°C) and then severe hypothermia (less than 28°C) the metabolic abnormalities progressively worsen to a state of coma and cardiac standstill. In most, if not all, victims of injury, it can be assumed that they are or will become hypothermic during their resuscitation. This condition leads to a number of physiologic derangements that will hinder the return to a well-perfused state. Among these derangements are depressed hepatic metabolism (i.e., synthesis of acute-phase reactants, metabolism of citrate), a worsening of metabolic acidosis (due to hypoperfusion of cold extremities and increased energy consumption due to shivering), impaired platelet function (decreased aggregation caused by diminished production of thromboxane B_2) and a shift of the oxygen-hemoglobin dissociation curve to the left (increasing its affinity for oxygen). The management of hypothermia is first preventive and second therapeutic, by warming fluids and inspired gases and by using external heating devices. The specific heat-transfer problem that needs to be addressed in resuscitating with blood is how to rapidly infuse at temperatures of 35°C a solution that is stored at 4°C and has a high viscosity. Whether packed red blood cells or additive red cells are used, the temperature gradient to be overcome is the same. An ideal fluid warmer is one that has a minimum flow rate of 150 mL/min, has a low priming volume and low pressure drop, is compatible with blood and is safe, compact and inexpensive.

There are a number of fluid-warming devices on the market, and new technology has facilitated the development of the ideal fluid warmer. In a comparison of available devices, the single-channel counter-current heat exchanger was found to have the most optimal flow characteristics, although the multichannel counter-current heat exchanger also worked well.[15] With these systems now readily available at moderate cost, the prevention and treatment of hypothermia in the injury victim has been greatly facilitated.

In certain patients who undergo massive transfusion after traumatic injury, diffuse pathologic bleeding develops. There is now abundant evidence that this "medical" bleeding develops because of the patient's generalized state of hypoperfusion, usually associated with hypothermia and acidosis. This is important to recognize, because the treatment of this problem is to warm the patient and to reverse the state of circulatory inadequacy not to administer massive volumes of blood components for their clotting factors.

Coagulopathy

The coagulopathy of massive transfusion has been attributed to the "washout" of platelets and clotting factors, and to their deterioration in stored blood. Clinical hemostasis requires about one-third normal levels of clotting factors, most notably the labile Factors V and VIII. Even after one blood volume exchange this amount is retained, and although levels are depressed, stored blood also preserves some of these factors. Factor VIII is an acute-phase reactant that is rapidly produced in response to injury. Studies done on patients undergoing multiple plasma exchange indicate that the factor most dangerously depleted is fibrinogen, which can affect coagulation. However, fibrinogen does not deteriorate in stored packed red cells, so unless many units of washed cells are used, depletion of fibrinogen should not occur. Based on these data, there is little evidence to support the prophylactic use of plasma or cryoprecipitate, which are rich in clotting factors.[6,16] These components should be used only when the patient's state of hypothermia and hypoperfusion has been reversed (as measured by end organ function) and there are documented abnormalities in the coagulation profile.[17]

Platelets are the other major component that deteriorate in storage and have been implicated in non-surgical bleeding problems. The thrombocytopenia associated with massive transfusion reaches its nadir 2 days after injury and usually returns to normal by day 4.[18] In studies comparing groups of patients who received platelet transfusion with those who did not, no difference was found in platelet count or in bleeding problems.[19] In a patient with normal bone marrow function it is very difficult to push the platelet count to a level below 50×10^9/L. Platelet function is an important aspect of thrombocytopenia-induced coagulopathy and must be taken into consideration with respect to platelet transfusion. As has been discussed, hypothermia induces changes in platelet aggregation, as do a multitude of medications. In the situation of a non-bleeding patient with normally functioning platelets, platelet transfusion need not be given prophylactically unless the count falls below 20×10^9/L. In the bleeding patient with normal function, platelet transfusion is generally indicated for a

count below 50 × 10^9/L. In both situations aggressive steps must be taken to rewarm and reperfuse the patient.

Transmission of Disease

Potentially the most frightening complication of blood transfusion is the transmission of disease that manifests itself weeks to years later. As the number of persons infected with the human immunodeficiency virus (HIV) increases, the need for vigilant screening of the donor pool also increases. Although HIV transmission through blood transfusion has declined, cases are still reported to occur when screening programs are in place. The development of more sensitive screening and awareness among donors should help to diminish the risk of HIV in blood recipients.[20] Despite the public's preoccupation with HIV transmission, the most commonly transmitted viral disease remains non-A, non-B hepatitis, now known as hepatitis C.

This disease, recognized as non-A, non-B hepatitis since 1974, has now been studied thoroughly and its clinical course well established. It is now understood that it has an even greater tendency than hepatitis B to produce chronic liver disease. Persistent alanine aminotransferase (ALT) elevation develops in more than 50% of cases, and in up to half of these an indolent form of chronic active hepatitis will develop subsequently with an increased risk of cirrhosis and primary hepatocellular carcinoma.[21]

Identification of the complete hepatitis C virus (HCV) nucleic acid sequence has permitted the development of an HCV antibody immunoassay. The prevalence of antibodies to the virus varies worldwide. The ability to screen for the virus and surrogate testing for ALT and the antibody to hepatitis B core antigen since 1986, have dropped the risk of hepatitis C transmission from 10% to 5% at a cost of about 5% of the donor population. Additional donor awareness about HIV and the ability to screen for antibody to HIV have resulted in a further drop, so that the risk today of post-transfusion HCV is less than 2%.[21]

Immunosuppression

In recent years increased attention has been given to the possibility of a persistent form of immunosuppression in blood transfusion recipients. Initial evidence suggests that this effect might be dose related. This has potentially important ramifications for the trauma patient who receives massive transfusions, particularly because sepsis is the major non-neurologic cause of death associated with trauma and thermal injury, carrying with it an overall mortality of more than 60%.[15,22] Much of the evidence suggesting this immunosuppressive effect in humans comes from patients with cancer and renal transplant recipients.[6,23-25] It is difficult to study this phenomenon in the trauma patient because of the immunosuppressive effects of soft tissue trauma and hemorrhage, both of which are usually present.

Most of the laboratory evidence for suppression of the immune system after blood loss comes from small-animal models. Within this context, hemorrhage has been found to depress the proliferation of blood lymphocytes and to reduce the production of certain cytokines (interleukin-2). These effects persist despite resuscitation and can last up to 3 days.[26-28] Within the humoral immune system, hemorrhage has been found to depress the ability of the B cell to react to known antigens.[29,30] Additionally, impaired phagocytosis may be associated with the increased production of other cytokines (tumour necrosis factor and interleukin-1) or the release of endotoxin by bacteria translocating from the gastrointestinal tract.[29] The net result is to leave the victim of blood loss more susceptible to sepsis for an undetermined time after injury.[29,31,32]

Because of these findings it will be very difficult to determine if the transfusion of blood into the traumatized patient has an immunosuppressive effect attributable to the blood alone. To date, studies in cancer patients and renal transplant recipients do provide some circumstantial evidence for this.[23-25] However, after hemorrhage and soft tissue trauma all efforts should be directed toward restoring homeostasis, and if blood transfusion is indicated, it should be given. To deny blood therapy because of a supposed depressive effect on the immune system would be incorrect on the basis of the evidence that exists today.

Conclusions

Work on blood substitutes continues, but recent medical history is littered with hopeful solutions that proved to be unsatisfactory. The best hope appears to be purified polymerized hemoglobin. In a recently published study, sheep tolerated a 95% exchange transfusion without evidence of clinical distress and with stable hemodynamics. The final hematocrit in this group was 24 ± 0.5%.[33] Many of the problems associated with stroma-free hemoglobin (i.e., physiologic P_{50}, oncotic pressure, depletion of plasma proteins) are gradually being overcome.[34] The prospects for having a synthetic oxygen-carrying solution that is disease free for use as a partial or total substitute for red blood cells appears closer now then

ever before. Until it is available at reasonable cost, however, blood remains the closest to being an ideal fluid. Although blood must be used in selected situations, because it is a limited resource and because of the potential long-term complications of blood transfusion, it remains the fluid of choice for resuscitation in the critically injured patient with signs of tissue hypoperfusion.

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Mobiflex®

(Tenoxicam Tablets) 20 mg
PHARMACOLOGICAL CLASSIFICATION
Anti-inflammatory, Analgesic Agent

ACTIONS AND CLINICAL PHARMACOLOGY

Non-steroidal anti-inflammatory agent (NSAID) with analgesic and antipyretic properties. Mechanism of action not completely known. Tenoxicam inhibits prostaglandin biosynthesis both in vitro and in vivo (protects mice against arachidonic acid induced toxicity). In vitro tests of leucocyte peroxidase also suggest tenoxicam may act as a scavenger for active oxygen at site of inflammation. Effects probably explain in part, activity in treatment of painful inflammatory and degenerative diseases of musculoskeletal system. Does not act by pituitary adrenal stimulation.

INDICATIONS

Symptomatic treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and extra-articular inflammations eg. tendinitis, bursitis, and periarthritis of shoulders or hips.

CONTRAINDICATIONS

Should not be administered to: patients with active peptic ulcer or active inflammatory diseases of gastrointestinal tract; patients who have shown hypersensitivity to the drug; patients in whom acute asthmatic attacks, urticaria, rhinitis or other allergic manifestations are precipitated by ASA or other NSAID's. Fatal anaphylactoid reactions have occured in such individuals.

Before anesthesia or surgery, should not be given to elderly patients, those at risk of renal failure, or those with increased risk of bleeding, because of increased risk of acute renal failure and possibility of impaired hemostasis.

WARNINGS

Peptic ulceration, perforation and gastrointestinal bleeding, sometimes severe and occasionally fatal reported during therapy with NSAID's including Mobiflex®. Caution should be exercised when a NSAID such as Mobiflex® used in patients with history suggestive of peptic ulcer, melena, or any gastrointestinal disease. Physician must weigh benefits of treatment against possible hazards.

Patients taking any NSAID including this drug should be instructed to contact a physician immediately if they experience symptoms or signs suggestive of peptic ulceration or gastrointestinal bleeding which can occur without warning symptoms or signs at any time.

Elderly, frail and debilitated patients appear to be at higher risk from a variety of adverse reactions from NSAID's. Mobiflex® should be used with special caution in these patients.

Use in Pregnancy and Lactation – Safety of Mobiflex® during pregnancy and lactation not established. Use not recommended.

No teratogenic effects observed in animal reproductive studies. Rats receiving tenoxicam during pregnancy showed delayed delivery. Tenoxicam readily passes into the milk of lactating rats.

Use in Children – Not recommended for use in patients under 16 years as dose and indications not established.

PRECAUTIONS

Gastro-intestinal system: If peptic ulceration or gastrointestinal bleeding occur during treatment drug should be immediately withdrawn.

No definitive evidence that concomitant administration of histamine H2-receptor antagonists and/or antacids will either prevent occurrence of gastrointestinal side effects or allow continuation of therapy when and if these adverse reactions appear.

Renal function: As with other NSAID's, long-term administration of tenoxicam to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome reported.

A second form of renal toxicity seen in patients with prerenal conditions leading to reduction in renal blood flow or blood volume, where renal prostaglandins have supportive role in maintenance of renal perfusion. In these patients, administration of a NSAID may cause dose-dependent reduction in prostaglandin formation and precipitate overt renal decompensation. Those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly at greatest risk. Discontinuation of NSAID therapy usually followed by recovery to pre-treatment state.

Reversible elevation of BUN and serum creatinine reported with Mobiflex®. Thought to result from inhibition of renal prostaglandin synthesis resulting in changes in medullary and deep cortical blood flow with attendant effect on renal function. Patients with impaired renal function or on diuretics, elderly patients and those with congestive heart failure or liver ascites, more at risk. During long-term therapy, kidney function should be monitored periodically.

Hepatic Function – As with other NSAID's, borderline elevations of one or more liver tests may occur. Abnormalities may progress, remain essentially unchanged, or be transient with continued therapy. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom abnormal liver test has occured, should be evaluated for evidence of development of more severe hepatic reactions. Severe hepatic reactions including jaundice and fatal hepatitis reported with this drug as with other NSAID's. Although rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), discontinue drug.

During long-term therapy, liver function tests should be monitored periodically.

Fluid and Electrolyte Balance – Fluid retention and edema observed in patients treated with Mobiflex®. As with many other NSAID's, possibility of precipitating congestive heart-failure in elderly patients or those with compromised cardiac function should be borne in mind. Use with caution in patients with heart failure, hypertension or other conditions predisposing to fluid retention.

With NSAID treatment, there is potential risk of hyperkalemia particularly in patients with conditions such as diabetes mellitus or renal failure; elderly patients; and patients receiving concomitant therapy with B-adrenergic blockers, angiotensin converting enzyme inhibitors or some diuretics. Serum electrolytes should be monitored periodically during long-term therapy, especially in patients at risk.

Hematology – Drugs inhibiting prostaglandin biosynthesis interfere with platelet function to some degree; therefore, patients who may be adversely affected by such action should be carefully observed when Mobiflex® administered.

Blood dyscrasias associated with use of NSAID's rare, but could be with severe consequences.

Infection – In common with other NSAID's Mobiflex® may mask usual signs of infection.

Ophthalmology – Blurred and/or diminished vision reported with use of Mobiflex® and other NSAID's. If such symptoms develop drug should be discontinued and ophthalmologic examination performed; ophthalmic examination should be carried out at periodic intervals in any patient receiving drug for extended period.

Hypersensitivity Reactions – As with other NSAID's, allergic reactions may occur. Manifestations include urticaria, bronchospasm and anaphylaxis, and in rare instances, severe skin reactions e.g. Stevens-Johnson syndrome and Lyell Syndrome.

Drug Interactions: ASA or Other NSAID's – Plasma concentrations of tenoxicam reduced to approx. 80% of normal concentrations when single doses administered in conjunction with ASA (2,600 to 3,900 mg/day). At steady state, simultaneous administration of ASA does not appear to have significant effect on plasma concentration of tenoxicam. Use in conjunction with ASA or another NSAID not recommended since data not available demonstrating that combination produces greater improvement than that achieved with either drug alone, and potential for adverse reactions increased.

Protein-Bound Drugs – As with other NSAID's, Mobiflex® is highly protein-bound, and therefore, might be expected to displace other protein-bound drugs, such as anticoagulants, oral hypoglycemics (sulfonylureas), phenytoin, and sulfonamides.

Short term pharmacodynamic studies demonstrated that tenoxicam does not potentiate anticoagulant effect of coumarin-type anti-coagulants nor hypoglycemic effect of sulfonylurea drugs. However, when a NSAID such as Mobiflex® administered concomitantly with anticoagulants, oral hypoglycemics, or other highly protein bound drugs, patients should be monitored and dosage adjustments made, if necessary.

Diuretics/Antihypertensives – As with other NSAIDs, Mobiflex® can attenuate blood pressure lowering effect of hydrocholorathiazide and peak excretion rates of NA^+ and $C\ell^-$ in patients with hypertension. Close monitoring of patients advisable. Excretion of electrolytes not significantly affected when tenoxicam (2-day loading dose of 40 mg daily, followed by 20 mg daily) administered to normotensive patients receiving furosemide therapy (40 mg daily). Some NSAID's reported to reduce antihypertensive effects of certain beta-blockers. Interaction between Mobiflex® and beta-blockers not studied.

Digoxin – In elderly patients, with normal plasma creatinine levels, plasma digoxin levels not altered by concomitant administration of Mobiflex® (30 mg daily).

Antacids – Administration of 15 ml of aluminum hydroxide or aluminum and magnesium hydroxide antacid just prior to single 20 mg oral dose of Mobiflex® did not affect bioavailability.

Cholestyramine – Average half-life of tenoxicam, after single 20 mg intravenous dose, reduced from 67.4 hrs. to 31.9 hrs. following administration of cholestyramine (4 g in 200 ml water p.o.t.i.d.). Apparent drug clearance of tenoxicam increased by 105%.

Lithium – NSAID's reported to increase steady state plasma lithium concentrations. Recommended these concentrations be monitored when initiating, adjusting and discontinuing Mobiflex® treatment.

Methotrexate – Co-administration of some NSAID's and methotrexate associated with reduced renal tubular secretion of methotrexate, higher plasma concentrations, and severe methotrexate toxicity. Therefore, caution should be exercised when NSAID's, such as Mobiflex®, administered concurrently with methotrexate. Interaction between Mobiflex® and methotrexate not studied.

ADVERSE REACTIONS

Most common adverse reactions encountered with NSAID's are gastrointestinal, of which peptic ulcer, with or without bleeding, is most severe. Fatalities have occurred, particularly in the elderly. In approx. 12,000 patients administered Mobiflex® (tenoxicam) 10-40mg/day, (approx. four/fifths receiving 20 mg/day), incidence of peptic ulceration and of gastrointestinal bleeding (including hematemesis and melena) was 0.1-0.6%.

Approx. incidences of other adverse effects listed by systems are: Gastrointestinal: (10.4-23.0%) – Dyspepsia (0.1-9.7%), nausea (2.0-6.7%), constipation (0.5-2.9%), abdominal pain (0.7-3.3%), diarrhea (0.5-2.3%), flatulence (0.04-1.9%), vomiting (0.2-1.1%), ulcerative stomatitis (0.1-0.7%), gastritis (0.1-0.8%), esophagitis (0.2%), abdominal discomfort (1.4-2.2%), pyrosis (1.3-1.9%), epigastric discomfort (0.2-0.4%), epigastric pain (1.8-2.5%), hyperacidity (0.02-0.4%), anorexia (0.05-0.4%), indigestion (0.1-0.2%), meteorism (0.2-0.4%), gastric pressure (0.5-1.0%), mouth dryness (0.1-0.3%). Glossitis, stomatitis, dysphagia, reflux esophagitis each reported in less than 0.1%.

Dermatologic: (1.6-3.9%) – Rash (0.2-1.4%), pruritis (0.3-1.3%), sweating (0.06-0.3%), exanthema (0.2-0.3%), itching (0.05-0.4%). Photosensitivity reaction, seborrhea, urticaria, eczema, nail disorder each reported in 0.1% or less of patients. One case of angioedema reported.

Central Nervous System: (2.0-9.1%) – Headache (0.9-4.3%), dizziness (0.8-3.3%), malaise (0.04-0.8%), parasthesia (0.02-0.5%), somnolence (0.1-0.7%), vertigo (0.2-0.4%), confusion (0.2%), fatigue (0.1-0.9%), depression (0.6%), insomnia (0.1-0.2%). Leg cramps, nervousness, fever, and paresis each reported in 0.1%.

Cardiovascular: Hypertension (0.02-0.3%), palpitations (0.02-0.2%), flushing (0.02-0.03%), purpura (0.02-0.2%). Tachycardia reported in less than 0.1%.

Hematologic: Anemia (0.04-0.3%), leukopenia (0.04-0.4%). Thrombocytopenia reported in 0.1% or less.

Renal: Haematuria (0.02-0.2%), edema (0.2-1.3%), micturition frequency (0.02-0.3%), polyuria (0.03-0.1%). Dysuria, cystitis, increased BUN, increased creatinine, and albuminuria each reported in less than 0.1% of patients. Isolated cases of abnormal renal function and one case of renal failure reported.

Hepatic: (0.06-0.4%) – Abnormal hepatic function (0.3%). Jaundice, increased SGOT, SGPT, gamma GT and bilirubin each reported in less than 0.1%. Hepatitis, hepatic coma and hepatic failure each reported once.

Respiratory: (0.02-0.65%) – Dyspnea (0.2%), bronchospasm (0.1%). Eyes, Ears, Nose, Throat: – Vision abnormal (0.02-0.3%). Diplopia, conjunctivitis, tinnitus, deafness, epistaxis, abnormal lacrimation each reported in 0.1% or less.

SYMPTOMS AND TREATMENT OVERDOSE

Cases of overdoses not reported. In event of overdosage with Mobiflex®, supportive and symptomatic therapy indicated.

DOSAGE AND ADMINISTRATION

Single daily dose of 20 mg Mobiflex® (tenoxicam) should be taken orally at the same time each day. Higher doses should be avoided as they do not usually achieve significantly greater therapeutic effect, but may be associated with higher risk of adverse events.

In some patients a 10 mg (1/2 tablet) daily dose may be sufficient. Smallest effective dose should be prescribed.

Use in elderly – Mobiflex® should be used with special caution in elderly patients since they may be less able to tolerate side effects than younger patients. Also more likely to be receiving concomitant medication or have impaired hepatic, renal or cardiovascular function.

AVAILABILITY

Yellow film coated, oblong 20 mg tabs, single scored on one side, imprinted 'ROCHE'. Available in white opaque density polyethylene bottles of 100 tabs.

References:

1. Mobiflex® Product Monograph, Hoffmann-La Roche Limited, June 1991.
2. Netter P et al. Premarketing risk to benefit study of tenoxicam – a new nonsteroidal anti-inflammatory drug. *Drug Invest* 1990;2(Suppl. 3): 22-30.
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The Maintenance of Competence (MOCOMP) Program: Motivating Specialists to Appraise the Quality of Their Continuing Medical Education Activities

I. John T. Parboosingh, MB, ChB, FRCOG, FRCSC;* S. Tunde Gondocz, MSc†

The goal of the Maintenance of Competence (MOCOMP) Pilot Project is to develop a comprehensive CME strategy that will motivate specialists to continuously update their clinical practice. In its 1st year the pilot program has taken several significant steps. A credit system has been implemented to facilitate recognition of CME of the highest educational quality and to encourage specialists to compare their CME efforts with those of their colleagues. The self-directed CME curriculum currently followed by the typical MOCOMP Program member has been described. A diary has been implemented for specialists to record CME activities and their potential impact on practice. The MOCOMP Program is the first attempt to motivate self-directed continuing medical education (CME) through the use of a diary and the first attempt to use this instrument to encourage critical appraisal of personal CME habits.

Le but du projet pilote de maintien des compétences (MOCOMP) est de développer une stratégie globale de FMC qui va inciter le spécialiste à continuellement remettre à jour sa pratique clinique. Dans sa première année d'application, le programme pilote a franchi plusieurs étapes importantes. Un système de crédits a été instauré en vue de faciliter la reconnaissance d'une FMC des plus hauts standards de qualité et d'encourager les spécialistes à comparer leurs efforts de FMC à ceux de leurs collègues. On décrit ici le programme courant de FMC auto-gérée suivi par un participant type au programme MOCOMP. Un journal a été dévelopé pour permettre aux spécialistes de consigner leurs activités de FMC et d'enregistrer l'impact qu'elles peuvent avoir sur leur pratique. Le programme MOCOMP constitue la première tentative pour promouvoir la formation médicale continue (FMC) auto-gérée par l'utilisation d'un journal; c'est aussi la première utilisation de cet instrument pour encourager une évaluation critique des habitudes personnelles de FMC.

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Most programs of maintenance of competence (MOCOMP) operate through legislation, which mandates continuing medical education (CME) or re-certification by examination. Nineteen specialty boards in the United States have introduced time-limited certification, and mandatory CME is in place in many states. The Royal Australian College of Obstetricians and Gynaecologists has linked mandatory CME to licensure since 1988.

The MOCOMP Program of the Royal College of Physicians and Surgeons of Canada will achieve its objectives by encouraging specialists to apply the principles of total quality management to their CME efforts. This involves examining the *resources* used, the *outcome* of their CME efforts and the *process* whereby these outcomes are achieved.

CME resources are the time committed and the CME methods used (e.g., reading, conferences, rounds). Data on the CME resources used by members of the MOCOMP Pilot Project (*MOCOMP Bulletin* January 1993) show that teaching and research (Type III CME activities) account for more than 50% of the time spent undertaking CME. Al-

though scholarly activities certainly contribute to MOCOMP, the relationship is not always easily described. Furthermore, this CME activity is more likely to be driven by the needs of students and research programs than by the needs of patients. The data suggest a need to define and record the outcomes of CME efforts, namely the clinical problems in current practices that have been reviewed and updated. The model of a self-directed CME curriculum (Fig. 1) describes the process whereby MOCOMP Program members use CME resources to achieve the outcomes that have impact on their clinical practice.

Physicians obtain information on a daily basis from a multitude of sources. Some professional activities (e.g., rounds, journal reading) are used primarily to scan for new information that may enhance clinical practice, whereas others (e.g., consultations, teaching, research) are undertaken primarily for other purposes. Both are rich sources of new ideas and opportunities to update patient care practices. This CME activity, whereby physicians scan their professional environment for new ideas, is referred to as level I CME activity in our model. These CME activities are too numerous to be recorded by busy practitioners. As important as they are, level I activities rarely motivate specialists to initiate a change in practice. Some of the information derived by scanning the environment, however, captures the attention of the specialist, who perceives an opportunity to improve on the management of a clinical problem.

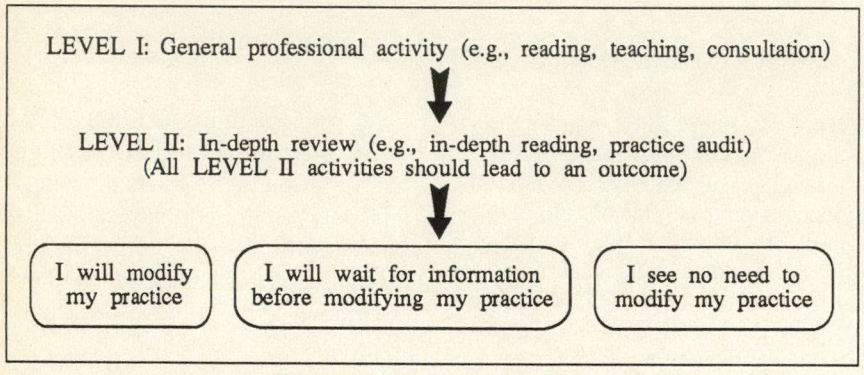

FIG. 1. Model of self-directed continuing medical education (CME) curriculum.

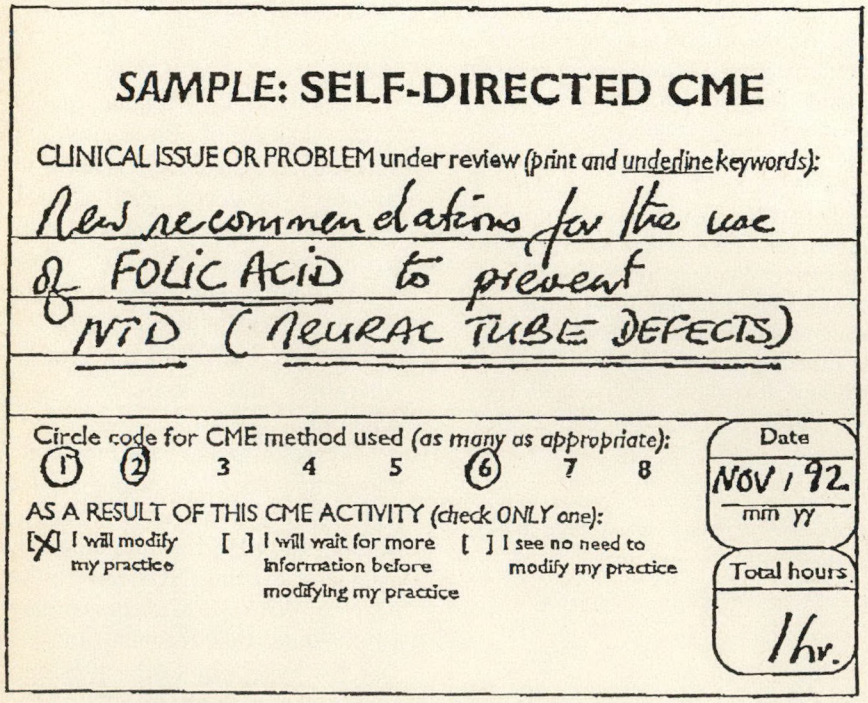

FIG. 2. Record of self-directed CME taken from MOCOMP diary.

CME resources (e.g., reading, discussions, programs, rounds) are now used in a more focussed manner to seek answers to the following three questions:

- What is the state-of-the-art method of managing this problem?
- What is my current method of managing this problem?
- What method of management are my colleagues using?

This CME activity, termed level II CME, differs from level I activity in that it focuses on a specific clinical problem and requires a more in-depth use of CME resources. Level II CME is goal oriented and always comes to one of three possible conclusions (or outcomes) regarding the management of the clinical problem under review: (a) "I have decided to make a change in my management of this clinical problem as a consequence of this CME activity"; (b) "I will wait for further information before making the decision to modify my practice"; or (c) "I see no need to change my practice; I am satisfied with my current approach to the management of this clinical problem."

The recording of self-directed CME in the MOCOMP diary (Fig. 2) has been restricted to level II CME activity — those activities that address specific topics in sufficient

depth for specialists to express the potential impact on their practice.

MOCOMP Program members will receive feedback of their CME activities in the form of an annual CME profile.

The MOCOMP Annual CME Profile

A summary of diary entries, including attendance at conferences registered in the MOCOMP Program will be sent to each specialist annually along with aggregate data computed from submissions by colleagues in the same specialty and practice setting. The main purpose of providing an annual CME profile is to assist specialists to appraise, critically, the quality of their CME activities. It is designed to encourage specialists to review their CME activities, discuss their results with their colleagues and plan their CME for the coming year. The profile will consist of two sections.

Section A: Group and Type II CME

This section of the annual CME profile will give specialists a summary of the number of MOCOMP credits earned, the mean credit rating and the number of hours spent attending rounds and conferences as well as aggregate data obtained from colleagues in the same specialty and practice setting.

Section B: Self-directed CME

This section will provide a summary of the number of individual topics submitted by the specialist in the year and the number of hours spent in self-directed CME as well as data, in aggregate form, submitted by colleagues.

The annual CME profile will include, for the individual specialist, a list of the keywords, the CME methods used and the outcome designated to each topic recorded in the MOCOMP diary during the year (Table I).

A directory of keywords, CME methods used and outcomes designated to topics recorded during the year by colleagues will also be included with the CME profile. The topics entered into the diary should be compared with the specialist's practice profile or case mix. All specialists should be working toward obtaining data on their case mix from computer records and using these data to determine the direction of their CME efforts.

The topics reviewed by the specialist in the past year should be compared with those reviewed by colleagues in the same specialty and practice setting. This exercise, whereby we are kept informed of the CME activities of our colleagues (the topics they studied, the CME methods used and the outcome designated to each topic), is intended to motivate the individual to keep up to date.

A national specialty society may use aggregate data obtained from the annual CME profiles of its members to plan educational programs. The data from the CME profiles of members of a national specialty society may serve as an important method of needs assessment for a national education program. For instance, the fact that members have reviewed a specific topic during the year and are waiting for more information before changing their practice may be an indication for a national or regional education session on that topic. The data from the CME profiles will provide a society with information on the CME methods used by its members. This information may be used to plan future needs such as computer learning programs and audiotapes. Also, the data from CME profiles may be used to monitor the response of society members to new information. For instance, a society may promote the recommendations that result from a multicentred randomized trial. The response to these recommendations can be monitored by searching for the relevant keywords and identifying the potential impact on practice (outcome codes) recorded in the CME profiles of its members.

Summary

The Royal College MOCOMP Pilot Project has taken several significant steps in its 1st year. A credit system has been implemented to facilitate recognition of CME of the highest educational quality and to encourage specialists to compare their CME efforts with those of their colleagues. The self-directed CME curriculum currently followed by the typical MOCOMP Program member has been described. A diary has been implemented for specialists to record CME activities and

Table I. Example of an Entry from an Annual Continuing Medical Education (CME) Profile

Item no.	CME code	Keywords	Outcome code
4*	1,2,6	Folate, NTDs	1
5†	1,2,6	PROM, antibiotics	2

*The role of folate in preventing fetal neural tube defects (NTDs) has been reviewed, using journal reading, a literature search and preparing a seminar (CME codes 1, 2 and 6 respectively); the outcome code (1) indicates the specialist's intention to modify current practice as a consequence of this review.

†The role of antibiotics in premature rupture of the membranes (PROM) has been reviewed by the same methods as those in item 4 (CME codes 1, 2 and 6); the outcome code (2) indicates the specialist's intention to wait for more information before changing practice.

their potential impact on practice. Data will be fed back in the form of an annual CME profile.

The MOCOMP Program is the first attempt to motivate self-directed CME through the use of a diary and the first attempt to use this instrument to encourage critical appraisal of personal CME habits. This unique component of MOCOMP has created much attention around the world where physicians are concerned about regulation of CME through examination. The program is developing standards for lifelong learning which, when evaluated appropriately, should be introduced into residency training programs. Finally, a credible program of research is developing around the MOCOMP project to answer questions regarding the relationship between CME and quality of care and, in the future, to provide information concerning the relationship between performance in residency training programs, CME habits in practice and the quality of care provided by practising specialists.■

BOOK REVIEWS

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trove of information on a group of remarkable people. The illustrations are both intriguing and plentiful. They show in the faces of both surgeons and patients the *zeitgeist* of their times.

The third section of the book is devoted to a wide variety of special subjects and covers the historical aspects of almost everything from amputations to orthopedic implants.

The fourth section is a station stop at the turn of the century — a pause to reflect on the state of the art at that time, what had been achieved and what was to come.

The book ends with reference to the impetus wars have given to trauma surgery, which arose from the sheer necessity to keep soldiers alive and capable of fighting again, or at least to rehabilitate the veterans. Homer's observations on war injuries are well recorded in the *Iliad*, and Roman Army surgeons 2000 years ago were early developers of pylons for immediate fitting to battlefield amputees.

David LeVay was a practising consultant orthopedic surgeon in London, England, for over 30 years, after which he spent a year working in Africa and Australia. He has always been a writer and at various times an editor and a translator of French and German works. He is also a gifted author, having completed the monumental task of assembling historical facts and knowledge on what is now orthopedic surgery. He has chosen a very attractive way of presenting his information as a blend of history, anecdote and reference. This book will provide endless pleasure for all who have an interest in the human frame, its failure and its repair. The book will appeal to anyone involved in medical care who is curious about its origins or who has heard at college or university names of the medical pioneers. Who knows, you may even find out what happened to Virchow!

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SABISTON REVIEW OF SURGERY. David C. Sabiston Jr. 291 pp. Illust. W.B. Saunders Company, London; Harcourt Brace Jovanovich, Inc., Philadelphia; HBJ-Holt-Saunders Distribution Services, Toronto. 1992. $37.95. ISBN 0-7216-3534-2

This paperback book is a companion to the 14th edition of *Textbook of Surgery: The Biological Basis of Modern Surgical Practice.*

According to the preface, medical students, surgical residents and practising surgeons will benefit from reading this book; it will be useful for revision of basic surgical science in preparation for the Board examinations, for orthopedic surgeons, neurosurgeons, otolaryngologists, plastic surgeons, maxillofacial surgeons and neurologists. Moreover, the book claims to be beneficial for residents in colorectal surgery, pediatric surgery and vascular surgery.

It comprises a series of questions on the content of each chapter of the main textbook. Each question is followed by a brief critique, and the correct answer is given. The number of questions for each chapter range from 12 ("The management of acute trauma") to 125 ("Cardiac surgery").

The critiques are readable, compact, well-written and clear, and the book is probably helpful in emphasizing the aspects of each chapter that the authors feel to be of importance.

I found that the format is not conducive to proper study. Each critique and answer is placed immediately after the question. The temptation to skip to this part before thinking over the question and truly testing one's knowledge is almost overwhelming. It would be better if the questions were together and the critiques were in a separate section, similar to the format employed in the SESAP syllabus.

It seems inherently improbable that one compact volume could be helpful to everybody from a medical student to a subspecialist in one area of general surgery although, clearly, there are parts that may be helpful to each particular level of training.

Overall, I found this to be an interesting companion for anybody who happens to be in possession of Sabiston's textbook (14th edition). It is fun to dip

continued on page 70

The Value of Prostate-Specific Antigen Levels in Pelvic Lymph Nodes for Diagnosing Metastatic Spread of Prostate Cancer

Daniel A. Shoskes, MD; John Trachtenberg, MD, FRCSC

Curative radical therapy for prostate cancer depends on accurate diagnosis of metastatic spread to pelvic lymph nodes. The authors measured prostate-specific antigen (PSA) levels in homogenized pelvic lymph nodes to determine the antigen's diagnostic value and its correlation with histologic findings. No PSA was detectable in the lymph nodes of either women or of men without prostate cancer. A dilution of prostate cancer tissue with nodal tissue showed that PSA is detectable in this assay to a concentration of 1:100 000. In 38 patients who underwent pelvic lymph node dissection for staging stage B prostate cancer the histologic findings were correlated with PSA content. All nine patients with histologic evidence of metastatic disease had measurable PSA in their nodes. Of the 29 patients with no histologic evidence of metastatic disease, 23 had no detectable PSA in their nodes. The six patients with negative histologic findings and positive findings for PSA had no progression of disease at 18-month follow-up. The authors conclude that the measurement of PSA in pelvic lymph nodes can add substantial information to that obtained by standard histologic examination.

Le traitement radical du cancer de la prostate à visée curative dépend du diagnostic précis de l'envahissement métastatique des ganglions pelviens. Les auteurs ont mesuré les taux d'antigène prostatique spécifique (APS) dans un homogénéisat de ganglions lymphatiques pelviens, afin d'établir l'intérêt de cet antigène pour le diagnostic et sa corrélation avec l'examen histologique. Aucun APS n'a été décelé dans les ganglions lymphatiques de femmes ou dans ceux d'hommes qui n'avaient pas le cancer de la prostate. La dilution de tissu prostatique cancéreux et de tissu ganglionnaire a montré que l'APS était décelable par cette technique de dosage jusqu'à conurrence de 1:100 000. Chez 38 patients soumis à une dissection des ganglions pelviens pour la détermination du stade B de l'évolution du cancer de la prostate, les résultats histologiques ont été mis en rapport avec la teneur en APS. Les neuf patients qui présentaient des signes histologiques de métastases avaient tous des taux mesurables d'APS ganglionnaire. Des 29 patients sans signes histologiques d'envahissement métastatique, 23 n'avaient pas d'APS décelable dans les ganglions. Les six patients ayant des résultats histologiques négatifs et un test positif pour l'APS n'avaient pas montré d'évolution de la maladie après 18 mois de surveillance. Les auteurs concluent que le dosage de l'APS dans les ganglions lymphatiques pelviens peut ajouter une information importante à l'examen histologique standard.

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The optimal treatment for clinically localized prostate cancer remains controversial. Radical curative therapy (radiotherapy or surgery) is based on the premise that the tumour has not spread beyond the confines of the prostate. The standard diagnostic manoeuvre prior to radical therapy is a bilateral pelvic lymph node dissection, including the obturator and external iliac nodes. Processing the nodes by frozen section at the time of radical prostatectomy is labour intensive, delays surgery and is associated with a 10% to 20% false-negative rate.

Prostate-specific antigen (PSA) is a serine protease that is specific to the prostate and has enjoyed widespread use as a serum marker for detecting and for monitoring prostate cancer.[1-3] As well, it can be used in an immunoperoxidase stain to identify metastatic prostate cancer in the lymph nodes[4,5] and in other tissues.[6] The existence of PSA in the pelvic lymph nodes of healthy men is not known, and there are no data available on the ability to detect nodal spread of prostate cancer by the measurement of tissue PSA. To address these issues, we studied the tissue content of PSA in normal lymph nodes and in malignant lymph nodes in an attempt to correlate histologic findings with the presence of the tumour marker.

Materials and Methods

Controls

To determine the presence of PSA in normal pelvic lymph nodes, PSA was measured in the pelvic nodes of 42 women and men (both young and old) without prostate cancer. The nodes from women and men older than 40 years were obtained at the time of cystectomy for transitional cell carcinoma; nodes from men 40 years of age or younger were obtained from cadaveric organ donors. The serum PSA level was normal in all men. No prostate cancer was noted in the histologic analysis of the prostates removed during cystoprostatectomy.

Assay Sensitivity

To determine the maximum sensitivity of the assay to detect lymph node PSA, normal lymph nodes from female cadaveric organ donors were serially diluted with malignant prostatic tissue obtained from radical prostatectomy specimens. The lymph nodes were minced, homogenized and mixed with homogenized prostate cancer tissue of known PSA content. Serial dilutions were continued to a concentration of 1:1 $\times 10^{-6}$ of prostate. Each assay was adjusted to 2 mg of protein/mL of assay. All PSA levels were determined by Hybritech R reagents and techniques (Hybritech Div. Eli Lilly Inc., Canada, Toronto). All assays were performed in triplicate.

Study Group

Thirty-eight men with clinical stage B[7] prostate cancer having negative findings on investigation for metastatic disease consented to radical prostatectomy. The investigations for metastatic disease consisted of measurement of the serum prostatic acid phosphatase (enzymatic) level, total body bone scan and abdominal and pelvic computed tomography (CT). PSA was less than 25 ng/mL (normal less than 2.25 ng/mL) in all cases. Before prostatectomy, a modified pelvic lymph node dissection was performed to include obturator and external iliac nodes. All nodal tissue was submitted for frozen section histologic examination. In addition, the highest node in the iliac dissection was bisected and half was snap frozen in liquid nitrogen, then stored at −70°C for later analysis for PSA. The other half was sent for histologic examination. Patients with positive lymph nodes on quick histologic section did not undergo radical prostatectomy.

Nodes for PSA determination were thawed and homogenized, then sonocated. After centrifugation, the specimen was weighed, then analysed for protein content. All specimens were adjusted in concentration to 2 mg of protein/mL, then processed by the Hybritech R PSA assay.

Results

Pure homogenates of prostate cancer tissue had PSA levels greater than 200 μg/L (Table I). Female lymph nodes had no measurable PSA. When the homogenate of female lymph nodes was serially diluted with the homogenate of prostate cancer tissue, PSA was detectable to a dilution of 1:100 000. Similar-

Table I. Sensitivity of Prostate-Specific Antigen (PSA)*

Tissue	Dilution	PSA (μg/L)
PC	No dilution	> 200
Lymph node 1	No dilution	Not detected
Lymph node 2	No dilution	Not detected
Lymph node 3	No dilution	Not detected
PC 1	1:10	> 200
PC 2	1:10	> 200
PC 3	1:10	> 200
PC 1	1:100	> 200
PC 2	1:100	> 200
PC 3	1:100	> 200
PC 1	1:1000	> 200
PC 2	1:1000	> 200
PC 3	1:1000	> 200
PC 1	1:10 000	37.1 ± 1.2
PC 2	1:10 000	25.2 ± 2.2
PC 3	1:10 000	20.2 ± 2.2
PC 1	1:100 000	4.2 ± 0.4
PC 2	1:100 000	5.2 ± 0.3
PC 3	1:100 000	4.7 ± 0.4
PC 1	1:1 000 000	Not detected
PC 2	1:1 000 000	Not detected
PC 3	1:1 000 000	Not detected

*Prostate cancer (PC) was serially diluted with homogenized female lymph-node tissue. All assays were adjusted to 2 mg protein/mL.

Table II. Presence of PSA in Lymph Nodes of 42 Patients Without Prostate Cancer

Sex (age, yr)	No. of patients	Location of lymph node	PSA
Female	6	Pelvis	Not detected
Female	4	Abdomen	Not detected
Male (≤ 40)	8	Pelvis	Not detected
Male (≤ 40)	8	Abdomen	Not detected
Male (> 40)	8	Pelvis	Not detected
Male (> 40)	8	Abdomen	Not detected

ly, in all lymph node specimens from women or men without prostate cancer, no PSA was detected (Table II).

Of the 38 men with prostate cancer, 8 had positive lymph nodes on frozen section histologic examination. All had PSA detected in their lymph node homogenates (Table III). One further patient had negative nodes on frozen section but was later found to have positive metastatic nodes on permanent section. This patient had detectable PSA in the lymph nodes.

Of the 29 men with negative lymph nodes on histologic examination, 23 had no detectable lymph node PSA. Six men, however, had detectable lymph node PSA despite a negative histologic diagnosis. None of these patients subsequently had recurrent or metastatic disease, although the follow-up was short (range from 5 to 18 months).

Table III. Biochemical and Pathologic Comparison of PSA in Pelvic Lymph Nodes

Patient no.	Histologic findings*	Tissue PSA	Serum PSA (ng/mL)
1	–	Not detected	12
2	–	Not detected	8
3	+	Detected	9
4	–	Not detected	15
5	–	Detected	9
6	–	Not detected	11
7	–	Detected	12
8	+	Detected	8
9	+	Detected	17
10	–	Not detected	6
11	+	Detected	12
12	–	Detected	8
13	–	Not detected	9
14	–	Detected	15
15	–	Not detected	9
16	–	Not detected	5
17	–	Not detected	12
18	+	Detected	18
19	–	Not detected	17
20	–	Not detected	5
21	–	Detected	12
22	–	Not detected	8
23	+	Detected	9
24	–	Not detected	15
25	+	Detected	9
26	–	Not detected	11
27	–	Not detected	12
28	–	Not detected	8
29	+	Detected	17
30	+	Detected	15
31	–	Detected	12
32	–	Not detected	8
33	–	Not detected	4
34	–	Not detected	6
35	–	Not detected	3
36	–	Not detected	5
37	–	Not detected	4
38	–	Not detected	6

*– = negative, + = positive

Discussion

By definition, for radical therapy of prostate cancer to be curative, the lesion must be localized to the prostate. Preoperative assessment of nodal spread is limited by the efficacy of the imaging and biochemical modalities available. CT can only detect substantially enlarged nodes, while pedal lymphangiography may miss obturator or presacral nodes. Serum PSA values, when markedly elevated, almost always suggest locally aggressive or metastatic disease, or both;[8] however, there is considerable overlap at intermediate levels. Pelvic lymph node dissection is the gold standard for diagnosing stage D1 disease. The reliance on quick-section interpretations at the time of surgery may understate by as much as 10% to 20%.

This preliminary study set out to establish that the concentration of PSA found in pelvic lymph nodes of men with prostate cancer could be used to determine the presence of lymph node metastasis. The use of a biochemical marker theoretically could be more sensitive and specific than histologic examination, particularly with low volume of disease. Because the presence of any nodal disease portends a significantly worse prognosis,[9] this greater sensitivity could spare patients the morbidity of noncurative radical therapy. For those who believe that lymph node metastasis is not a contraindication to radical therapy,[10] the diagnosis of D1 disease still adds prognostic information and aids in the treatment stratification. With the increased interest in laparoscopic pelvic lymph node dissection, PSA assay of the removed nodal tissue mass may be easier than standard histologic means (Gerald W. Chodak, personal communication, 1992).

By using appropriate controls, we demonstrated that PSA could not be detected in normal lymph nodes and that PSA could be measured in very low concentrations in cancerous nodes, probably in the order of 1 cancer cell per 10 000 normal cells. Put another way, this theoretically could detect one cancer cell in less than 0.1 mg of tissue.

This study also demonstrated an excellent correlation between the

presence of PSA in pelvic nodes and the presence histologically of metastases in pelvic nodes. All the men with positive histologic findings had PSA detected in their nodes. Six of 23 men with negative histologic findings, however, were found to have PSA in the pelvic nodes. It is interesting to speculate whether this result is in keeping with the observation that metastatic disease still develops in 20% to 35% of men who undergo node dissection for prostate cancer and have negative findings on permanent sections. Further follow-up of these patients will determine whether this assay has a 25% false-positive rate or whether in fact it allows the identification of patients with unsuspected low-volume metastatic disease.

Finally, although the current PSA assay takes too long for practical intraoperative use, the development of newer enzymatic assays seeking an "all-or-nothing" effect could eventually be faster and less subjective than histologic analysis. These solid-state assays have been developed for the determination of small concentrations of substances in plasma, and the entire procedure usually takes less than 15 minutes. They require no special expertise or processing and would be extremely inexpensive to perform. The tests are presently being developed commercially. The ideal situation, however, will probably combine the information the two tests provide, because tissue PSA may be able to detect metastasis too small to see with light histology, and very poorly differentiated tumours that do not express PSA[5,11] still could be recognized by histologic appearance.

Conclusions

Measurement of PSA in nodal tissue is a viable diagnostic tool that correlates well with histologic examination for metastatic prostate cancer. PSA in nodes of women and of men without prostate cancer was undetectable, whereas all men with positive nodes on histologic examination had measurable PSA. Six men with negative histologic findings had positive nodal PSA, suggesting either a 25% false-positive rate or that this technique can detect previously unmeasurable low-volume metastatic disease. Resolution of this will require larger numbers with longer follow-up because of the slow growth rate of the disease.

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A Review of 1486 Transurethral Resections of the Prostate in a Teaching Hospital

Eric P. Estey, MD; David R. Mador, MD, FRCSC; Malcolm S. McPhee, MD, MSc, FACS, FRCSC

The authors reviewed retrospectively 1486 consecutive transurethral resections of the prostate (TURP) gland performed in a teaching hospital between 1985 and 1987. The death rate was 0.8% in an institution where senior residents were the primary resectionists in approximately 75% of TURPs. The results of this review are compared with those of a 1974 study of 2223 patients. They indicated that TURP was a reasonably well-tolerated surgical procedure in the training environment and was associated with lower mortality and morbidity and a shorter hospital stay for the patient than in the 1974 study. The authors believe that with proper supervision and instruction, resident urologists can obtain satisfactory results while gaining competence and experience in performing TURPs.

Les auteurs ont étudié de façon rétrospective 1486 résections transurétrales de la prostate (RTUP) consécutives pratiquées dans un hôpital d'enseignement entre 1985 et 1987. Le taux de mortalité a été de 0,8 % dans un établissement où les résidents séniors étaient les premiers intervenants dans 75 % des RTUP. Ces résultats ont été comparés à ceux d'une étude réalisée en 1974 chez 2 223 patients. Ils indiquent que la RTUP est une intervention chirurgicale raisonnablement bien tolérée en milieu de formation, et qu'elle est reliée à une mortalité et à une morbidité plus faibles et à un séjour hospitalier plus court que pour les patients de 1974. Les auteurs croient qu'avec une surveillance et des instructions adéquates, un résident en urologie peut obtenir des résultats satisfaisants tout en acquérant compétence et expérience dans l'exécution des RTUP.

Over 50 years have passed since transurethral resection of the prostate (TURP) gland was devised to relieve bladder outlet obstruction for those with benign or malignant disease. It has been estimated that the probability of a 40-year-old man undergoing a prostatectomy during his lifetime is 29%, and 90% of patients who undergo an operation for bladder outlet obstruction will have a TURP.[1,2] The mortality from TURP has declined steadily over the past 30 years, with rates as low as 0.2% quoted in the American Urological Association Cooperative Study in 1988.[3] The literature contains numerous reviews indicating that TURP is a reasonably safe procedure; however, few surveys have evaluated the safety of TURP for neophyte resectionists.

The purpose of this review is to evaluate the urologic care provided in a teaching hospital to determine if resident participation influences patient morbidity or mortality. A common surgical procedure, TURP, is the basis of this evaluation.

Patients and Methods

Hospital charts of all 1486 consecutive patients who underwent TURP in one institution between 1985 and 1987 were reviewed. Each record was examined with respect to 25 variables. This review deals with patient evaluation, resection methods and early postoperative complications.

The evaluation was performed at the Royal Alexandra Hospital, Edmonton, a teaching institution affiliated with the University of Alberta. Senior urology residents obtain a portion of their training at this centre under the supervision of staff urologists. Endoscopy is an important part of their training. The urology resident is the primary resectionist in approximately 75% of the TURPs performed at the hospital. The resident receives supervi-

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sion and instruction from the attending urologist during the operation with periodic endoscopic assessment of the resection.

The resections were carried out in the conventional fashion, resecting prostatic adenoma down to the fibres of the surgical capsule. Resections were performed with intermittent irrigating resectoscopes, using either 1.5% glycine solution or distilled water as an irrigant. All patients with a positive urinary culture, bacteriuria or indwelling Foley catheters were given appropriate antibiotics pre- and postoperatively. Others were maintained on appropriate antibiotics for several days postoperatively. A Foley catheter, with intermittent or continuous bladder irrigation, was maintained for at least 24 hours postoperatively. Postoperative hospital stay included the time from surgery to discharge or patient death.

Major nonfatal complications were noted. The overall mortality included any death that occurred while the patient was hospitalized, even if it was not directly related to the prostatectomy.

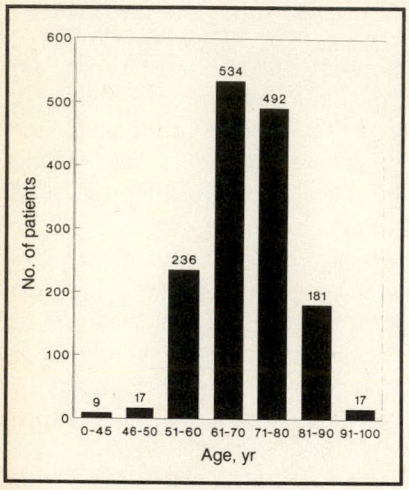

FIG. 1. Age distribution of patients who underwent transurethral resection of prostate (TURP) between 1985 and 1987.

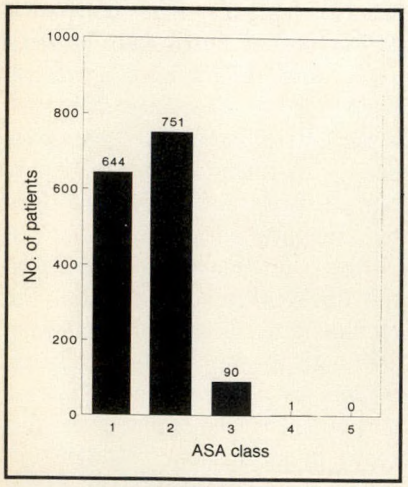

FIG. 2. American Society of Anaesthesiologists (ASA) classification of physical condition. 1 = no systemic disease, 2 = mild systemic disease, 3 = moderate systemic disease, 4 = severe systemic disease, 5 = moribund.

Findings

Patients

The average age was 63 years (Fig. 1). Physical condition was based on the American Society of Anaesthesiologists (ASA) physical status classification[4] from 1 (no systemic disease) to 5 (moribund patients with little chance for survival). The patients were fairly evenly divided between class 1 and class 2 (644 patients [43.3%] and 751 [50.5%]). Only 91 patients (6.2%) were class 3 or 4 (Fig. 2).

Laboratory Findings

The serum creatinine level was determined before TURP. Table I shows the distribution of patients with normal and elevated serum creatinine levels according to whether 1.5% glycine or distilled water was used as an irrigating fluid. The group with elevated serum creatinine levels and using distilled water had a death rate of 3.8%.

Operative Findings

The operative technique and results are noted in Table II. The patients underwent TURP with intermittent irrigating resectoscopes using 1.5% glycine in 36% of cases and distilled water in 64% of the cases. Average time for the operation (patient in theatre until transfer to recovery room) was 60 minutes. Anesthesia was fairly evenly distributed between general and spinal. The average decrease in the hemoglobin level was 14.2 g/L, and 9% of the patients required at least one unit of packed cells within 10 days of operation. The average postoperative hospital stay was 5.75 days. The average stay decreased during the 3-year period of the study by 1 day.

Pathological Findings

The weight of prostatic tissue resected ranged from 0.6 g to 160 g (Fig. 3). The average weight of resected prostate was 24.3 g. Pathological examination of the

Table I. Serum Creatinine Levels Before Transurethral Resection of the Prostate (TURP), According to Type of Irrigant Used

	Water		Glycine	
Creatinine, μmol/L	Patients, no. (%)	Deaths, no. (%)	Patients, no. (%)	Deaths, no. (%)
≤ 130	830 (88.6)	5 (0.6)	445 (84.4)	3 (0.7)
> 130	106 (11.4)	4 (3.8)	82 (15.6)	0
Total*	936 (100)	9 (0.46)	527 (100)	3 (0.56)

*In 23 patients the serum creatinine level was not measured before operation.

specimens revealed that 85% were benign and 15% were malignant.

Complications

Major nonfatal complications occurred in 7.8% of the patients (Table III). Cardiovascular and thromboembolic events complicated the course of 1.1% of our patients. Documented hyponatremia and transurethral resection syndrome were found in only 0.5%. Patients who were readmitted for postoperative bleeding or repeat resection were only accounted for if they were readmitted to the Royal Alexandra Hospital.

Minor complications were inconsistently documented in the hospital records and therefore are not included in this review.

Mortality

Twelve patients in this series died — a death rate of 0.8%. The average age of these patients was 79 years. Thirty-nine percent of those who died were more than 70 years old. The death rate for patients over 70 years of age was 1.7% compared with 0.2% for those less than 70 years of age. The median ASA classification was 3.

Preoperatively 57% of patients had mild to moderate systemic disease (ASA class 2 or 3). Of those who died, 67% were in ASA physical class 3 preoperatively. Four patients (0.3% of the total) died after elective admission for TURP. The other eight who died were long-term admissions and were referred to the urology service. There were no intraoperative deaths. Eight patients (0.5%) died within 30 days of their prostatectomy. Of these, two had intraoperative myocardial infarction, two had pulmonary embolism and the remaining four died of respiratory or cardiac arrest more than 10 days postoperatively. The four patients who died without obvious precipitating factors all had severe underlying systemic disease. None of the patients who died had urosepsis or electrolyte abnormalities. However, in patients with renal dysfunction (an elevated serum creatinine level) in whom distilled water was used as the irrigant, the death rate was 3.8%.

Nine percent of the patients received blood transfusions for a low hemoglobin level as well as operative blood loss.

Residents were the primary resectionists for the surgery of 7 (58%) of the 12 patients who died.

Table II. Operative Information

Irrigation fluid, % of patients	
1.5% glycine	36
Distilled water	64
Anesthesia, % of patients	
Spinal	55
General	45
Average operation time, min	60
Average decrease in hemoglobin, g/L	14.2
Patients requiring blood transfusions, %	9

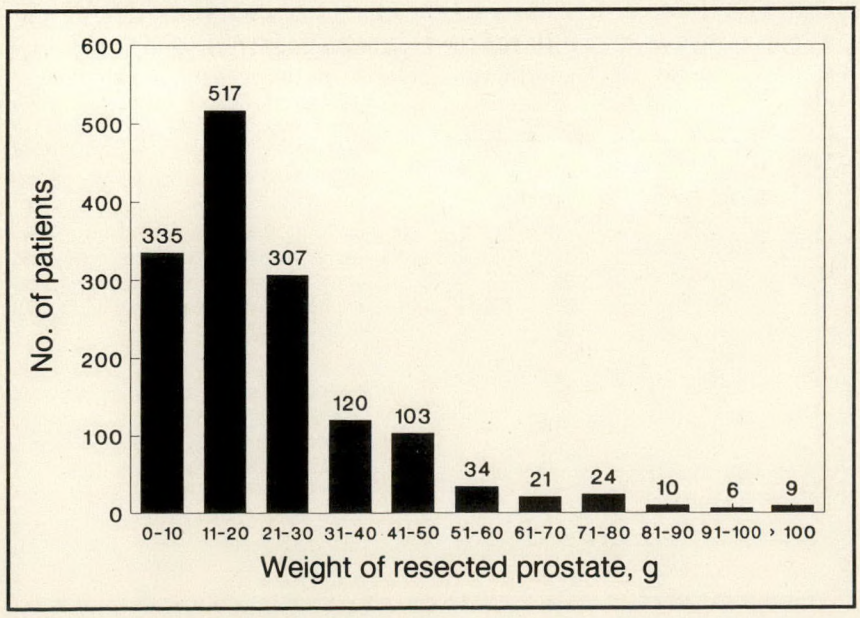

FIG. 3. Weight of prostate resected.

Discussion

The most remarkable finding in this series with respect to the death rate was the fact that 3.8% of patients having an elevated serum creatinine level and distilled water used as the irrigating solution during surgery died. Distilled water as an irrigating fluid has obvious benefits of low cost and optical superiority over other solutions. However, because of the risks of hemolysis and subsequent renal failure, many urologists believe that distilled water is contraindicated in TURP despite its advantages.[5,6] As shown in this and other series, in patients without renal impairment, the choice of irrigating solution does

Table III. Nonfatal Complications, %

Complication	No. (%) of patients
Thromboembolic events	5 (0.3)
Myocardial infarction	12 (0.8)
Transurethral resection syndrome/hyponatremia	7 (0.5)
Repeat resection — within 1 yr	25 (1.7)
Bleeding* — < 60 d	67 (4.5)
Total	116 (7.8)

*Requiring readmission

not appear to affect outcome; however, care must be taken when using distilled water in those with reduced renal function. The apparent safety of distilled water as an irrigating solution is probably accounted for by improved surgical techniques limiting fluid absorption and by the surgeon's experience. However, the use of distilled water cannot be universally recommended, especially when residents in the early stages of their careers are beginning to learn TURP, because there may be a significant risk to the patient.

To put this study into perspective, we compared the findings with those of a previous study by Melchior and associates in 1974.[7] They reported on the morbidity in a series of 2223 consecutive patients who underwent TURP.[7] In their study, as in this one, both staff and resident urologists were included. The comparisons are made in Table IV. The two series have a similar ratio of staff to resident as the primary resectionist. The patients in our series were slightly younger, the group having a mean age of 63 years. In both series the mean weight of specimen resected was similar; however, the surgery was performed, on average, 24 minutes faster, and approximately 15% fewer patients received blood transfusions at our institution.

The patients in our series were in hospital approximately 1 day less. This might reflect either an earlier removal of the catheter or a change in patient care over the 17 years between the two studies. Presently, it is the practice at our hospital to remove the catheter the 1st day postoperatively if bleeding is minimal. Furthermore, with hospitals currently attempting to control spending and the implementation of continuing quality improvement measures, the hospital stay postoperatively for a patient undergoing TURP is now approximately 3 days in our institution.

The overall death rate in Melchior's review was 1.3%. In this series, the death rate within 30 days of operation was lower at 0.5%. Most of the deaths in both series occurred in elderly patients with moderately severe multisystem disease, and the TURP probably contributed little to their death.

Conclusions

From a review of TURP in a teaching hospital, the short-term results appear favourable in comparison with other large reviews on this very common surgical procedure. In this series, having senior residents perform the procedure does not have any adverse effect on patient morbidity or mortality. With proper supervision and instruction from staff urologists, residents are able to gain experience and technical competency and maintain low complication rates.

Table IV. Comparison of Current Series With That of Melchior et al[7]

Variable	Current series (n = 1486)	Melchior et al[7] (n = 2223)
Primary resectionist, %		
Staff	25	39
Resident	75	61
Average age, yr	63	61
Average operation time, min	60	84
Blood given for operation, % of patients	9	24
Average specimen weight, g	24	21
Mortality, %	0.8	1.9
Average postoperative hospital stay, d	5.7	6.5

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Outpatient Laser Cone Biopsy Under Local Anesthesia

Gavin C.E. Stuart, MD; Jill G. Nation, MD

The authors report on 60 patients who had abnormal findings on cervical cytologic examination, necessitating conization of the cervix. The procedure was done in an ambulatory setting, with a carbon-dioxide laser unit and local anesthesia. The average operative time was 16.9 minutes. Fifty-one (85%) patients experienced no complications, and there were no cases of excessive bleeding. In all patients, the specimen was satisfactory for histologic review. Only 5% (three) of patients would have preferred to have the procedure performed under general anesthesia.

Laser cone biopsy of the cervix can be performed in an outpatient setting, with local anesthesia. Morbidity is minimal and there is potential for economic saving when compared with conventional methods for biopsy of the cervix.

Les auteurs ont étudié 60 patientes qui avaient eu un examen cytologique anormal du col utérin nécessitant une conisation du col. L'intervention fut pratiquée en milieu ambulatoire, sous anesthésie locale, à l'aide d'un laser au bioxyde de carbone. Le temps opératoire moyen fut de 16,9 minutes. Cinquante-et-une patientes (85%) n'eurent aucune complication et il n'y eut aucun cas de saignement excessif. On obtint chez toutes les patientes un échantillon satisfaisant pour examen histologique. Seulement trois patientes (5%) auraient préféré subir l'intervention sous anesthésie générale.

La biopsie conoïde du col au laser peut être effectuée en milieu ambulatoire, sous anesthésie locale. La morbidité est minime et il y a possibilité d'une économie par rapport aux méthodes classiques de biopsie du col utérin.

Since 1976, laser vaporization of cervical intraepithelial neoplastic lesions has been reported to be of value in the management of this condition.[1] The procedure has been performed in both inpatient and outpatient settings, with either local or general anesthesia. However, excisional cone biopsy for diagnostic purposes has generally been performed in an operating room under local or general anesthesia with either the scalpel or laser. The purpose of this paper is to report the use of the laser in performing excisional cone biopsies of the cervix under local anesthesia in an outpatient setting in 60 patients. The ability to carry out this procedure satisfactorily without the need for hospital admission or general anesthesia greatly reduces the morbidity usually associated with cone biopsy and results in considerable cost saving.

Patients and Methods

Sixty consecutive women, who were referred to the Colposcopy Clinic of the Tom Baker Cancer Centre, in Calgary, and who required a diagnostic cone biopsy of the cervix were the subjects of this report. The average age was 29.8 years (range from 22 to 43 years). Twenty-four women had delivered at least one infant previously and the remainder were nulliparous.

All women had a history of cervical cellular abnormalities. Repeat cytologic investigation was done before colposcopic assessment, and directed biopsy was done in all the women. The indications for diagnostic cone biopsy are listed in Table I. Endocervical curettage was not done routinely in all new patients but did constitute part of the regular follow-up in those who had previously received therapy for cervical intraepithelial neoplasia (CIN). An unsatisfactory examination was one in which the entire squamocolumnar junction could not be seen or the area of white epithelium extended into the cervical canal. The colposcopic diagnosis prior to the cone biopsy is recorded in Table II. The new patient with benign atypia underwent cone biopsy because the initial cytologic findings were cells inconsistent with CIN grade III. After adequate examination, women in our clinic who are found to have CIN grade I only are not actively treated but are observed in regular follow-up. The five women with histologic evidence of CIN grade I underwent a cervical conization because of a discrepancy between cytologic and histologic findings. Of the 60 women, 40 were noted to have concomitant cytologic or histologic changes consistent with the presence of human papilloma virus.

Informed consent for laser cone biopsy was obtained from all the

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women. They attended the Ambulatory Surgery Unit at the clinic 1 hour before their scheduled procedure. Lorazepam, 1 mg, was offered as an anxiolytic medication. All procedures were conducted in the treatment area, with oxygen and resuscitative equipment immediately available. Pulse and blood pressure were monitored automatically throughout the procedure on a digital display with pulse oximetry. All procedures were performed by the same gynecologist. An anesthesiologist was not present. A nurse attended throughout to observe the patient and to provide distraction through conversation.

After repeat colposcopic examination, the area to be excised was outlined with a Xanar-20 carbon-dioxide laser (Xanar, Div. of Coherent Medical, Palo Alto, Calif.) at a power density of 2420 watts/cm^2. This setting was chosen for a 1 mm spot size with maximal energy output. Following this outline, the patient was offered a paracervical block (1% xylocaine without epinephrine), which was administered with 5 mL of solution injected at the base of each uterosacral ligament and then an additional 10 mL injected circumferentially on the cervix just distal to the line of excision. After establishment of a paracervical block, the line of excision was extended to a depth of 10 to 15 mm to include the projected squamocolumnar junction. A small, 20-cm skin hook was used to deflect the specimen from the path of the laser beam. Once the specimen was mobilized in a cylindrical fashion, a long Allis clamp (Codman Surgical Inc., Randolph, Mass.) was applied to the cut edges of the specimen, carefully avoiding trauma to the surface epithelium. An Allis clamp can be applied without crushing viable tissue, hence preserving the histologic definition of the specimen. By placing this clamp under traction and occasionally torsion, a conical incision can be made across the base of the specimen with the laser beam. After removal of the specimen, the base of the area was treated with the laser at a power density of 960 watts/cm^2 to achieve complete hemostasis. In five women, excisional laser cone biopsy was performed in combination with ablation of visible disease beyond the excised margins.

After the procedure, the women were asked to remain in the unit for at least 1 hour for observation of any delayed vasovagal response or other complication. All were contacted by telephone 1 week later as part of the follow-up. The procedure was evaluated subjectively by asking the women if they would choose to have the procedure done again under local anesthesia as opposed to general anesthesia if it was necessary. They were reviewed in the clinic 1 month after the biopsy to ensure adequate healing of the cervix. Repeat cytologic and colposcopic assessment was conducted after a 6-month interval.

Histologic review was completed on all phosphate-buffered, formalin-fixed specimens by staining with hematoxylin and eosin.

Results

Nine patients (15%) declined the offer of anxiolytic medication before the procedure and received no premedication. Eighteen patients (30%) did not wish to receive any local anesthetic or paracervical block. Three of the 60 patients had the procedure completed by choice without any premedication or local anesthesia. They tolerated the procedure well.

The procedure was completed in all patients. Exact blood loss was not recorded but was minimal with the use of gauze swabs and the application of ferric subsulfate (Monsel's) solution in all but two women. These two required the insertion of a Grafco vaginal tampon (Graham-Field Inc., Hauppauge, NY) as a vaginal pack, and this was removed the morning after the procedure. The time spent by the patient in the procedure room averaged 16.9 minutes (range from 10 to 40 minutes). The patient who remained for 315 minutes did so because of transportation difficulties rather than for medical reasons.

Fifty-one (85%) of the 60 women experienced no significant complications (Table III). Five women, all of whom had a paracervical block administered, experienced cramping pain and required oral analgesics

Table I. Indications for Diagnostic Cone Biopsy

Indication	No. of patients (%)
Positive endocervical curettage	34 (57)
Unsatisfactory examination	22 (37)
Microinvasive cancer	2 (3)
No lesion seen	1 (2)
Adenocarcinoma in situ	1 (2)
Total	60 (100)

Table II. Pathological Findings in 60 Patients Before Laser Cone Biopsy

Findings	Referral cytology	Directed biopsy	Colposcopy
Benign atypia	7	1	1
CIN I	11	5	6
CIN II	17	24	24
CIN III	14	27	29
Negative	11	3	0
Total	60	60	60

CIN = cervical intraepithelial neoplasia

before being discharged. Three women experienced a vasovagal response as evidenced by transient bradycardia and hypotension. One woman was admitted to hospital 4 days after the procedure with a clinical diagnosis of pelvic inflammatory disease and required intravenous antibiotic therapy. None of the women experienced bleeding that required a return visit to the clinic. Retrospectively, when questioned, three women (5%) stated that if they had to undergo the procedure again they would elect to have the procedure performed under general rather than local anesthesia.

The cervical cone biopsy was adequate for histologic review in all patients. The average dimensions of the specimen were 20 × 16 × 10 mm. The final pathological diagnosis is reported in Table IV. No cases of invasive cancer were detected in this group.

Comments

In this paper we have addressed the need to perform a cone biopsy of the cervix under general anesthesia in the hospital operating suite, a situation which results in greater patient morbidity and increased cost, because of the need for an anesthesiologist and an operating-room facility, compared with the use of local anesthesia in a clinic setting.

Table III. Complications of Laser Cone Biopsy

Complication	No. of patients (%)
None	51 (85)
Pain	5 (8)
Vasovagal response	3 (5)
Pelvic inflammatory disease	1 (2)
Total	60 (100)

Table IV. Final Diagnosis of Laser Cone Biopsy

Final diagnosis	No. of patients (%)
No evidence of dysplasia	7 (12)
Benign atypia	2 (3)
CIN I	16 (27)
CIN II	4 (6)
CIN III	30 (50)
Adenocarcinoma in situ	1 (2)
Total	60 (100)

It has been clearly documented[2-4] that a cone biopsy of the cervix can be performed with the carbon-dioxide laser with less morbidity than with a conventional scalpel. Complications that occur with reduced frequency when the laser is used include bleeding, both immediate and delayed, cervical stenosis and premature delivery. The ability to perform this procedure in an outpatient setting has been reported previously,[5] but in the majority of patients general anesthesia was used. In 1987, Indman[6] reported on 101 women who underwent laser conization of the cervix in an office setting with anaproxen sodium as premedication and a paracervical block using 0.5% bupivacaine hydrochloride. Indman recommended the use of vasopressin intraoperatively.

Our report further documents the efficiency of this procedure in an outpatient setting, with local anesthesia and a modified technique. Three of our patients had a vasovagal response in the form of bradycardia and hypotension. In the report by Indman[6] transient hypertension associated with the use of bupivacaine and vasopressin was described in two patients. Although the risk of cardiovascular complications appears to be low, it is recommended that, if the procedure is to be done in an ambulatory setting without the presence of an anesthesiologist, the pulse rate should be monitored routinely and supplemental oxygen and Trendelenberg positioning should be available. In this series, without the use of vasopressin or epinephrine, bleeding was not a problem. Any loss of blood not controlled by the use of the laser beam at a diffused setting can usually be controlled by the use of topical ferric subsulfate solution.

Although the technique of diagnostic conization of the cervix can be accomplished in an ambulatory setting with local anesthesia alone, the technique must be acceptable to the patient. Recognizing the limitations of retrospective questioning, we found that only 5% of the women would have elected to have the procedure repeated under general anesthesia. We cannot comment on the role of premedication with lorazepam because there is no control group for comparison. It would appear, however, that the role of the nurse or other medical attendant, as a distractor for the patient, is essential and may be of more value as an anxiolytic and analgesic than the medication used.

Laser conization appears to be an effective, well-tolerated technique that can be used in the ambulatory setting with only local anesthesia. The economic advantages are likely to be significant while delivering appropriate patient care with minimal morbidity.

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Pr VASOTEC®

(enalapril maleate, Frosst Std.)

Tablets 2.5, 5, 10, 20 mg

Pr VASOTEC® I.V.

(enalaprilat)

1.25 mg/mL

Angiotensin Converting Enzyme Inhibitor

INDICATIONS AND CLINICAL USE

VASOTEC® is indicated in the treatment of essential or renovascular hypertension; usually administered in association with other drugs, particularly thiazide diuretics. Consider the risk of angioedema (see WARNINGS). Normally used when a diuretic or beta-blocker was ineffective or associated with unacceptable adverse effects. Can also be tried as initial agent where a diuretic and/or beta-blocker is contraindicated or could cause serious adverse effects.

Oral enalapril is also indicated in the treatment of congestive heart failure, as adjunctive therapy in patients not responding adequately to digitalis and diuretics.

Use of ACE inhibitors during the second and third trimesters of pregnancy can cause injury or death of a developing fetus. When pregnancy is detected, discontinue VASOTEC® as soon as possible (see WARNINGS; Use in Pregnancy).

VASOTEC® I.V. (enalaprilat) is an active metabolite of enalapril; the onset of action after administration occurs within 15 minutes, with the maximum effect within 1 to 4 hours.

VASOTEC® I.V. is indicated for the treatment of hypertension when oral therapy is not practical. VASOTEC® I.V. has been studied with only one other antihypertensive agent, furosemide, which showed additive effects on blood pressure. Due to insufficient experience in the treatment of accelerated or malignant hypertension, VASOTEC® I.V. is not recommended in such situations (see DOSAGE and ADMINISTRATION).

CONTRAINDICATIONS

Hypersensitivity to any component; history of angioneurotic edema related to ACE inhibitor therapy.

WARNINGS

Angioedema, with laryngeal edema and/or shock, have been reported and may be fatal. In such cases, discontinue drug promptly and observe patient until swelling subsides. Swelling confined to the face, lips, and mouth usually resolves without treatment, although antihistamines may be useful in relieving symptoms. However, where there is involvement of the tongue, glottis and larynx, likely to cause airway obstruction, prompt administration of subcutaneous adrenaline (0.5 mL 1:1000) may be indicated. Patients with a history of angioedema, unrelated to ACE inhibitor use, may be at increased risk (see CONTRAINDICATIONS).

Symptomatic hypotension has occurred, usually during initial therapy or when the dose was increased, and is more likely in patients who are volume-depleted. In patients with severe congestive heart failure, excessive hypotension may be associated with oliguria and/or progressive azotemia. For patients in whom the excessive hypotension could result in severe or fatal complications, i.e. those with severe congestive heart failure, ischemic heart or cerebrovascular disease – start therapy under close medical supervision, usually in a hospital. Such patients should be followed closely for the potential fall in blood pressure during first two weeks of therapy or when enalapril or a diuretic is increased. If hypotension occurs, place patient in supine position and if needed, administer IV infusion of normal saline. A transient hypotensive response is not a contraindication to further doses of enalapril or enalaprilat.

Neutropenia/agranulocytosis and bone marrow depression have been caused by ACE inhibitors. Current experience with enalapril shows incidence to be rare. Consider periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease.

Use of ACE inhibitors in pregnancy can cause fetal and neonatal morbidity and mortality. When pregnancy is detected, discontinue VASOTEC® as soon as possible. Rarely, no alternatives to an ACE inhibitor will be found and mothers should be apprised to the potential hazards to the fetus. Ultrasound should be performed to assess fetal development, well-being and volume of amniotic fluid. If oligohydramnios is observed, discontinue VASOTEC® unless lifesaving for the mother. A non-stress test and/or a biophysical profiling may be appropriate however, if concerns persist, a contraction stress testing should be considered. Oligohydramnios may only appear after fetus has sustained irreversible injury.

Closely observe infants exposed *in utero* to ACE inhibitors for hypotension, oliguria and hyperkalemia, and initiate appropriate corrective medical procedures.

Human Data: Exposure to ACE inhibitors during second and third trimesters has been associated with hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure and death of the fetus. Oligohydramnios, associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development also has been reported. Prematurity and patent ductus arteriosus also reported but unknown if due to ACE inhibitor use. It is not known whether exposure limited to the first trimester can adversely affect fetal outcome.

PRECAUTIONS

Impaired renal function: Renal function should be assessed before initiating therapy with enalapril or enalaprilat. Patients with renal insufficiency may require reduced or less frequent doses, and their renal function must be monitored appropriately (see DOSAGE). Renal failure, which has been reported mainly in patients with severe congestive heart failure or underlying renal disease including renal artery stenosis, is usually reversible when treated promptly.

Some hypertensive patients with no apparent renal disease have developed increases in BUN and creatinine while on concurrent diuretic/enalapril therapy. Dosage reduction or discontinuation of one or both drugs may be required.

Hyperkalemia: In clinical trials, hyperkalemia (>5.7 mmol/L) was observed in approximately 1% of hypertensive patients, and caused discontinuation of therapy in 0.28% of such patients. Risk factors for hyperkalemia development may include renal insufficiency, diabetes mellitus, and concomitant use of agents to treat hypokalemia (see ADVERSE REACTIONS).

Valvular Stenosis: Theoretically, patients with aortic stenosis, who do not develop as much afterload reduction, might be at risk of decreased coronary perfusion when treated with vasodilators.

Surgery/Anaesthesia: During major surgery or anaesthesia with hypotensive agents, enalapril blocks angiotensin II formation secondary to compensatory renin release. Hypotension that develops due to this mechanism can be corrected by volume expansion.

Impaired liver function: Hepatitis, jaundice (hepatocellular and/or cholestatic),elevation of liver enzymes and/or serum bilirubin, which have occurred in patients with or without pre-existing liver abnormalities, were usually reversed on discontinuation of enalapril or enalaprilat. For any unexplained symptoms, particularly within the first months of treatment, a full set of liver function tests and other necessary investigations are recommended. Consider discontinuation of enalapril or enalaprilat when appropriate. Use enalapril or enalaprilat with particular caution in patients with pre-existing liver abnormalities. Obtain baseline liver function tests before initiating drug and monitor response and metabolic effects closely.

Cough: A dry, persistent cough has been reported, which usually disappears after withdrawal or lowering the dose of enalapril or enalaprilat.

Nursing mothers: Enalapril and enalaprilat are secreted in human milk in trace amounts therefore, nursing should be interrupted.

Pediatric use: This use is not recommended because enalapril and enalaprilat have not been studied in children.

Hemodialysis patients: Anaphylactoid reactions have been reported with high-flux membranes (eg. polyacrylonitrile [PAN]) and treated concomitantly with an ACE inhibitor. If symptoms such as nausea, abdominal cramps, burning, angioedema, shortness of breath and severe hypotension occur, stop dialysis immediately. The symptoms are not relieved by antihistamines and the use of a different type of dialysis membrane or class of antihypertensive agent should be considered.

Drug Interactions

Hypotension - Patients on Diuretic Therapy: Particularly when diuretics recently initiated, patients occasionally experience hypotension after initiating therapy with enalapril or enalaprilat. To minimize the hypotensive effects, discontinue the diuretic or increase the salt intake prior to starting the drug. If the diuretic cannot be discontinued, patients should be placed under close medical supervision for at least one hour after the initial dose of enalaprilat (see WARNINGS).

Agents Increasing Serum Potassium: Since enalapril and enalaprilat decrease aldosterone production, elevation of serum potassium may occur. Diuretics such as spironolactone, triamterene or amiloride, or potassium supplements should be given cautiously for documented hypokalemia only and should be monitored frequently. Potassium containing salt substitutes should be used with caution.

Agents Causing Renin Release: Diuretics, for example, augment the antihypertensive effect of enalapril and enalaprilat.

Agents Affecting Sympathetic Activity: Ganglionic blocking agents or adrenergic neuron blocking agents, for example, may be used with caution. Beta-adrenergic blockers add some further antihypertensive effect to enalapril.

Lithium Salts: Lithium clearance may be reduced; therefore, monitor serum lithium levels carefully if they are administered.

ADVERSE REACTIONS

VASOTEC®: In controlled clinical trials involving 2314 hypertensive patients and 363 heart failure patients, the most severe adverse reactions were: angioedema (0.2%), hypotension (2.3%) and renal failure (5 cases). In hypertensive patients, hypotension occurred in 0.9% and syncope in 0.5%, with a discontinuation rate of 0.1%. In heart failure patients, hypotension occurred in 4.4% and syncope in 0.8%, with a discontinuation rate of 2.5%. The most frequent clinical adverse reactions in controlled clinical trials were: headache (4.8%), dizziness (4.6%) and fatigue (2.8%). Discontinuation of therapy was required in 6.0% of the 2677 patients.

	Hypertension % (2314 Patients)	Heart Failure % (363 Patients)
CARDIOVASCULAR		
Hypotension	0.9	4.4
Chest Pain	0.9	1.7
Palpitations	0.6	0.3
Myocardial Infarction, Acute	0.2	0.6
Myocardial Infarction, Recurrent	—	0.3
GASTROINTESTINAL		
Nausea	1.4	1.1
Vomiting	0.8	1.7
Dysphagia	0.1	—
Diarrhea	1.4	3.0
Abdominal pain	0.7	1.4
RENAL		
Renal failure	0.1	0.6
Oliguria	1 case	—
Proteinuria†	0.1	—
DERMATOLOGIC		
Rash	1.4	1.9
Pruritus	0.4	1.4
NERVOUS SYSTEM		
Headache	5.2	2.2
Dizziness	4.3	6.6
Insomnia	0.5	0.3
Nervousness	0.6	—
Somnolence	0.6	—
Paresthesia	0.6	—
ALLERGIC		
Cough	1.3	1.4
Angioedema	0.2	—
HEMATOLOGIC		
Anemia	0.1	—
Leukopenia	1 case	—
MISCELLANEOUS		
Muscle cramps	0.6	0.3
Dyspnea	0.6	1.1
Hyperhidrosis	0.7	—
Impotence	0.4	0.3
Fatigue	3.0	1.4
Taste disturbance	0.4	0.3

† Defined as >1 g/24h or >0.5 g/12h on two consecutive measurements, at least one month apart.

ABNORMAL LABORATORY FINDINGS

Hyperkalemia: (see PRECAUTIONS).

Creatinine, Blood Urea Nitrogen: Increases were reported in about 20% of patients with renovascular hypertension and about 0.2% of patients with essential hypertension on enalapril alone. Increases, which usually were reversible upon discontinuation of enalapril or concomitant therapy, were reported in 9.7% of heart failure patients who were receiving diuretics and/or digitalis.

Hemoglobin and Hematocrit: Decreases (mean approximately 0.34 g% and 1.0 vol%, respectively) occurred frequently, but were rarely of clinical importance. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Hepatic: Elevations of liver enzymes and/or serum bilirubin have occurred (see PRECAUTIONS).

ADVERSE REACTIONS REPORTED IN UNCONTROLLED TRIALS AND/OR MARKETING EXPERIENCE

With an incidence of 0.5 to 1%: Insomnia, impotence, renal dysfunction, renal failure and oliguria.

With an incidence < 0.5%:

Cardiovascular: Myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see WARNINGS); cardiac arrest; pulmonary embolism; rhythm disturbances; angina pectoris. **Gastrointestinal:** Anorexia; ileus; pancreatitis; dyspepsia; constipation. **Hemopoeitic:** Neutropenia; thrombocytopenia; bone marrow depression. **Hepatic:** Liver function abnormalities; hepatitis; jaundice (hepatocellular and/or cholestatic). **Nervous System/Psychiatric:** Vertigo; depression; confusion; ataxia. **Respiratory:** Bronchospasm/asthma; rhinorrhea. **Other:** Erythema multiforme; exfoliative dermatitis; Stevens-Johnson syndrome; toxic epidermal necrosis; urticaria; photosensitivity; alopecia; flushing; tinnitus; hearing impairment; glossitis; blurred vision. A symptom complex has been reported which may include fever, serositis, vasculitis, myalgia, arthralgia/arthritis, a positive ANA, elevated erythrocyte sedimentation rate, eosinophilia and leukocytosis. Rash, photosensitivity or other dermatologic manifestations may occur. These symptoms have disappeared after discontinuation of therapy.

LABORATORY TEST FINDINGS: Hyponatremia

VASOTEC® I.V.: Since enalapril is converted to enalaprilat, those adverse reactions associated with VASOTEC® tablets might also be expected to occur with VASOTEC® I.V. The incidence of symptomatic hypotension is 3.4% with VASOTEC® I.V. Other adverse experiences occurring in greater than 1% of patients were headache (2.9%) and nausea (1.1%). Adverse reactions occurring in 0.5 to 1.0% of patients in controlled clinical trials include myocardial infarct, fatigue, dizziness, fever, rash and constipation.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Limited human data are available. The most likely manifestation of overdosage would be hypotension, which can be treated by I.V. infusion of normal saline solution. Enalaprilat may be removed from the general circulation by hemodialysis.

DOSAGE AND ADMINISTRATION

VASOTEC®
FOR ORAL ADMINISTRATION ONLY

Dosage must be individualized. The absorption of enalapril maleate is not affected by food.

HYPERTENSION

Initiation of enalapril requires consideration of extent of blood pressure elevation, salt restriction and recently used antihypertensive agents, the dosage of which may need to be adjusted.

The recommended initial dose of enalapril maleate in patients not on diuretics is 5 mg once a day. Adjust dosage according to blood pressure response; the usual range is 10 to 40 mg daily, in a single dose or divided in two doses. Some patients on once-daily dosage may have diminished antihypertensive effect toward the end of dosing interval and require an increase in dosage, or twice daily administration. If blood pressure is not controlled, a diuretic may be added. Raising the daily dose above 40 mg is not recommended because adverse reactions may be increased.

Occasionally symptomatic hypotension may occur following the initial dose, more likely in patients currently taking a diuretic. Therefore, if possible, discontinue the diuretic two to three days before initiating enalapril therapy (see WARNINGS). If the diuretic cannot be discontinued, use an initial dose of 2.5 mg.

In the absence of sufficient experience in the treatment of accelerated or malignant hypertension, enalapril is not recommended in such situations.

Dosage in the Elderly (over 65 years): Start at 2.5 mg daily. Some elderly patients may be more responsive than younger patients.

Dosage Adjustment in Renal Impairment: (see PRECAUTIONS - Hemodialysis patients)

Guidelines for reducing doses in hypertensive patients:

Renal Status	Creatinine Clearance mL/min(mL/s)	Initial Dose mg/day
Normal renal function	>80 mL/min (>1.33 mL/s)	5 mg
Mild impairment	≤80 >30 mL/min (≤1.33 >0.50 mL/s)	5 mg
Moderate to severe impairment	≤30 mL/min (≤0.50 mL/s)	2.5 mg
Dialysis patients	—	2.5 mg on dialysis days*

* Enalaprilat is dialysable. Dosage on nondialysis days should be adjusted depending on the blood pressure response.

CONGESTIVE HEART FAILURE

Use in conjunction with a diuretic and digitalis. Initiate therapy under close medical supervision, usually in a hospital. Monitor blood pressure and renal function before and during treatment with enalapril, because severe hypotension, and more rarely, consequent renal failure have been reported (see WARNINGS and PRECAUTIONS).

When initiating enalapril consider the recent diuretic therapy and possibility of severe salt/volume depletion. Before beginning enalapril reduce diuretic therapy if possible.

The recommended initial daily dose is 2.5 mg. While managing symptomatic hypotension, increase dose gradually, depending on individual response, to the usual maintenance dose of 10-20 mg daily, given in a single dose or divided in two doses. This dose titration may be performed over a two- to four-week period, or more rapidly if indicated by residual signs and symptoms of heart failure. The maximum daily dose is 40 mg.

VASOTEC® I.V. FOR INTRAVENOUS ADMINISTRATION ONLY

VASOTEC® I.V. vials should be inspected visually and should not be used if particulate matter or discoloration is observed.

VASOTEC® I.V. may be administered intravenously as supplied, or mixed with up to 50 mL of one of the following diluents:

5% Dextrose Injection
0.9% Sodium Chloride Injection
0.9% Sodium Chloride Injection in 5% Dextrose
5% Dextrose in Lactated Ringer's Injection

Diluted solutions should be used within 24 hours.

The dose is 1.25 mg every 6 hours administered intravenously over at least 5 minutes. A clinical response is usually seen within 15 minutes. Peak effects after the first dose may not occur for up to four hours after dosing. The peak effects of the second and subsequent doses may exceed those of the first.

No dosage regimen for VASOTEC® I.V. has been clearly demonstrated to be more effective in treating hypertension than 1.25 mg every 6 hours. However, in controlled clinical studies in hypertension, doses as high as 5 mg every 6 hours were well tolerated for up to 36 hours. There has been inadequate experience with doses greater than 20 mg per day.

In studies of patients with hypertension, VASOTEC® I.V. has not been administered for periods longer than 48 hours. In other studies, patients have received VASOTEC® I.V. for as long as 7 days.

The dose for patients being converted to VASOTEC® I.V. from oral therapy for hypertension with enalapril maleate is 1.25 mg every 6 hours administered intravenously over at least 5 minutes. For conversion from intravenous to oral therapy, the recommended initial dose of VASOTEC® tablets is 5 mg once a day with subsequent dosage adjustments as necessary.

Patients on Diuretic Therapy

For patients on diuretic therapy, the recommended starting dose for hypertension is 0.625 mg administered intravenously over at least 5 minutes. A clinical response is usually seen within 15 minutes. Peak effects after the first dose may not occur for up to 4 hours after dosing, although most of the effect is usually apparent within the first hour. If after 1 hour there is an inadequate clinical response, the 0.625 mg dose may be repeated. Additional doses of 1.25 mg may be administered at 6 hour intervals.

For conversion from intravenous to oral therapy, the recommended initial dose of VASOTEC® tablets for patients who have responded to 0.625 mg of enalaprilat every 6 hours is 2.5 mg once a day with subsequent dosage adjustment as necessary.

Dosage Adjustment in Renal Impairment

The usual dose of 1.25 mg of enalaprilat every 6 hours is recommended for patients with a creatinine clearance >30 mL/min [>0.50 mL/s] (serum creatinine up to approximately 3 mg/dL [265.2 µmol/L]). For patients with creatinine clearance ≤30 mL/min [≤0.50 mL/s] (serum creatinine ≥3 mg/dL [≥265.2 µmol/L]), the initial dose is 0.625 mg (see WARNINGS).

If after 1 hour, there is an adequate clinical response, the 0.625 mg dose may be repeated. Additional doses of 1.25 mg may be administered at 6 hour intervals.

For dialysis patients, the initial dose should be 0.625 mg every 6 hours. (see PRECAUTIONS - Hemodialysis patients).

For conversion from intravenous to oral therapy, the recommended initial dose of VASOTEC® is 5 mg once a day for patients with creatinine clearance >30 mL/min [>0.50 mL/s] and 2.5 mg once daily for patients with creatinine clearance ≤30 mL/min [≤0.50 mL/s]. Dosage should then be adjusted according to blood pressure response.

AVAILABILITY OF DOSAGE FORMS

Barrel-shaped, biconvex tablets, engraved with code number on one side and VASOTEC on other.

VASOTEC® 2.5 mg - yellow, scored, engraved 14.

VASOTEC® 5 mg - white, scored, engraved 712.

VASOTEC® 10 mg - rust-red, engraved 713.

VASOTEC® 20 mg - peach, engraved 714.

All strengths available in bottles of 100 tablets.

VASOTEC® I.V. 1.25 mg per mL, is a clear, colourless solution and is supplied in vials containing 2 mL.

PRODUCT MONOGRAPH AVAILABLE ON REQUEST

(490iv-a,11,92)

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5527, 5959, 5974, 6657

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Disseminated Leiomyomatosis Peritonealis: Report of a Case in a Postmenopausal Woman

Gia-Khanh Nguyen, MD

Disseminated leiomyomatosis peritonealis (DLP) is a rare condition that to date has been reported only in premenopausal women. The author reports a case of DPL occurring in a postmenopausal woman who had undergone total hysterectomy 30 years before and had received no hormonal therapy subsequently. The lesions were multiple and consisted of smooth-muscle cells that proliferated from medium-sized blood vessels. The author concludes that the patient's lesions likely represent a histologic variant of DLP.

La léiomyomatose péritonéale disséminée (LPD) est une affection rare qui n'a été signalée, à ce jour, que chez la femme en préménopause. L'auteur décrit un cas de LPD survenant chez une femme en période postménopausique qui avait subi une hystérectomie totale 30 ans plus tôt et n'avait pas reçu d'hormonothérapie subséquente. Les lésions étaient multiples et étaient constituées de cellules de muscle lisse qui proliféraient à partir de vaisseaux sanguins de taille moyenne. L'auteur conclut que les lésions retrouvées chez cette patiente représentent vraisemblablement une variante histologique de la LPD.

Disseminated leiomyomatosis peritonealis (DLP) is an infrequently reported lesion. About 30 cases have been documented.[1-8] It has been found exclusively in women during their childbearing years. Most cases were detected incidentally at cesarean section.[1-7] DLP lesions in women taking contraceptive steroids and in women who were not on contraceptive pills have also been reported.[5] One patient with an ovarian granulosa-cell tumour was found to have DLP at laparotomy.[8] I report a case of DLP incidentally found at laparotomy in a postmenopausal woman.

Case Report

A 63-year-old white woman, para 5 gravida 5, was admitted to the University of Alberta Hospitals for an elective cholecystectomy for cholelithiasis. Her medical history included a total abdominal hysterectomy performed at 30 years of age for a benign endometrial lesion associated with persistent vaginal bleeding. No peritoneal lesions were noted during that operation. She had mild hypertension controlled by hydrochlorothiazide and a low-salt diet. She had not been on hormonal therapy since her hysterectomy.

At laparotomy, several subperitoneal round nodules of brownish tissue, ranging from 0.5 to 3 cm in diameter, were found attached to the parietal peritoneum and the antimesenteric borders of both small and large intestine. They covered about 7% of the peritoneal surface. A few small nodules were present under the pelvic serosa. Frozen-section examination of a large peritoneal nodule gave a histologic diagnosis of neurofibroma. The patient underwent an exploration of the common bile duct and a cholecystectomy. Her postoperative course was smooth, and she was discharged from the hospital 10 days later. She is currently well with no evidence of malignant disease, 10 years after her cholecystectomy.

Pathological Examination

The largest fragment of peritoneal nodules was ovoid and measured $3 \times 3 \times 2$ cm. It was firm, and its cut surface was glassy white with no hemorrhagic necrosis. Five tissue blocks, 1 mm^3 of fresh tissue, were fixed in 4% buffered glutaraldehyde and processed according to the routine techniques for transmission electron microscopic (EM) study. Several tissue blocks were fixed in formalin and processed for light microscopic examination. Tissue sections 5 μm thick were stained with hematoxylin and eosin, Masson's trichrome and reticulin stains.

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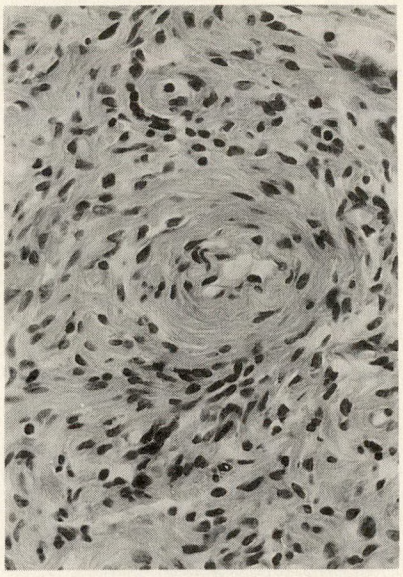

FIG. 1. Peritoneal lesion shows proliferation of smooth-muscle cells radiating from media of muscular blood vessel (hematoxylin–eosin, original magnification × 100).

Light Microscopic Findings

The submitted lesions were subperitoneal round nodules consisting of bundles of spindle-shaped cells with a considerable amount of collagen tissue and numerous muscular blood vessels of different size and variable mural thickness. Many of them appeared to be arteriolar in type. Radiating from the media of these vessels were spindle-shaped smooth-muscle cells with cigar-shaped nuclei (Fig. 1). They encircled the vessels and spread away in the mass lesion in an irregular pattern. Less than one normal mitotic figure was noted per 10 high-power fields. No nerve trunks were identified. Reticulin fibres and thin bundles of collagen fibres were seen scattered between smooth-muscle cells. The histologic findings suggested that the lesions represented angiomyomatosis.

Ultrastructural Findings

Ultrathin sections of the lesion confirmed a spindle-cell lesion that was rich in blood vessels. The spindle-cell component consisted of mature smooth-muscle cells with abundant intracytoplasmic bundles of microfilaments with focal densities (Fig. 2). Pinocytotic vesicles were noted along the cell membrane, which was often surrounded by incomplete basal lamina. These cells appeared to be derived from the media of adjacent small blood vessels. The supporting stroma contained delicate bundles of collagen fibres and occasional fibroblasts with irregular and indented nuclei and abundant intracytoplasmic

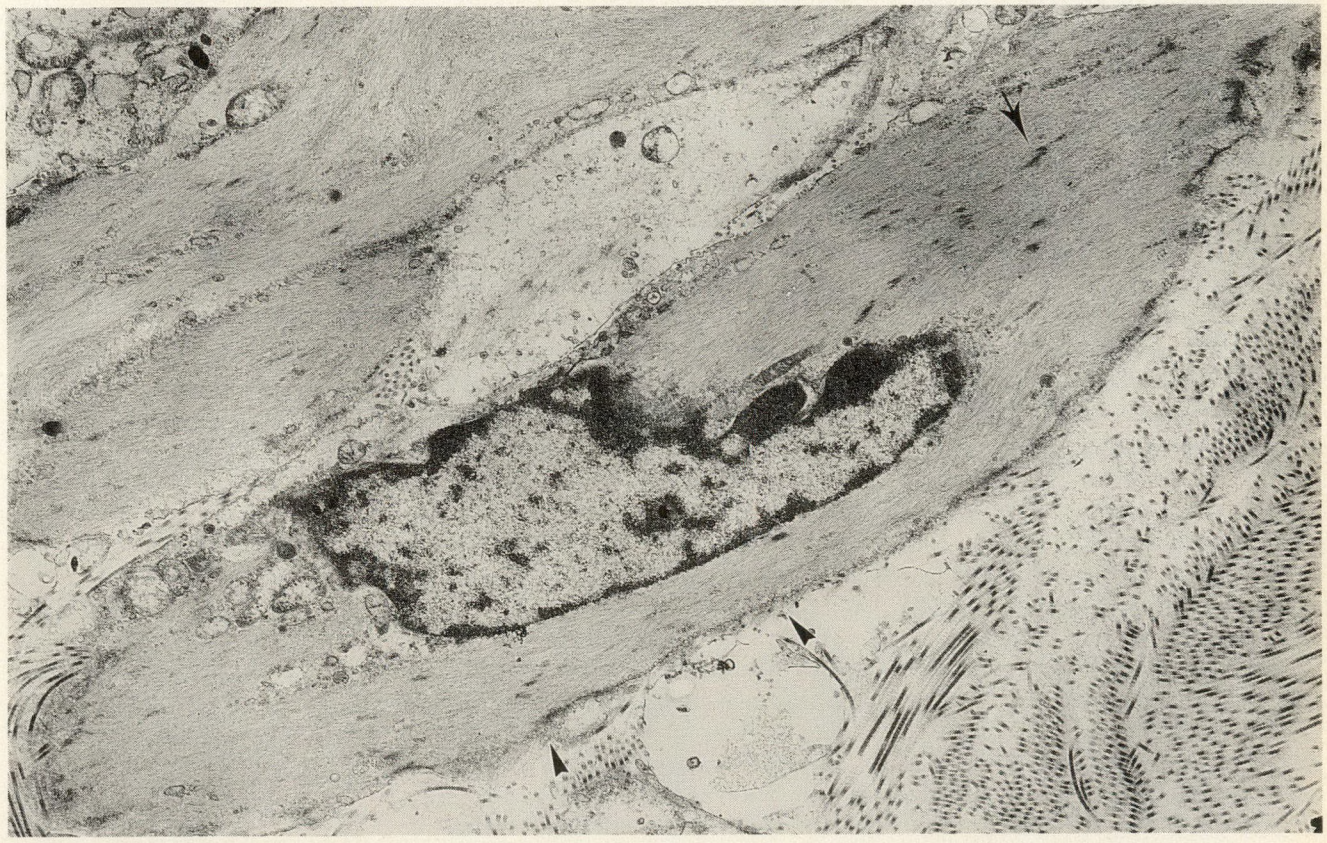

FIG. 2. Proliferated mature smooth-muscle cells show irregular and elongated nuclei, intracytoplasmic bundles of microfilaments with focal densities (arrow), membranous pinocytotic vesicles (arrow heads) and incomplete basal lamina. Collagen fibres can be seen in interstitial spaces (uranyl acetate and lead citrate stains, original magnification × 16 000).

rough endoplasmic reticula. No nerve axons or cells with digitating cytoplasmic processes were identified, nor were there cells with the features of a myofibroblast. The EM findings suggested a smooth-muscle lesion of vascular origin.

Discussion

The peritoneal lesions in this patient were highly unusual. They clearly arose from the media of the subperitoneal arterioles. Their histologic features were in keeping with those of an angiomyoma, which has not been described in the literature, although solitary angiomyoma is a common tumour of the subcutis, accounting for 25% to 50% of all superficial leiomyomas.[9] Our patient's peritoneal lesions were different from those of infantile myofibromatosis (IM), peritoneal leiomyosarcoma and benign metastasizing leiomyoma of the uterus in several aspects.

In patients with IM, the lesions can be solitary or multicentric with visceral involvement.[10] In about 89% of patients with IM the condition is diagnosed during the first 2 years of life. Histologically, the lesions are composed of short curving bundles of spindle-shaped cells and collagen tissue extending in a fingerlike fashion into the surrounding tissue with a hemangiopericytoma-like pattern at the centre.[10] Histochemical and EM studies suggest that the constituent cells are myofibroblasts. The lesions in IM have a tendency to regress, and they may be hamartomatous in nature as suggested earlier by Shnitka, Asp and Horner,[11] Bartlett, Otis and Laasko[12] and Beatty.[13] Leiomyosarcoma involving the peritoneum is characterized by nodules of smooth-muscle cells with marked cellular atypia and a high mitotic index.[1] The benign metastasizing leiomyoma generally presents as one or more pulmonary nodules. When leiomyosarcoma occurs in the pelvis, the metastatic nodules tend to locate near the round ligaments of the uterus and iliac veins.[1]

Lesions of DLP are seen in women during their childbearing ages. They usually regress after pregnancy but may persist.[5] These findings indicate that estrogen and progesterone do play an important role in the pathogenesis of DLP. The experimental work of Fujii and associates[14] on guinea pigs also supports this hypothesis. Microscopically, DLP is characterized by numerous subperitoneal nodules of spindle cells consisting of smooth-muscle cells, a mixture of smooth-muscle cells and myofibroblasts or altered smooth-muscle cells and fibroblasts. These cells are seen arranged in fascicles orientated in irregular or perpendicular patterns similar to those of the common uterine leiomyoma.[1-8] No lesions reported were found arising from smooth-muscle cells of the media of blood vessels.[1,3-8] However, in one report, the lesions appeared to originate from a muscular blood vessel. The DLP lesions are most likely formed by fibroblastic replacement of subperitoneal decidua in pregnant women.[5,6] They seem to arise from an abnormal metaplastic change of submesothelial stem cells in nonpregnant patients whose ovarian hormonal levels can be normal or elevated.[4,5] It is most likely that this patient's peritoneal lesions represent a histologic variant of DLP. The abundance of collagen fibres might indicate that the lesions formed a long time before they were incidentally found at laparotomy for cholecystectomy. They might have formed years or months after the patient's previous total abdominal hysterectomy in 1948 and persisted.

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Spontaneous Rupture of the Spleen in Patients With Infectious Mononucleosis

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The author describes two cases of spontaneous splenic rupture occurring with infectious mononucleosis in young, previously healthy patients. The reports illustrate the variable clinical presentation — from sudden, fatal hemorrhage to bleeding that stops spontaneously. Although conservative nonoperative treatment may be successful in carefully selected cases, laparotomy with splenectomy appears to be the safest therapeutic approach.

When a nonoperative approach is selected, the patient should be observed in a critical-care facility with immediate access to an operating room. Normal activity should not be resumed until the spleen has returned to its normal size as demonstrated by computed tomography or ultrasonography.

L'auteur décrit deux cas de rupture spontanée de la rate survenant en cours de mononucléose infectieuse chez des patients jeunes, préalablement en bonne santé. Les deux cas illustrent l'étendue du tableau clinique allant de l'hémorragie soudaine et fatale, au saignement qui s'arrête spontanément. Même si un traitement conservateur, non chirugical, peut suffire dans certains cas choisis, la laparotomie avec splénectomie paraît être l'abord thérapeutique le plus sûr.

Si une approche non chirurgicale est choisie, le malade devrait être gardé dans un service de soins intensifs ayant un accès immédiat au bloc opératoire. Les activités normales ne devraient être reprises qu'une fois la rate revenue à sa taille normale, vérifiée par la tomographie par ordinateur ou l'échographie.

Infectious mononucleosis is a common disorder, particularly among young, previously healthy individuals. Although splenomegaly is reported in approximately half of these patients,[1,2] the disease usually runs a benign course without untoward long-term sequelae. However, it has been reported[3] that 0.5% of these patients, who present with abdominal pain, suffer spontaneous splenic rupture, which is associated with a high death rate. Therefore, physicians should be acutely aware of the possibility of spontaneous splenic rupture in infectious mononucleosis. Even when the diagnosis is made there is controversy concerning the management and outcome.[4,5]

We present two cases of spontaneous rupture of the spleen in previously healthy young individuals, in whom the presentation, management and outcome were quite different.

Case Reports

Case 1

An 18-year-old girl had been healthy until she experienced a sore throat and mild fever with some cervical lymphadenopathy. She was seen by her family physician who treated her with erythromycin for what appeared to be pharyngitis due to *Streptococcus*. She was advised to stay in bed until the fever subsided. Four days later, approximately 12 hours before being admitted to hospital, she experienced increasing pain in the abdomen and felt dizzy on getting out of bed. There was no history of recent trauma. She fainted during one episode of dizziness. Approximately 6 hours later she was found to be unresponsive, so she was admitted to hospital. At Sunnybrook Health Science Centre there was electrical cardiac activity but no palpable spontaneous peripheral pulse. External cardiopulmonary resuscitation was applied. Large-bore intravenous lines were established with administration of emergency blood. The abdomen was quite distended.

At emergency laparotomy, there was gross blood throughout the peritoneal cavity. A bleeding spleen was delivered into the wound and quickly removed by clamping the hilum of the spleen. Hemostasis was then established and fluid infusion continued in the operating room. At the termination of the operation the patient's vital signs had stabilized. Her blood pressure was 110/70 mm Hg and her heart rate was 110 beats/min, but her pupils remained fixed and dilated and her core temperature was recorded as 32°C. Upon closure of the abdomen diffuse bleeding was noted in the wound and the patient

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was given fresh frozen plasma and platelets. She also received 10 units of packed cells in the operating room for resuscitation.

She was transferred to the intensive care unit where her neurologic status did not improve. Signs of disseminated intravascular coagulation developed with persistent prolongation of the prothrombin (more than 30 seconds) and partial thromboplastin (150 seconds) times and a depression of her platelet count. She continued to have bright red bloody drainage from her peritoneal drains. In our opinion the hypocoagulable state resulted from the hypothermia. Her hypocoagulability was relatively resistant to platelets, plasma, cryoprecipitate and 1-deamino-8-D-arginine vasopressin (DDAVP). Subsequently, severe respiratory failure, necessitating the administration of 100% oxygen, and high positive end-expiratory pressures (up to 20 cm H_2O) developed, with demonstration of florid pulmonary edema consistent with acute respiratory distress syndrome. Acute renal failure gradually developed, and, because of the continuing hemorrhage from her peritoneal drains, the possibility of mechanical bleeding in the abdomen was considered. She was returned to the operating room, and her abdomen was re-explored. The ligatures in the splenic hilum and other areas of the abdomen were intact, and no mechanical source of bleeding was identified. After 72 hours of normothermia and correction of her coagulation defect there was still no improvement in her neurologic status. Acute renal failure developed with continuing deterioration of her respiratory status. Primarily because of her persistent deep coma with no brain stem reflexes after normothermia further aggressive therapy was discontinued and the patient died.

At autopsy there was still considerable blood in the peritoneal cavity. The enlarged spleen, which weighed 350 g, was examined grossly and histologically. There was evidence of denudation of the capsule in the area of the hilum (Fig. 1). Histologic examination of the spleen demonstrated findings consistent with infectious mononucleosis. From a blood sample taken at the time of admission the latex agglutination test gave a positive result for infectious mononucleosis.

Case 2

A 29-year-old man, who was otherwise healthy and athletic, presented to the emergency department of Sunnybrook Health Science Centre 6 hours after experiencing abdominal pain and faintness. He gave a history of malaise and sore throat for 7 days for which penicillin had been prescribed. He denied any history of trauma or unusual exertion.

His blood pressure was 110/70 mm Hg, his pulse rate was 70 beats/min and regular and his chest was clear. Abdominal examination revealed diffuse tenderness. The hemoglobin level was 129 g/L and the leukocyte count was 14.5 $\times$ 10^9/L with a lymphocytosis (lymphocyte count 7.2 $\times$ 10^9/L [normal 1 to 4 $\times$ 10^9/L]). After 2 L of fluids were administered over approximately 6 hours his hemoglobin level was 109 g/L. The presumptive diagnosis was a perforated viscus, but upright chest films and an upper gastrointestinal series with Gastrografin contrast medium gave negative results, and ultrasonography demonstrated free intraperitoneal fluid raising the possibility of a lacerated spleen.

Because the patient was relatively stable and his pain had occurred approximately 6 hours previously, he was taken to the critical care unit where his blood pressure was measured frequently and his cardiac status was monitored. It was decided to treat him conservatively for a ruptured spleen. A latex agglutination test gave a positive result for infectious mononucleosis.

A smear of a peripheral blood sample showed abnormal lymphocytes consistent with infectious mononucleosis. Computed tomography (CT) of the abdomen demonstrated a laceration through the spleen, which appeared to have tripled in size compared with the size of a normal spleen on CT scans (Fig. 2). The patient remained stable over the next 5 days with no further deterioration in his vital signs or drop in hemoglobin level. He was then transferred out of the critical care unit and slowly mobilized. Upon discharge from hospital 7 days after admission, he was taking iron orally and had specific instructions not to be involved in any vigorous activity and to return to the hospital immediately if abdominal pain or dizziness recurred.

At follow-up 8 weeks later his hemoglobin level and leukocyte count were normal (153 g/L and 4.9 $\times$ 10^9/L respectively). Upon repeat CT of the abdomen 12 weeks after his admission the size of the spleen had decreased to normal and the laceration had healed. The patient was advised to avoid vigorous sports and body contact sports for at least 3 months and to report any abdominal pain immediately.

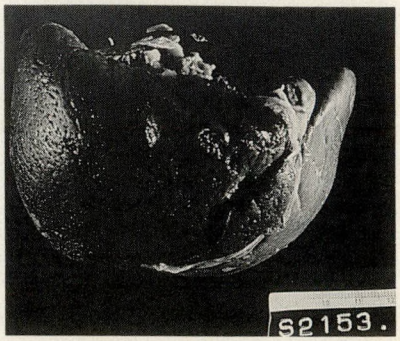

FIG. 1. Case 1. Gross appearance of spleen showing denudation of capsule and large splenic laceration.

Discussion

These two cases demonstrate that spontaneous rupture of the spleen can occur in association with infectious mononucleosis and that the course is variable and may include a fatal outcome.

Several authors[4] have cautioned against conservative management of a ruptured spleen associated with infectious mononucleosis because of a higher death rate than in traumatic rupture of the spleen. However, our case 2 demonstrates that conservative management and close observation can be successful.

The mechanism of splenic rupture in infectious mononucleosis is not completely understood. Splenomegaly appears to be a common accompaniment of splenic rupture in this disorder.[1,2] Edema, increase in cell size and lifting of the splenic capsule would suggest that stretching of the capsule may result in spontaneous hemorrhage. Intense inflammatory reaction and vasculitis may also contribute. As seen in both these cases the splenomegaly can occur very rapidly in infectious mononucleosis in contrast to other causes of splenomegaly, and this may predispose to splenic rupture. However, a history of trauma usually precedes splenic rupture in splenomegaly from other causes. It has beeen claimed that splenic rupture is unlikely during the first 2 weeks of infectious mononucleosis.[6] However, our two cases have demonstrated that rupture can occur within 1 week. Although spontaneous rupture of the spleen is rare, it is the most common cause of death in patients with infectious mononucleosis.[7]

The timing of return to normal activities remains unclear. As in our case 2, it seems reasonable to restrict activity until the spleen has returned to normal size. Recommendations for return to sports activities in athletes vary from 3 weeks to 6 months after clinical resolution of the illness.[3,8,9] A reasonable recommendation is that vigorous activity should not be resumed until the spleen has returned to normal size as determined by imaging techniques.

Because of the usually benign course and the ubiquitous nature of infectious mononucleosis, complacency may exist among many physicians. However, splenic rupture in infectious mononucleosis is a serious complication, and precautions should be taken once the diagnosis is made to avoid vigorous sports activity. The patient should be alerted to the possibility of spontaneous rupture of the spleen. Any significant abdominal pain should prompt further investigation and medical supervision of care. Shoulder tip pain or any signs of severe abdominal pain require CT or ultrasonography for evaluation of the abdomen. Splenomegaly, even in the absence of a fall in hemoglobin, calls for bed rest for the patient and close observation. As with traumatic splenic rupture conservative management requires close observation in an intensive care setting, so that emergency laparotomy can be carried out if there is any deterioration of the patient's condition.

All criteria for spontaneous splenic rupture in infectious mononucleosis as outlined by Rutkow[7] were met in our case 1. In case 2, although the spleen could not be evaluated histologically, all other criteria were met.

It has been estimated that spontaneous rupture of the spleen occurs in 0.5% of cases of infectious mononucleosis,[3] and the death rate for splenic rupture has been reported to be as high as 30%.[8] In Rutkow's report[7] all patients survived when splenic rupture was recognized and treated early. This emphasizes the need for rapid diagnosis and treatment.

The argument for surgical removal is that the risks associated with blood transfusion for ongoing hemorrhage are of similar magnitude to those of sepsis following splenectomy and that the abnormal spleen seen at operation may also be more prone to rupture later.[9] However, as seen in case 2, these spleens do return to normal size. If a period of observation and conservative management is considered,

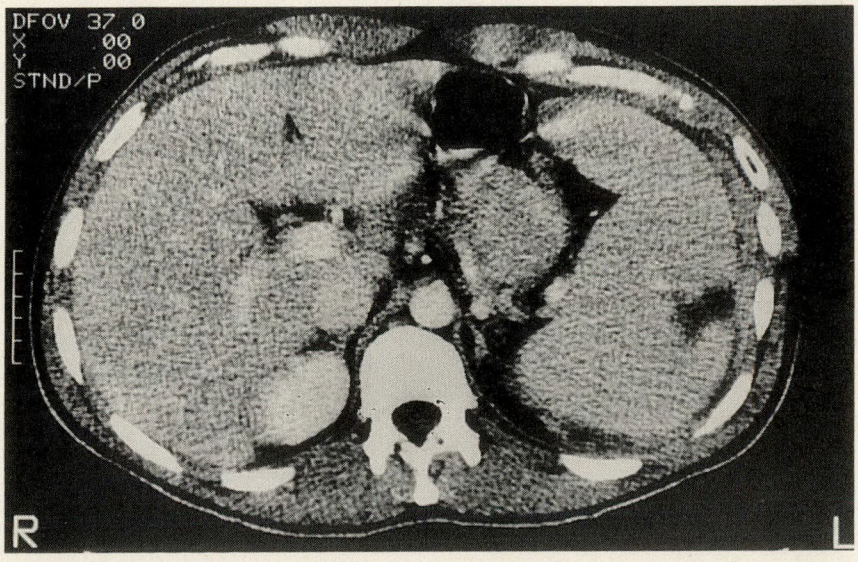

FIG. 2. Case 2. Computed tomography scan of abdomen demonstrating splenomegaly, large laceration of spleen and intraperitoneal blood.

the patient should be under close supervision until the spleen returns to normal size.

A case of sudden death due to spontaneous splenic rupture in infectious mononucleosis, as in case 1, has also been reported previously.[10] This suggests that the magnitude of the hemorrhage from splenic rupture can vary from simple small subcapsular hematomas to exsanguinating hemorrhage. Where critical care facilities for close observation and immediate surgery are not available, splenectomy appears to be the safest treatment.[11]

In case 2 nonoperative management was prompted by the fact that the symptoms were present for at least 6 hours before the patient presented to the emergency department with stable vital signs. Had this patient presented with hemodynamic instability or signs of continuing hemorrhage the decision to operate would have been easier. The patient was also fully informed of the risk of nonoperative management as well as the risk of blood transfusions. It was decided that if blood transfusions became necessary to maintain hemodynamic stability in this patient then operative intervention would be the course of action.

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SESAP VII Critique / Critique SESAP VII

Item 360

Pulmonary complications after operation are a leading cause of morbidity and mortality. The site of surgical incision has a pronounced effect on the development of postoperative respiratory complications. Thoracic and upper abdominal operations are associated with the highest risk.

Diaphragmatic function is markedly altered after upper abdominal operation. Abdominal pain, inflammation, and local irritation are believed to be responsible for the decrease in lung volumes found postoperatively. Intercostal nerve blockade is helpful in decreasing patient discomfort, but has not produced the expected beneficial effect on lung volumes after midline incisions.

Patients with chronic obstructive pulmonary disease are at high risk for postoperative pulmonary complications because of decreased maximum expiratory flow rates that make them unable to produce an adequate cough. Without treatment, 60% of these patients develop a pulmonary complication. Preoperative bronchodilators, antibiotics, and physiotherapy decrease the postoperative complication rate to 22%.

The lower limit of FEV_1 below which patients should not be given general anesthesia has not been clearly defined. Patients at risk should be studied with preoperative pulmonary function tests. An FEV_1 less than 65% of the predicted value indicates significant disease, and preoperative preparation is warranted prior to abdominal operation. The decrease in vital capacity postoperatively is not related to the specific anesthetic agent used.

C

Reference

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Sulfhydryl-Containing Agents in the Treatment of Gastric Bleeding Induced by Nonsteroidal Anti-inflammatory Drugs

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In a double-blind study involving 172 patients, the author investigated the effect of sulfhydryl-containing agents (cysteine and methylmethionine sulfonium chloride [MMSC]) on hematemesis resulting from erosive gastritis induced by nonsteroidal anti-inflammatory drugs.

The 56 patients who received cysteine (200 mg orally four times a day) and the 59 patients who received MMSC (500 mg orally four times a day) were significantly ($p < 0.01$) more hemodynamically stable, with no rebleeding, than the 57 patients who made up a control group. Endoscopy carried out 48 hours after admission demonstrated that gastric erosions were still present in a significantly ($p < 0.01$) higher number of patients in the control group (20 [35%]) than in patients receiving cysteine (6 [11%]) and in patients receiving MMSC (7 [12%]).

Eighteen patients (32%) in the control group required blood transfusion because of continued bleeding or rebleeding compared with only 3 patients (5%) receiving cysteine and 2 patients (3%) receiving MMSC ($p < 0.01$). Emergency surgery was necessary in 13 patients (23%) in the control group and in 1 patient (2%) in the group receiving cysteine who had rebleeding. Four patients in the control group died postoperatively.

The results show that sulfhydryl-containing agents stimulate the healing of erosive gastritis induced by nonsteroidal anti-inflammatory drugs and protect against the complications of bleeding produced by the gastritis.

Dans cette étude à double insu impliquant 172 patients, on a étudié l'effet de composés ayant des groupements sulfhydryles (cystéine et chlorure de méthylméthionine sulfonium [CMMS]) sur l'hématémèse résultant de la gastrite érosive provoquée par les anti-inflammatoires non stéroïdiens.

Les 56 patients qui reçurent la cystéine (200 mg, quatre fois par jour, par voie orale) et les 59 patients qui reçurent le CMMS (500 mg, quatre fois par jour, par voie orale) se sont avérés significativement plus stables ($p < 0,01$) au plan hémodynamique, puisqu'ils n'eurent aucune récidive hémorragique, que les 57 patients qui formaient le groupe témoin. L'endoscopie pratiquée 48 heures après l'entrée à l'hôpital a révélé des érosions gastriques encore présentes chez un nombre significativement plus élevé ($p < 0,01$) de patients du groupe témoin (20 [35 %]) que chez ceux qui avaient reçu la cystéine (6 [11 %]) ou le CMMS (7 [12 %]).

Dix-huit patients (32 %) du groupe témoin nécessitèrent des transfusions à cause d'une persistance ou d'une récidive des saignements, comparativement à seulement 3 patients (5 %) du groupe cystéine et 2 (3 %) du groupe CMMS ($p < 0,01$). Une intervention chirurgicale d'urgence fut requise chez 13 patients (23 %) du groupe témoin et 1 patient (2 %) du goupe cystéine qui éprouvèrent une rechute hémorragique. Quatre patients du groupe témoin sont décédés en postopératoire.

Ces résultats démontrent que les composés possédant des groupements sulfhydryles stimulent la guérison de la gastrite érosive provoquée par les anti-inflammatoires non stéroïdiens et protègent des complications des saignements causés par la gastrite.

Some nonsteroidal anti-inflammatory drugs (NSAIDs), such as acetylsalicylic acid or indomethacin, irritate the gastrointestinal mucosa, causing bleeding or ulceration, or both.[1,2] The irritation ranges in severity from a few small acute ulcers to erosive gastritis, in which the entire gastric mucosa is inflamed and studded with erosions. The latter condition may produce life-threatening bleeding that requires surgical intervention. The death rate associated with such intervention is at least 30%.[3,4]

Sulfhydryl-containing agents, such as DL-cysteine and methylmethionine sulfonium chloride (MMSC), have been shown, in the rat,[5] to convey gastric mucosal cytoprotection by sustaining the physicochemical properties of the mucosal barrier, thus affording protection against injury from ischemia or noxious substances. Sulfhydryls bind the oxygen-derived free radicals that mediate tissue damage.[6,7] These radicals were recently shown to be directly implicated in gastroduodenal ulceration, and scavenging them protects against ulceration by maintaining mucosal integ-

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rity in the face of deleterious agents.[8-10] Sulfhydryl-containing agents make an essential contribution to protein synthesis,[11] and the repair of tissue loss requires large quantities of sulfur-containing amino acids.[11] The gastrointestinal mucosa is highly anabolic and will rapidly incorporate these amino acids, which will then donate sulfur for the sulfation of the acid mucopolysaccharides of gastrointestinal mucin as well as for the synthesis of mucosal and mesenchymal tissues.[11] Furthermore, it has been reported that sulfhydryls stimulate the release of gastric mucin glycoproteins in rats.[7] Zalewsky and Moody[12] noted that mucus cells on the surface and in gastric pits contained a highly sulfated mucin, and Starkey, Snary and Allen[13] demonstrated that the gel structure of gastric mucin depends on disulfide bridges. These actions suggest that sulfhydryl-containing agents may promote the repair of breaches of the gastrointestinal mucosa and, thus, maintain the integrity of this mucosa and enhance its ability to withstand forces tending to injure it.

Since the possibility exists that sulfhydryl-containing agents might be beneficial in the treatment of NSAIDs-induced upper gastrointestinal bleeding, the present study was undertaken. It covered the period October 1978 to December 1980.

Patients and Methods

Sulfhydryl-containing Agents

A 4% solution of DL-cysteine and a 10% solution of MMSC (Sigma Chemical Co., St. Louis, Mo.) were prepared in double-distilled water and placed in 300 mL dark glass bottles. The double-distilled water was given to the control patients.

Study Design

The study was prospective, randomized, double blinded and controlled. It was conducted on consecutive patients with rheumatoid arthritis or osteoarthritis who presented with hematemesis caused by NSAIDs-induced gastric erosions. Patients were randomized by drawing sealed envelopes.

Treatment was begun immediately after the diagnosis was made. A patient was judged suitable for the study when all of the following applied: hematemesis started within 2 hours of presentation; the patient had received no treatment; there were no clinical signs of shock or any apparent hemodynamic disturbance (pulse rate less than 100/min, systolic blood pressure more than 100 mm Hg, hemoglobin level more than 10 g/dL, packed red cell volume in men more than 0.4 and in women more than 0.37). Exclusion criteria included any of the following: erosions extending beyond the stomach; previous upper gastrointestinal hemorrhage; a history of dyspepsia; bleeding diathesis or any hematologic disorder; well-established causes for the development of stress-induced acute gastric mucosal injury (trauma, surgery, burns, shock or sepsis); treatment with any gastrointestinal ulcer healing agent during the 4 weeks before presentation; hiatus hernia; esophageal erosions or ulcers; coexistent or previously noted gastric or duodenal ulceration; a visible vessel, a spurting vessel or a clot adherent to a vessel seen during endoscopy; previous anti-ulcer surgery; the use during the month preceding the bleeding episode of corticosteroids, antineoplastic agents, antimalarial agents, gold preparations, multiple NSAIDs, anticholinergic agents, phenothiazines or tetracyclines; the presence of significant symptoms from other gastrointestinal disorders that would make it difficult to evaluate efficacy and safety of the trial drugs (e.g., severe irritable bowel syndrome); cardiorespiratory problems; hepatic or renal disorders; pregnancy or alcoholism.

NSAIDs-induced erosive gastritis was diagnosed when at endoscopic examination, with the patient sedated, most of the gastric mucosa showed hemorrhagic inflammation studded with erosions (breaches of the mucosa regardless of their shape, size, site or number).

When patients with hematemesis were judged suitable for the study, a complete history was obtained, followed by physical examination. After a complete fast the patients were admitted to the hospital and hydrated intravenously. Endoscopy was undertaken within 6 hours of admission. After erosive gastritis was diagnosed, patients were randomized to one of the study groups and allowed free fluids and milk (the intravenous line was disconnected soon after these were taken). Standard hematologic and biochemical measurements were made, and urinalysis was performed and repeated daily until patients were discharged home or until complications developed. Plain abdominal radiography was always undertaken to exclude visceral perforation. Patients whose condition remained stable with no further hematemesis were examined by endoscopy again 48 hours after the start of treatment (preceded by a complete fast for 3 hours) to study the integrity of the gastric mucosa. These patients were then allowed solid food, and if that was well tolerated for 24 hours, the treatment was withdrawn, and they were discharged home. Resumption of the NSAIDs was not permitted until a week later.

A central venous line was inserted when clinical signs of shock or hemodynamic disturbance devel-

oped, or when rebleeding occurred. Restoration of the circulating blood volume was attained by blood transfusion, and the effectiveness of resuscitation was determined by clinical observations and monitoring of central venous pressure.

The decision to abandon conservative management and to undertake emergency surgery — vagotomy and antrectomy with underrunning of any obviously bleeding points — was based on the following criteria: for patients older than 60 years — four units of blood required within 24 hours or one episode of rebleeding; for patients 60 years of age or younger — eight units of blood required in 24 hours or two episodes of rebleeding during the same admission.

The compliance of patients with their regimen and any adverse reactions to this regimen that they experienced were carefully monitored on special charts.

The end point for this study, when the treatment code was broken, was when patients were discharged home or when they required insertion of a central venous line.

Ethical Considerations

This investigation was approved by the Ethical Committee on Human Experimentation at the hospital, and every patient gave written informed consent.

Study Groups

Two hundred and thirteen consecutive patients who presented with hematemesis caused by NSAIDs-induced erosive gastritis were randomized. In the first group, patients were given 5 mL of double-distilled water orally every 6 hours. In the second group, patients were given 5 mL of 4% cysteine (200 mg) orally every 6 hours. In the third group, patients were given 5 mL of 10% MMSC (500 mg) orally every 6 hours. All patients were given the same volumes of solutions and they were treated for 3 days unless their condition deteriorated.

Statistical Analysis

A sample size of 150 patients was initially chosen, with 50 patients in each group. On the basis of a two-tailed *t*-test, such a size will detect a significant difference of 30% between active and placebo therapy ($p < 0.05$) with a probability of 80% for the overall sample. Because of the anticipated problems of nonevaluability of some patients, which could weaken any conclusion drawn, the aim was to enter approximately 70 patients in each group. The differences detectable within any subgroup are considerably larger than 30%.

Results are expressed as percentages or the mean value. The χ^2 test with Yates' correction was used to determine statistical significance ($p < 0.05$) of observed differences in the percentage incidence between the groups, and the Mann–Whitney "U-statistic" test for nonparametric data was used to establish the statistical significance of observed differences in mean values among the study groups.

Life-table analyses with Mantel–Cox (log rank) and Breslow generalized Wilcoxon's statistics were used to evaluate the statistical differences in the results of treatment between the groups. Pair-wise comparisons were made between groups with or without sulfhydryl-containing agents. Cox proportional hazards models were then used to investigate the effect of these agents on the outcome of treatment when account was taken of the other patient factors as covariants.

Exclusion of Patients From Efficacy Analysis

Patients were excluded from the efficacy analysis on the basis of the following rules, which were rigidly applied: adverse reaction to the therapeutic regimen; intolerance of the therapeutic regimen; failure to comply with the regimen; the use of any form of medication, other than the trial regimen, to avoid therapeutic activities of unknown origin.

The decision to exclude patients from the efficacy analysis was undertaken before breaking the treatment code. Additional intention-to-treat analyses were performed reincluding such patients and using various theoretically possible outcomes to examine what influence their exclusion had on the conclusions reached.

Results

Patient Characteristics

Seventy-two patients (45 women and 27 men) with an age range of 28 to 74 years (mean 57 years) were randomized to the control group. Seventy patients (38 women and 32 men) with an age range of 25 to 71 years (mean 55 years) were randomized to the cysteine group. Seventy-one patients (43 women and 28 men) with an age range of 27 to 76 years (mean 59 years) were randomized to the MMSC group. These patients were randomized from a total of 391 patients seen during the study period. Fifteen patients in the control group, 14 patients in the cysteine group and 12 patients in the MMSC group were excluded (Table I). The characteristics of the remaining patients were similar with respect to numbers, age range, sex ratio, number of smokers and social drinkers (Table II). None of the patients were

heavy consumers of alcohol, but all drank coffee every day. The daily coffee intake and amount of smoking (all cigarettes) were comparable among the groups. Thirteen women in the control group, 15 women in the cysteine group and 11 women in the MMSC group had used the contraceptive pill at some time in their lives.

Comparison Between the Groups

No significant differences were noted among the three groups with respect to the indication for NSAIDs, the type of NSAIDs used or the duration of therapy (Table II).

Approximately 10% of patients in each of the groups given sulfhydryl-containing agents experienced adverse effects. These were mostly headache, nausea, dyspepsia and abdominal pain. They were sufficiently troublesome, however, to lead to withdrawal of medication in four patients receiving cysteine and in two patients receiving MMSC. Three patients in the cysteine group and two patients in the MMSC group were intolerant of their regimen (Table I). There were no obvious treatment-related changes in hematologic or biochemical values.

Table I. Patients in Study Groups and Reasons for Exclusion

Inclusion/exclusion	Group		
	Control	Cysteine	MMSC*
No. patients entered	72	70	71
No. available for complete assessment	57	56	59
No. excluded	15	14	12
Excluded because of:			
Drug intolerance	0	3	2
Adverse effects	0	4	2
Prohibited drugs used	3	1	2
Noncompliance	12	6	6

*Methylmethionine sulfonium chloride

Table II. Patient Characteristics

Characteristics	Group		
	Control ($n = 57$)	Cysteine ($n = 56$)	MMSC ($n = 59$)
Age, yr			
Range	28 – 71	27 – 69	29 – 75
Mean	56	59	57
Sex			
Men	22	24	23
Women	35	32	36
Smokers	27	24	30
Social drinkers, ≤ 14 units/wk†	22	25	27
Indication for NSAIDs‡			
Rheumatoid arthritis	32	35	30
Osteoarthritis	25	21	29
Duration of NSAIDs therapy, mo			
< 3	41	47	44
3 – 12	9	5	8
> 12	7	4	7
NSAIDs used			
Diclofenac	22	19	24
Piroxicam	11	14	16
Mefenamic acid	10	9	11
Naproxen	7	8	4
Ibuprofen	6	4	4
Other	1	2	0

†One unit = 284 mL of beer, 100 mL of wine or 40 mL of liquor
‡Nonsteroidal anti-inflammatory drugs

Clinical Progress

Thirty-nine patients (68%) in the control group remained stable 48 hours after admission and had no further hematemesis or signs of continued blood loss. The number of patients in the cysteine group (53 [95%]) and MMSC group (57 [97%]) achieving the same outcome was significantly ($p < 0.01$) higher. The second endoscopic examination demonstrated signs of hemorrhagic inflammation in every stomach inspected; however, erosions were present in a significantly ($p < 0.01$) higher number of controls relative to the cysteine (6 [11%]) and MMSC (7 [12%]) groups. The clinical progress of these patients continued, and they were all discharged home after 3 days of hospitalization. It follows that the number of patients tolerating solid food and then allowed home was significantly ($p < 0.01$) larger in the cysteine and MMSC groups than in the control group (Table III).

Eighteen controls (32%) required blood transfusion because of continued blood loss (8 patients [14%]) or an episode of rebleeding (10 patients [18%]). Two patients (4%) taking cysteine required blood because of continued hemorrhage, and another patient in the same group (2%) required blood because of an episode of rebleeding. In the MMSC group, two patients (3%) required blood transfusion for continued bleeding. Emergency surgery was necessary in six control patients (11%) who continued to lose blood, in seven control patients (12%) who had an episode of re-

bleeding and in the only patient in the cysteine group (2%) who had rebleeding. Four control patients died postoperatively (one of cardiac arrest and three of bronchopneumonia) giving an operative death rate of 31% and an overall group death rate of 7%.

A series of Cox proportional hazards models was fitted using, as covariates, all factors other than treatment with the sulfhydryl-containing agents to obtain a group of patients and conditions that independently and significantly influenced recovery from the bleeding episode. Treatments with cysteine and MMSC were then added as separate covariates. Age over 60 years, an episode of rebleeding during the same admission, transfusion of blood, continued bleeding after hospitalization and shock all had a significantly ($p < 0.001$) detrimental effect upon the recovery rate. When these and all the other nonsignificant variables were allowed for, treatment with cysteine or MMSC continued to exert a significantly beneficial effect upon recovery from the hemorrhagic episode ($p < 0.01$).

Intention-to-treat analyses were performed to determine what might have happened if all patients had been evaluable. This required postulating that some patients would have remained stable and experienced no rebleeding or continued blood loss whereas others would have had further rebleeding or continued blood loss at various times.

When all the excluded patients were assumed to have remained stable after admission to the hospital and had no further blood loss or rebleeding or when they were assumed to have deteriorated, treatment with cysteine or MMSC continued to afford a significant therapeutic advantage ($p < 0.01$) in terms of the numbers of patients remaining stable and their complete recovery from the bleeding episode. This advantage, however, was lost when only the patients excluded from the control group were assumed to have remained stable and to have made a full recovery whereas all those excluded from the other groups were assumed to have deteriorated because of rebleeding or continued blood loss.

Discussion

NSAIDs can produce damaging effects on the gastric and duodenal mucosa, ranging from acute gastric mucosal injury to perforation of peptic ulceration.[1-3] The incidence of this injury is approximately 30% and may increase to 51% in patients taking multiple NSAIDs.[2] Inhibition of cyclo-oxygenase by NSAIDs leads to inhibition of prostaglandin synthesis, an action that can initiate the development of acute gastric mucosal injury.[14] Prevention of prostaglandin synthesis depresses gastric mucosal blood flow and bicarbonate secretion, reduces mucus production and causes atrophy of the gastric epithelium.[15] Thus, the mucosal defensive properties are impaired, allowing gastric acid to attack and injure the mucosa.[15,16]

This investigation demonstrates that sulfhydryl-containing agents stimulate the healing of acute gastric mucosal injury produced by NSAIDs and protect against the complications of the hemorrhagic episode caused by such injury (Table III). Continued hemorrhage and rebleeding are among the complications and are particularly serious because they may necessitate emergency surgery, which is associated with a death rate of up to 30%. The similarity in efficacy between cysteine and MMSC and the fact that the latter is converted via the transsulfuration pathway to cysteine[11] suggest that the actions of the sulfhydryl-containing agents used were provided by cysteine.

Adverse effects, whether mild or sufficiently troublesome to lead to withdrawal, occurred in small numbers of patients (Table I), and there were no obvious treatment-related changes in hematologic or biochemical values. These findings illustrate the safety of cysteine and MMSC. It would be an advantage if their daily doses could be reduced without compromising efficacy.

The compliance of patients with the regimen was carefully monitored, and any violation led to exclusion of the patient (Table I). Compliance was similar among the groups, so the results cannot be ascribed to differences in patient compliance or to an unintended bias

Table III. Clinical Course of Patients

Clinical course	Group, no. (%)		
	Control ($n = 57$)	Cysteine ($n = 56$)	MMSC ($n = 59$)
Condition stable after 48 h	39 (68)	53 (95)	57 (97)
Second endoscopy			
Hemorrhagic inflammation	39 (68)	53 (95)	57 (97)
Erosions	20 (35)	6 (11)	7 (12)
Blood transfusion for:			
Continued blood loss	8 (14)	2 (4)	2 (3)
Rebleeding	10 (18)	1 (2)	0
Surgery for:			
Continued blood loss	6 (11)	0	0
Rebleeding	7 (12)	1 (2)	0
Return to solid food after 48 h	39 (68)	53 (95)	57 (97)
Discharge after 3 d	39 (68)	53 (95)	57 (97)

in favour of a particular group, which may influence compliance.

Although sulfhydryl-containing agents can be detected on the breath, this was never raised by any patient as a significant source of inconvenience. Furthermore, it could not be seen as a source of bias in favour of any of the study groups, since the primary parameters of assessment were objective (Table III).

I am grateful to Dr. S.H. Alwash for the opportunity to undertake this work at the Medical City and to the nursing staff for their help during the course of the investigation. I am also grateful to Mrs. Jutta Gaskill and to Mrs. Moira Cairney for secretarial work.

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NOTICES
AVIS

Lake Tahoe Annual Vascular Conference

The course entitled "Strategies in Vascular Disease: Minimizing the Morbidity in Diagnosis and Treatment" will be offered at the Lake Tahoe Annual Vascular Conference to be held from Mar. 15 to 17, 1993, at the Resort at Squaw Creek in Olympic Village, Squaw Valley, Calif. The conference is sponsored by the Office of Continuing Medical Education, UC Davis School of Medicine and Medical Center. The course is designed for surgeons and radiologists who deal with the complexities and challenges of peripheral vascular disease. For information contact: Office of Continuing Medical Education, UC Davis Medical Center, 2701 Stockton Blvd., Sacramento, CA 95817; phone: (916) 734–5390

Symposium VIII on Operating Room Environment

This symposium will be held from May 3 to 5, 1993, at the Stouffer Harborplace Hotel in Baltimore. The symposium is presented by the American College of Surgeons in cooperation with the American Society of Anesthesiologists and the Association of Operating Room nurses. Five separate information sessions will be presented on timely operating-room topics of ethical conflicts in patient care, leadership, environmental hazards, operating-room efficiency and technology assessment. For more information contact: American College of Surgeons, Committee on Operating Room Environment, 55 E Erie St., Chicago, IL 60611–2797; phone: (312) 664–4050, ext. 250 or 361.

Progress in Gastrointestinal Surgery

A course entitled "Progress in Gastrointestinal Surgery" will be presented as the major topic of the 57th Annual Surgery Course, to be held from June 16 to 19, 1993, at the University of Minnesota. The course is presented by the Department of Surgery of the University of Minnesota Medical School. For more information contact: Office of Continuing Medical Education, University of Minnesota, Radisson Hotel Metrodome, Suite 107, 615 Washington Ave. SE, Minneapolis, MN 55414; phone: 1–800–776–8636; fax: (612) 626–7766

International Surgical Week

The 35th World Congress of Surgery of the International Society of Surgery with its integrated societies presents International Surgical Week from Aug. 22 to 27, 1993, in Hong Kong. For more information contact: Congress Secretariat, ISW Hong Kong, Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong; phone: (852) 819–2235; fax: (852) 855–1897.

Hematuria and Intravenous Pyelography in Pediatric Blunt Renal Trauma

Paul F. Middlebrook, MD, FRCSC;* John F. Schillinger, MD, FRCSC†

Because the traditional protocol for investigating blunt renal trauma in children has been questioned and because of societal awareness of health care costs, the authors carried out a retrospective review of blunt renal trauma in 138 children over a 5-year period to establish criteria for urgent radiologic investigation of those with suspected renal trauma. From their findings, they recommend that in the absence of the suspected major injuries and hypotension a threshold count of 40 red blood cells per high-power field is necessary before urgent intravenous pyelography should be done.

Vu la remise en question du protocole traditionnel d'investigation des traumatismes rénaux fermés chez l'enfant et la conscientisation du public à l'augmentation des frais de santé, les auteurs ont mené une étude rétrospective portant sur 138 enfants victimes de traumatismes rénaux fermés au cours d'une période 5 ans, afin d'établir les critères commandant l'examen radiologique d'urgence de ceux soupçonnés de traumatismes rénaux. Des résultats obtenus, ils recommandent qu'en l'absence de lésions importantes et d'hypotension, un seuil de 40 hématies par champ microscopique à fort grossissement soit nécessaire avant de pratiquer une pyélographie intraveineuse d'urgence.

Although hematuria is widely recognized as an indicator of potential urinary tract injury in trauma, controversy persists over the necessity of investigation in all patients having hematuria after blunt trauma and about the urgency with which such investigation should be performed. This controversy is further compounded by the fact that current management for most blunt renal injuries is conservative, so imaging results lead to few changes in management. The traditional method of investigating these patients has been with intravenous pyelography (IVP), although enhanced computed tomography (CT) is routinely used in many centres.

The majority of patients with blunt renal trauma have minor renal involvement. Traditionally, children have a greater propensity to pedicle injuries with minimal hematuria. Further, the incidence of congenital anomalies in children is higher than in adults, which may account for renal injury with minor trauma. Complicating this, is the incidence on routine analysis of microscopic hematuria in children with no morbid condition. Hitherto, we have investigated urgently all children with significant abdominal trauma who have hematuria. Recent articles questioning this approach plus a societal awareness of health care costs led to a retrospective appraisal of this approach.

Method

The standard management of blunt trauma patients with either gross or microscopic hematuria by the urology service at the Children's Hospital of Eastern Ontario, Ottawa, has been urgent imaging with IVP unless other suspected injuries warrant alternative initial procedures (e.g., CT). Patients with normal findings on IVP have been assumed to have minor renal contusions and have been managed with bedrest in hospital until their urine is clear. Major renal injuries have been managed with bedrest for at least 10 days and ambulation only after the urine is clear and further imaging indicates some resolution of the local lesion. The records of all patients with a diagnosis of renal trauma (including contusion, laceration, fracture and pedicle injury) seen at our institution between January 1986 and December 1990 were reviewed. For each patient, the following data were collected: age, sex, mechanism of injury, presenting blood pressure, severity of hematuria, result of initial imaging, final diagnosis, associated injuries, blood transfusion requirements and

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length of hospitalization. Note was also made of adverse reactions to the radiocontrast agent used in imaging these patients. For purposes of analysis, renal injuries diagnosed as contusions (including those with no identifiable lesion on imaging) were classified as minor. Major injuries consisted of renal lacerations, fractures and pedicle injuries. Hematuria was quantified as follows: gross, greater than 40 red blood cells per high-power field (rbc/hpf), 20 to 40 rbc/hpf and less than 20 rbc/hpf. A patient was considered to be hypotensive if the first recorded systolic blood pressure was below 100 mm Hg. Associated injuries were considered major if they, independently, would require hospitalization beyond 24 hours. The severity of renal injury was correlated with the severity of hematuria, the presence of hypotension, the presence of associated major injuries, the mechanism of injury, the duration of hospitalization and the need for blood transfusion.

Findings

The records of 138 children (104 boys, 34 girls) were reviewed. No child in the study had sustained penetrating renal trauma. The children ranged in age from 2 to 17 years (Fig. 1), with a trend toward the early to middle teenage years. Falls and traffic accidents were the most common mechanisms of injury (Table I). Only 12 children sustained major renal injuries.

Initial Imaging Investigations

IVP was the initial investigation in 121 children, ultrasonography in 12 children and CT in 3 (Table II). Two children did not undergo initial diagnostic imaging: one had minimal microscopic hematuria; the other, who was admitted in profound shock, underwent immediate laparotomy. IVP successfully identified all major renal injuries among the children who underwent this investigation.

A number of significant non-renal abdominal injuries were also detected (Table III), most of which were identified by IVP. The exceptions were three splenic contusions, one hepatic contusion and one hematoma in the gastrosplenic ligament. These were identified by ultrasonography or CT.

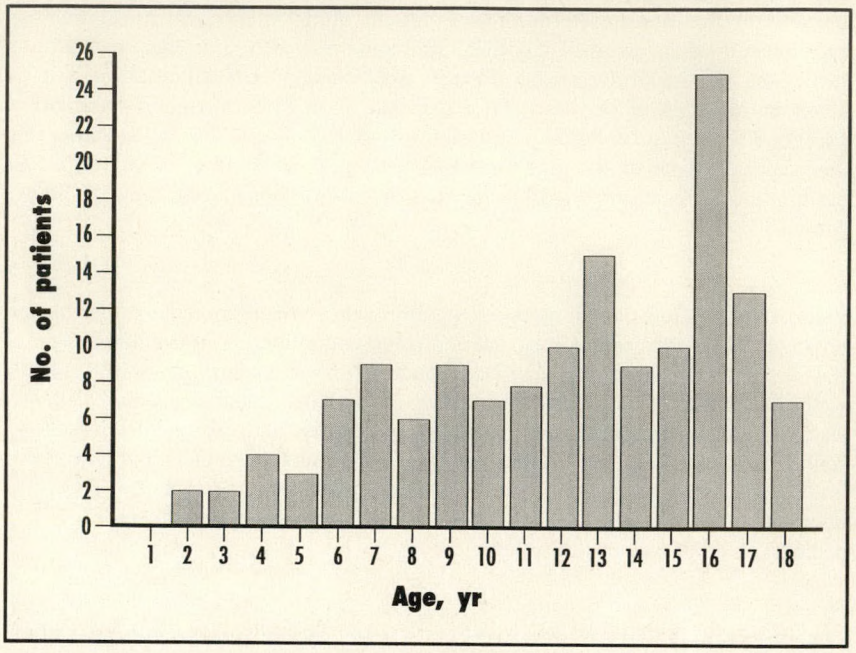

FIG. 1. Age range of 138 children with blunt renal trauma.

Table I. Mechanisms of Injury

Mechanism	No. of patients		
	Minor renal injury	Major renal injury	Total
Fall	47	7	54
Traffic accident	46	4	50
Sports	21	0	21
Blow	12	1	13
Total	126	12	138

Table II. Results of Initial Diagnostic Investigation*

Result	No. of patients			
	Intravenous pyelography	Ultrasonography	Computed tomography	Total
Normal	80	7	0	87
Contusion	32	4	2	38
Laceration	6	1	1	8
Fracture	3	0	0	3
Pedicle injury	0	0	0	0
Total	121	12	3	136

*No imaging in two patients: one had minimal microscopic hematuria; the other was admitted in profound shock with massive hemorrhage and underwent emergency laparotomy.

Severity of Hematuria

The severity of hematuria correlated with the presence of major renal injuries (Table IV). For those whose urinalysis results were recorded, no child with fewer than 40 rbc/hpf in the urine had a major renal injury. One had an isolated major renal injury with microhematuria (> 40 rbc/hpf) alone. This represents a positive predictive value of 21% for gross hematuria and 12% if all hematuria greater than 40 rbc/hpf is considered. The child admitted in profound shock with massive intra-abdominal injuries who underwent immediate laparotomy had no urine obtained for analysis. This was the only patient in the series who required laparotomy.

Congenital Renal Anomalies

Congenital renal anomalies were noted in four patients. Two had a duplex collecting system, which had previously been diagnosed in one child. One horseshoe kidney and one ureterocele were also identified. None of these patients sustained major renal injuries.

Hospital Stay

The mean hospital stay for those with minor renal injuries was 5.0 days (range of 0 to 14 days). The longer hospitalizations were due to associated nonrenal injuries. However, the mean hospital stay for the nine children with major renal injuries who were discharged was 18.5 days (range from 10 to 30 days).

Nonrenal Injuries

Forty-four major nonrenal injuries were sustained by 33 patients (Table III). Six (18%) of the 33 patients had major renal injuries compared with 12 (8.7%) of 138 patients in the total study population who had renal injuries.

Hypotension was seen in 12 patients, only 2 of whom had major renal injury. (Both had coexisting major nonrenal injuries.) Thus, only 2 (17%) of the 12 patients sustaining major renal injury had hypotension.

Other Considerations

Seven patients required blood transfusion in the form of packed red blood cells. Of these, five had sustained major renal injuries. In most of these cases, associated injuries were responsible for the blood loss, but one patient had an isolated major renal injury requiring transfusion. Four patients suffered complications directly related to their renal injuries or to investigation for these injuries. Although no patient had a major reaction to radiocontrast agents, two minor reactions were recorded requiring antihistamine therapy. One child had hypertension, which responded well to medical therapy. Persistent hematuria was seen in one patient who eventually required angioinfarction of a renal segment to control the bleeding. Both patients with complications not related to radiocontrast agents had major renal injuries.

Mortality

Three children died: two from a closed head injury and one from massive intra-abdominal and pelvic hemorrhage (the child who required emergency laparotomy for multiple abdominal and pelvic injuries). All three patients had sustained major renal injuries, but these were not considered directly responsible for the deaths.

Table III. Major Nonrenal Injuries in Trauma Patients With Hematuria

Type of injury	No. of injuries	
	Total no.	No. in patients with major renal injury
Major bone fracture	17	1
Splenic/hepatic laceration	11	6
Splenic/hepatic contusion	8	0
Significant head injury	6	2
Major thoracic injury	2	2
Total	44 (in 33 pts)	11 (in 6 pts)

Table IV. Hematuria in Renal Trauma Patients

Degree of hematuria, rbc/hpf*	No. of patients		
	Minor renal injury	Major renal injury	Total
Gross	38	10	48
> 40	41	1	42
20 – 40	21	0	21
< 20	25	0	25
2+ on dipstick (no microhematuria)	1	0	1
No urine sample available	0	1	1
Total	126	12	138

*Red blood cells per high-power field

Discussion

Although the incidence of major renal injuries in the pediatric literature varies from 0%[1] to 18%,[2] our incidence of 8.7% is consistent with that of most series (5% to 10%).[3–9]

Pedicle injuries are uncommon, and although they were absent in our series and that of others,[7] they may represent up to 2.5% of renal injuries, but they always occur with major associated injuries.[9]

Congenital anomalies are traditionally said to predispose the kidney to injury and are found in up to 17% of patients in blunt trauma series.[7] Our incidence of 2% differs little from that expected in the general population. The diagnosis of renal injury with blunt abdominal trauma has generated controversy over the imaging modality used, the indications for imaging and the urgency for performing imaging.

IVP is the traditional and most widely available imaging technique. In our series, only 22% of children with abnormal findings on IVP had major renal injury, but IVP missed no major renal injury subsequently found by other imaging techniques. However, 5 (26%) of 19 children with associated major nonrenal *abdominal* injuries had normal findings on IVP. This finding supports the conclusion of Taylor, Eichelberger and Potter,[8] who found that 73% of patients with traumatic hematuria had significant other abdominal injuries that were missed by IVP but were found by CT. They concluded, and we concur, that enhanced CT should be performed in any patient with hematuria and evidence of other abdominal injury. Ultrasonography with Doppler flow or with nuclear renography may be superior to IVP in defining renal or other solid-organ injuries but is not available consistently on an emergency basis in many centres, including our own.

The indications for renal imaging with blunt trauma are controversial. Some have reported the association of major renal injury with microscopic or no hematuria.[9] These instances are associated, however, with other major injuries. Others[3,4,10] have indicated that if microhematuria with hypotension or gross hematuria alone are the indications for imaging, then 99% to 100% of all major renal injuries will be identified.

In our series, 10 (91%) of 11 patients (one excluded because no urinalysis was available) with major renal injury had gross hematuria. One, however, had microscopic hematuria (greater than 40 rbc/hpf) only and no other associated injury or hypotension. The predictive factors for major renal injury are far from perfect. From several series[3,4,10] the values reported were: hypotension 17%, associated nonrenal injuries 18%, gross hematuria 21% and hematuria greater than 40 rbc/hpf 8% (our series). If we had applied the criterion of the threshold of hematuria being 40 rbc/hpf or greater, all major renal trauma would have been found by 90 imaging studies to detect 11 cases (Table IV), but 47 studies (34% of all studies) would have been eliminated (on an emergency basis at least).

From these studies and ours, we conclude that urgent renal imaging should be obtained in blunt abdominal trauma if there is gross hematuria or microscopic hematuria greater than 40 rbc/hpf. In these cases an IVP is adequate for diagnostic imaging. If other major trauma or hypotension is present or suspected, and either of these is associated with gross or microscopic hematuria of any degree, then contrast enhanced CT should be done. These criteria should be sufficient to pick up all major renal injuries including pedicle injuries.

It must be remembered that 4% of primary school children have microscopic hematuria on a single urinalysis.[11] Thus, children not meeting the above criteria but with less than 20 rbc/hpf should have a future repeat urinalysis before further investigation. Those with a count of 20 to 40 rbc/hpf should be put on bedrest and undergo non-urgent ultrasonography as a precaution against the error in the absolute precision of microscopic urinalysis.

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The Clinical Significance of Acute Hyperamylasemia After Blunt Trauma

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The clinical value of total serum amylase (TSA) levels measured after blunt trauma remains controversial. To test the utility of this measurement, the authors surveyed the routine admission TSA levels of 4316 adults who were victims of blunt trauma. Most patients (58.2%) had been injured in motor vehicle accidents, and all were admitted directly from the accident scene. Patients were divided into two groups based on the admission TSA level: more than 125 U/L (abnormal) and 125 U/L or less (normal). Of the 4316 patients, 3920 (90.8%) had a normal TSA level upon admission. Hyperamylasemia was associated with a greater injury severity score (ISS) and death rate, a lower admission Glasgow Coma Scale score and an increased incidence of facial fracture, brain injury, pancreatic and hollow-viscus injuries and hypotension ($p < 0.01$). However, the positive predictive value of an abnormal TSA level for pancreatic and hollow-viscus injuries was 1.5% and 3.0% respectively. Also, most patients with pancreatic (65%) and hollow-viscus (83%) injuries had a normal TSA level. There was no relation between the anatomic grade of pancreatic injury and the TSA level.

Acute hyperamylasemia after blunt trauma appears to be a poor predictor of pancreatic and hollow-viscus injuries. Therefore, urgent TSA determinations should not influence the clinical and radiologic evaluation of the blunt trauma victim.

L'intérêt clinique des niveaux d'amylase sérique totale (AST) mesurés après un traumatisme fermé demeure sujet à controverse. Dans le but de mesurer l'importance de cette mesure, les auteurs ont mené une enquête sur les taux d'AST mesurés de façon systématique chez 4316 adultes, victimes de traumatismes fermés. La plupart des patients (58,2 %) avaient été blessés dans des accidents de la circulation et tous sont arrivés directement de la scène de l'accident. Les patients furent divisés en deux groupes selon leur niveau d'AST à l'arrivée : 125 U/L ou plus (anormal) ou moins de 125 U/L (normal). Sur les 4316 patients, 3920 (90,8 %) avaient des taux d'AST normaux. L'hyperamylasémie a été relié à un indice de gravité des blessures (IGB) et à une mortalité plus élevés, à une cote plus faible sur l'échelle d'évaluation du coma de Glasgow, et à une incidence plus élevée des fractures faciales, des lésions cérébrales, des blessures du pancréas et des viscères creux, et d'hypotension ($p <$ 0,01). Toutefois, les valeurs prévisionnelles positives d'un AST anormal pour les blessures du pancréas ou des viscères creux ont été de 1,5 % et 3,0 %, respectivement. De plus, la plupart des patients ayant des lésions pancréatiques (65 %) ou des viscères creux (83 %) avaient des AST normaux. Il n'y avait aucune relation entre le grade anatomique des lésions pancréatiques et le niveau d'AST.

L'hyperamylasémie aiguë post-traumatique semble un mauvais prédicteur des blessures du pancréas ou des viscères creux. En conséquence, les dosages de l'AST en urgence ne doivent pas influencer l'évaluation clinique et radiologique des victimes de traumatismes fermés.

The role of serum amylase in the evaluation and management of nontraumatic pancreatic disorders is well established.[1,2] Determination of the total serum amylase (TSA) level was first reported as useful in the evaluation of the blunt trauma victim in 1943.[3] Since then there have been conflicting reports on the value of TSA in the acutely traumatized patient.[4–7] Hyperamylasemia is

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associated with severe brain injury, facial trauma and hypotension.[8–10] The recent literature appears to favour the hypothesis that acute TSA is not clinically useful in the blunt trauma victim.[11,12] However, this hypothesis has not been tested in a large group of blunt trauma victims whose TSA levels have been determined routinely.

Blunt pancreatic and hollow-viscus injuries are notoriously difficult to detect nonoperatively, and clinicians have sought reliable noninvasive diagnostic methods. Hyperamylasemia has been demonstrated in 61% to 90% of patients with blunt pancreatic injuries and is known to occur after bowel perforation and ischemia.[13–16] These data and the lack of superior laboratory tests have become the impetus for routine determination of TSA levels in the initial evaluation of the blunt trauma victim with possible intra-abdominal injury. It is our hypothesis that acute hyperamylasemia is a poor marker of pancreatic and hollow-viscus injury and that the incidence of acute hyperamylasemia should not influence the clinical and radiologic evaluation of the blunt trauma victim.

Patients and Methods

The R Adams Cowley Shock Trauma Center of the Maryland Institute for Emergency Medical Services Systems (MIEMSS) in Baltimore is the clinical hub of Maryland's statewide emergency medical services (EMS) system. Patients admitted to the trauma centre are managed with established institutional protocols by a trauma team consisting of an attending traumatologist, a trauma surgery fellow and three to four residents in surgery or emergency medicine.[17] Abdominal injury is diagnosed or excluded by diagnostic peritoneal lavage, computed tomography (CT) or repeated clinical examination. Blood for TSA determination is drawn routinely on admission to the Shock Trauma Center. TSA is measured by an enzymatic rate method (Beckman Synchron CX4; Beckman Instruments, Inc., Brea, Calif.) (normal, 125 U/L or less).

Between July 1987 and June 1990, 4404 adult (more than 14 years old) blunt trauma victims were admitted to the trauma centre directly from the accident scene (vital signs present). Of these, 4316 (98%) had TSA concentrations measured within 90 minutes of admission. Prospectively collected data were obtained on these 4316 patients from the MIEMSS–Dunham clinical trauma registry.[18] The study population of 4316 patients was divided into two groups: those with a normal TSA level (125 U/L or less) and those with an abnormal TSA level (more than 125 U/L). These groups were compared with respect to age, sex, mechanism of blunt injury, injury severity score (ISS), admission Glasgow Coma Scale (GCS) score, admission systolic blood pressure, results of ethanol screening, the incidence of facial and skull fractures and brain injury and the incidence of pancreatic, gastric, duodenal, small-bowel, colonic and rectal injuries. Ethanol screens were recorded as positive or negative. Brain injury was defined as an intracranial traumatic lesion demonstrated by CT. Hospital charts were examined for patients with a blunt pancreatic injury to anatomically grade the injury according to the guidelines of Moore and colleagues.[19]

The sensitivity, specificity, positive predictive value and negative predictive value for admission TSA level as a test for pancreatic or hollow-viscus injury were calculated. Patient groups were compared by Student's *t*-test or χ^2 analysis, as appropriate. All values are presented as means ± standard deviation.

Findings

The average age of the 4316 patients was 33.3 ± 15.8 years. Males made up 69.6% of patients. A majority of patients (2513 [58.2%]) had been involved in motor vehicle accidents. The remainder were victims of motorcycle accidents (320 [7.4%]), falls (610 [14.1%]), pedestrian trauma (309 [7.2%]), bicycle accidents (50 [1.2%]), blunt beatings (209 [4.8%]) and miscellaneous mechanisms of injury (305 [7.1%]). The mean ISS was 13.8 ± 12.4 and the mean admission GCS score 13.8 ± 2.7. Patients were transported from the field by helicopter (2856 [66.2%]) or land ambulance (1460 [33.8%]). Hypotension (admission systolic blood pressure less than 90 mm Hg) was present in 140 (3.2%) patients. The in-hospital death rate for these 4316 patients was 5.3% (229 patients).

Of the study population, 3920 (90.8%) had an admission TSA concentration in the normal range (125 U/L or less), and 396 patients (9.2%) had abnormal TSA concentrations (more than 125 U/L). Of the 396 patients with abnormal TSA levels, 309 (78.0%) had TSA levels ranging from 126 to 200 U/L, 62 (15.7%) had levels ranging from 201 to 300 U/L, and 25 (6.3%) had TSA levels greater than 300 U/L (Fig. 1).

When the 3920 patients with normal TSA levels and 396 patients with abnormal TSA levels were compared (Tables I and II), significant differences were found between the two groups for the following factors: ISS, GCS score, death rate and the frequency of admission hypotension, facial fractures, and brain, pancreatic, and hollow-viscus injuries ($p < 0.01$).

An abnormal TSA concentration was found in 30 (21.4%) of 140 patients admitted with a systolic blood pressure less than 90 mm Hg and in 366 (8.8%) of 4176 patients admitted with a systolic blood pressure greater than 90 mm Hg ($p < 0.001$).

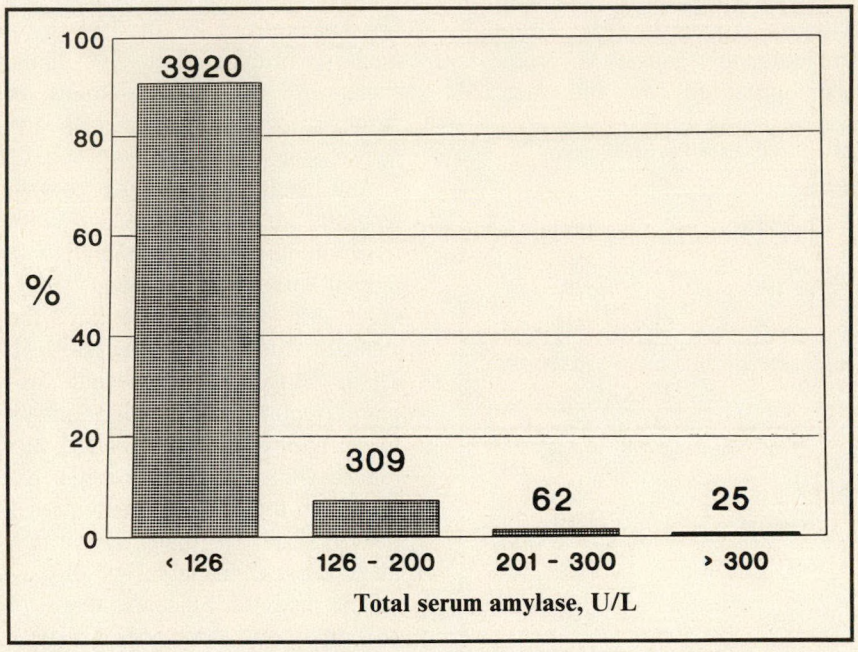

FIG. 1. Total serum amylase (TSA) levels among 4316 adult blunt trauma victims admitted directly from accident scene.

Table I. Comparison of Clinical Factors in Patients With Normal and Abnormal Total Serum Amylase (TSA) Levels

Clinical factor	TSA, U/L: Normal ($n = 3920$)	TSA, U/L: Abnormal ($n = 396$)	Significance, p value
Mean age, yr (SD)	33.0 (15.6)	35.9 (16.5)	NS
Males, %	69.8	68.4	NS
Mean injury severity score (SD)	13.1 (11.9)	18.2 (14.9)	< 0.001
Mean Glasgow Coma Scale score (SD)	13.9 (2.6)	12.9 (3.5)	< 0.001
Ethanol screen, % positive	31.4	35.3	NS
Motor vehicle accident, %	57.8	62.1	NS
Admission systolic blood pressure, < 90 mm Hg, %	2.8	7.6	< 0.001
Mortality, %	4.6	12.4	< 0.001

SD = standard deviation

Table II. Comparison of Injuries in Patients With Normal and Abnormal TSA Levels

Injury	TSA, U/L: Normal, no. (%) ($n = 3920$)	TSA, U/L: Abnormal, no. (%) ($n = 396$)	Significance, p value
Brain injury	495 (12.6)	69 (17.4)	< 0.01
Facial fracture	245 (6.2)	49 (12.4)	< 0.01
Skull fracture	351 (9.0)	43 (10.9)	NS
Pancreatic injury	11 (0.3)	6 (1.5)	< 0.01
Hollow-viscus injury	59 (1.5)	12 (3.0)	< 0.01

The 3006 males and 1310 females in the study population had similar incidences of abnormal TSA concentrations (9.0% and 9.5% respectively). An abnormal TSA concentration was equally prevalent among patients with positive and negative ethanol screens (10.2% and 8.7%, respectively). Of the 25 patients with TSA levels greater than 300 U/L, 10 had a positive ethanol screen.

Of the 3920 patients with normal TSA levels, 11 (0.3%) had pancreatic injuries and 59 (1.5%) a hollow-viscus injury, and of the 396 patients with abnormal TSA levels, 6 (1.5%) had pancreatic injuries and 12 (3.0%) a hollow-viscus injury (Tables II to IV).

The highest TSA level among the 17 patients with pancreatic injuries was 362 U/L. The 17 blunt pancreatic injuries were graded according to the system of Moore and colleagues,[19] and the injuries were evaluated according to the TSA levels (Table V).

No gastric or small-bowel injuries were sustained by the 25 patients with a TSA level greater than 300 U/L. One patient had a duodenal injury, and another had colonic and pancreatic injuries. The patient with the highest recorded admission TSA level (730 U/L) had no pancreatic or hollow-viscus injury.

The TSA values for patients with pancreatic, stomach, duodenal, small-bowel and large-bowel injuries are shown in Fig. 2.

At the MIEMSS Shock Trauma Center, the laboratory cost of a TSA level assay is $1.50 US. Therefore, the cost of the routine TSA measurements in these 4316 patients was $6474.

The sensitivity, specificity, positive predictive value and negative predictive value for abnormal TSA as a test for blunt pancreatic and

hollow-viscus injury are shown in Tables III and IV.

Discussion

Amylase, an enzyme that hydrolyzes glycoside bonds, is a product of two genes known as AMY 1 (salivary) and AMY 2 (pancreatic) coded on chromosome number 1.[20] The AMY 1 isoamylase, although predominantly salivary in origin, is also produced by the lacrimal glands, lungs, breasts and mullerian tissues. The AMY 2 isoamylase is produced only by the pancreas.[21] Pancreatic isoamylase represents approximately 33% of TSA in a healthy human subject.[22] Thus, there are two main sources of serum amylase: the pancreas and salivary glands.

Any insult to tissues that contain amylase may be associated with hyperamylasemia. Interestingly, malignant tumours of the lung, ovary, colon and pancreas may have the capacity to secrete amylase.[23] In 1929, Elman, Avneson and Graham[24] reported the association between pancreatic disease and hyperamylasemia. Since their initial observation, attention on the amylases has focused on their use in the diagnosis and management of pancreatic diseases. Since the report of Naffziger and McCorkle[3] in 1943, TSA determination has been used to assess the possibility of pancreatic injury in the trauma victim, but its usefulness in blunt trauma remains controversial.

In the multitraumatized patient, hyperamylasemia may result from circulatory shock, ingestion of ethanol or narcotics, starch plasma expanders and extra-abdominal injury.[8,10,25,26] Olsen[27] found that only 8% of patients with hyperamylasemia and blunt abdominal trauma had a pancreatic injury. In our patients, the positive predictive

Table III. Evaluation of Abnormal TSA Level as a Test for Blunt Pancreatic Injury*

	Pancreatic injury, no.		
TSA level	**Positive**	**Negative**	**Total**
Normal	11	3909	3920
Abnormal	6	390	396
Total	17	4299	4316

*Sensitivity, 35.3%; positive predictive value, 1.5%; specificity, 91.3%; negative predictive value, 99.7%

Table IV. Evaluation of Abnormal TSA Level as a Test for Blunt Hollow-Viscus Injury*

	Hollow-viscus injury, no.		
TSA	**Positive**	**Negative**	**Total**
Normal	59	3861	3920
Abnormal	12	384	396
Total	71	4245	4316

*Sensitivity, 16.9%; positive predictive value, 3.0%; specificity, 91.0%; negative predictive value, 98.5%

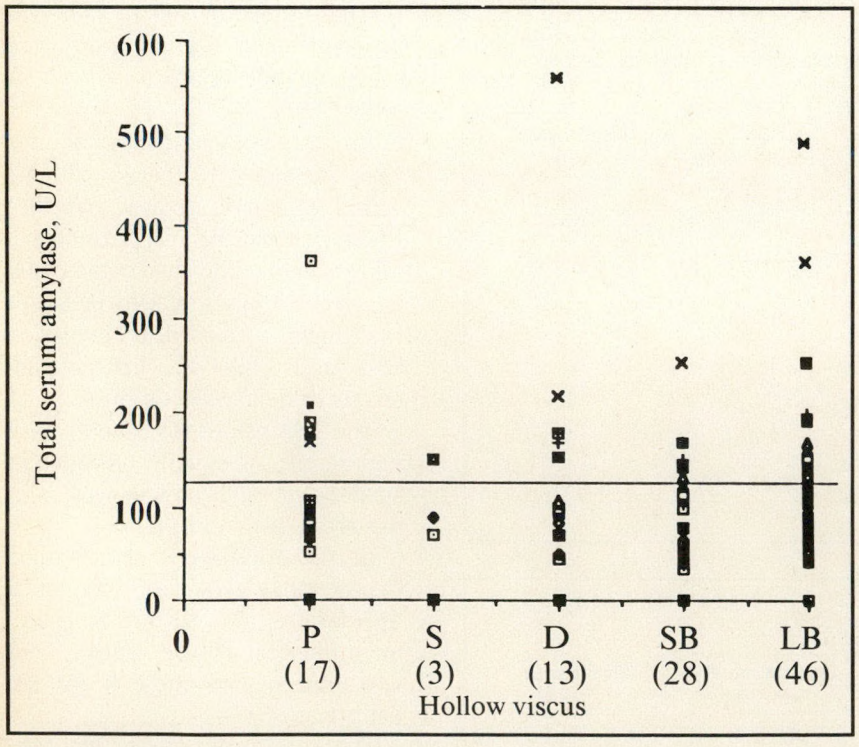

FIG. 2. Distribution of TSA among patients with blunt pancreatic and hollow-viscus injuries. Horizontal line indicates upper limit of normal (125 U/L) for TSA. P = pancreas, S = stomach, D = duodenum, SB = small bowel and LB = large bowel. Numbers in brackets indicate number of patients with respective injury.

Table V. Relationship Between Grade of Blunt Pancreatic Injury and Admission TSA Level in 16 Patients*

Grade[19]	TSA level, U/L
I	53,64,67,74,77, 95,96,98,170,178, 190,212
II	106,362
III	91
IV	86
V	None

*One patient had an unknown grade of pancreatic injury and a TSA level of 208 U/L.

value and sensitivity of hyperamylasemia as a test for pancreatic injury were 1.5% and 35.3% respectively. It is clear that an abnormal TSA level is a poor marker of pancreatic injury and that most patients with a pancreatic injury will have a normal TSA value. Reports of the efficacy of pancreatic isoamylases and lipase in evaluating the status of a blunt trauma victim have also been disappointing.[11,12] The quest for a simple blood test that will differentiate pancreatic from extrapancreatic injury continues.

It is well accepted that the serum amylase level does not correlate with the severity of acute pancreatitis.[28] There are many reports of severe pancreatic injuries in patients with normal TSA levels. In a series of 500 pancreatic injuries, only 65% of patients with complete pancreatic transection had elevated TSA levels.[14] In a study of endoscopic retrograde cholangiopancreatography in pancreatic trauma, the degree of hyperamylasemia did not correlate with ductal rupture.[29] Table V[19] relates the anatomic grade of the pancreatic injuries in our study to admission TSA levels. There was no clear relationship between the grade of pancreatic injury and the TSA level. Therefore, the admission TSA level is no measure of the severity of a pancreatic injury.

In both adults and children there are increasing reports of the conservative management of radiologically detected intra-abdominal injuries. Surprisingly, pancreatic injuries have been managed nonoperatively.[30,31] Clinical, laboratory and radiologic criteria are required for the proper institution of such conservative protocols. Our study clearly demonstrates that admission TSA determination is not an appropriate guide to the conservative management of patients with blunt pancreatic injuries.

Nontraumatic intestinal perforation and ischemia or infarction are associated with elevated TSA levels.[15] Pancreatic isoamylase is predominant because salivary amylase is degraded by gastric juice.[22] Blunt traumatic intestinal injuries have been associated with high serum amylase levels in 52% of cases.[16] Fig. 2 displays the distribution of TSA levels among patients with hollow-viscus injuries. As is evident, most hollow-viscus injuries (83.1%) are associated with normal TSA levels. The positive predictive value and sensitivity of abnormal TSA levels as a test for hollow-viscus injury were 3.0% and 16.9% respectively. Therefore, difficulty in the nonoperative diagnosis of blunt intestinal injury is not diminished by knowledge of the TSA levels.

Many factors may influence TSA concentrations in healthy subjects. Females have a higher mean TSA level than males.[32] In our trauma population, 9.5% of females and 9.0% of males had an abnormal TSA level. Mean TSA levels have been shown to increase with advancing age in both sexes.[32] In one study, TSA activity was very low in infants, reached adult levels in 10-year-old children and remained constant to the eighth decade, when there was a 40% increase.[33] The mechanism of age dependency of TSA concentration is thought to be an age-related decrease in renal function. It is interesting that there was no age difference between patients in the normal and abnormal TSA groups (Table I). However, trauma populations are skewed to young ages; thus, it is difficult to draw conclusions about the possible age dependency of TSA. There may be a genetic determinant of TSA, as observed by Tsianos and colleagues[34] in a study of residents of the United Kingdom. Dubick and associates[35] reported elevated serum amylase levels in cigarette smokers. These studies shed light on the complexity of amylase metabolism.

The relationship between brain injury and hyperamylasemia further confounds the clinical application of TSA levels in the trauma victim. It appears that severe brain injury, specifically intracranial bleeding, may activate pathways that increase TSA levels.[9] Vitale and colleagues[8] reported that 38% of patients with severe head injury had hyperamylasemia. In our study, 69 (12.2%) of 564 patients with an intracranial traumatic lesion on CT scan had hyperamylasemia. This group included patients with mild to moderate head injury, which may explain the lower incidence of hyperamylasemia. Patients in the abnormal TSA group had a significantly greater incidence of brain injury ($p < 0.01$) (Table II).

The pancreas is susceptible to ischemic injury, resulting in hyperamylasemia. Also, hyperamylasemia has been correlated with the degree of lactic acidosis and, separately, hypotension in the trauma victim.[10,36] In our study, patients with an abnormal TSA level had greater anatomic injury, as measured by ISS and GCS scores and an increased death rate ($p < 0.001$). The incidence of hypotension on admission was significantly higher in the abnormal amylase group ($p < 0.001$). Blood lactate concentration was not included in our study, but our findings indirectly support the association between lactic acidosis and hyperamylasemia. Thus, elevated TSA levels soon after a blunt traumatic event is an indirect predictor of the degree of anatomic and physiologic insult.

Hyperamylasemia has been well documented following oral or maxillofacial trauma. Isoamylase determinations confirmed the predominance of salivary hyperamylasemia in this subset of patients.[37] In our study population, 17% of patients

with facial fractures had an abnormal TSA level. Facial fractures were much more common in patients with an abnormal TSA level ($p < 0.01$) (Table II). Our findings confirm those of previous studies and cast further doubt on the utility of TSA estimation in the multiple trauma victim.

The association between alcohol consumption and pancreatitis is well described. Some have questioned whether acute alcohol consumption or binges raise serum amylase levels. Bloch, Weaver and Bouwman[20] reported that 30 of 58 clinically intoxicated individuals had hyperamylasemia, which was most frequently salivary in nature. In contrast, only 1% of patients with recent significant ethanol consumption had amylase elevations more than twice the upper limit of normal.[38] Our findings do not support a relationship between a positive ethanol screen following trauma and TSA, because the incidence of a positive ethanol screen was similar in patients with normal and abnormal TSA levels. Also, patients with a positive ethanol screen were equally as likely to have an abnormal TSA level as patients with a negative ethanol screen. The incidence of ethanol consumption in the blunt trauma victim appears to have no influence on acute TSA.

Blunt pancreatic injury is an uncommon lesion in blunt trauma. It is theorized that this is due to the well-protected retroperitoneal location of the pancreas and the high immediate mortality with associated intra-abdominal vascular injuries.[39] Blunt trauma victims should be assumed to have an intra-abdominal injury until such injury is excluded by either repeated clinical examinations, CT or diagnostic peritoneal lavage. In this study, the incidence of pancreatic injury (0.4%) among a large group of patients (4316) at risk for intra-abdominal injury would have been greater if we were to select patients with intra-abdominal injury or those undergoing laparotomy. However, the purpose of this study was to determine the utility of TSA determination in all trauma victims, not in a selected subgroup with heightened suspicion of abdominal injury.

It is important to emphasize that our study population consisted of patients transported directly from the accident scene. In Maryland's well-developed EMS system, prehospital response and transport times are minimized. The majority (66.2%) of patients are transferred from the accident scene by Maryland State Police helicopter. Thus, an admission TSA level is obtained on this group of patients very soon after the traumatic event. A rising TSA level after admission may indicate pancreatic injury.[40] Similarly, a patient transferred from a referring hospital, hours to days after trauma, may have a high TSA level. Our study did not evaluate the utility of TSA levels under these circumstances.

In the practice of surgery, utilization review and quality assessment of diagnostic tests have become increasingly important in efforts to curb escalating health care costs. For the 4316 patients in our study, the cost of routine TSA measurement was approximately $6500 over a 3-year period. Also, when faced with an elevated TSA level, clinicians may be inclined to perform expensive diagnostic procedures, delay enteral feedings and prolong nasogastric suctioning and hospital stay. With the demonstrated poor positive predictive value of TSA for pancreatic and hollow-viscus injury (1.5% and 3.0% respectively), enormous costs will be incurred to rule out intra-abdominal injuries. Clearly, early determinations of TSA in the trauma victim are of low cost-benefit. As the cost analysis of TSA has demonstrated, closer scrutiny of diagnostic procedures and tests that are regarded as routine in the evaluation of the trauma victim is required.

In conclusion, acute TSA determinations should not influence the clinical or radiologic evaluation of adults who are victims of blunt trauma.

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into and to read the critiques. I did not find it provided a true or penetrating test of any depth or breadth of surgical knowledge.

I believe this is a book that would be better borrowed than bought.

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SURGICAL REVASCULARIZATION OF THE HEART: THE INTERNAL THORACIC ARTERIES. Edited by George E. Green and Ram N. Singh. Illust. Igaku-Shoin Medical Publishers, Inc., New York. 1991. Price not stated. ISBN 0-89-640-198-7

The internal thoracic arteries have become standard conduits in coronary artery bypass surgery, due largely to the persistence and proselytizing of Dr. George Green, who pioneered the concept and who has edited this monograph.

This book's greatest virtue is a long chapter, written by Dr. Frank Sims, on the histologic features of the internal thoracic arteries, offering explanations for its resistance to atherosclerosis, and its excellent long-term patency. This chapter is lucidly written and contains excellent photomicrographs. It offers insight to surgeons on the rationale for the use of these vessels as bypass conduits.

The remainder of the text is devoted to issues that have been extensively covered elsewhere. The opening chapter is a concise history of coronary surgery by a participant in its beginnings, Dr. Donald Effler. Three chapters are devoted to the angiographic anatomy of these vessels, postoperative assessment of them and clinical results.

Eight chapters written by Dr. Green outline his philosophies and techniques of coronary bypass surgery, from making the incision and cannulating vessels for cardiopulmonary bypass to a discussion of postoperative management and complications. Since beginning these techniques, Dr. Green has used the operating microscope in place of the optical loupes favoured by most cardiac surgeons, and he extols the virtue of this instrument and his rationale for its use. There are many operative photographs detailing the differences in operative fields at different magnifications.

Dr. Green devotes a chapter to refuting the notion that spasm of these arteries can and does contribute to postoperative cardiac dysfunction. He has even reviewed the cinéangiograms of patients cited in case reports in the literature to back up his views.

The final chapter is a discussion of arterial conduits other than the internal thoracic arteries, including splenic, radial, right gastroepiploic and inferior epigastric arteries.

This small book should be of interest to many cardiac surgeons because of the interesting material on the histopathology of the internal thoracic arteries. The appeal of the remainder of the book will be limited, though the surgical technique of a fine and respected pioneer in coronary artery bypass surgery will always be of interest. It is conceivable that for housestaff it could serve as a primer for coronary artery surgery.

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THE PRINCIPLES OF TRAUMA SURGERY. Edited by Joseph A. Moylan. 343 pp. Illust. Gower Medical Publishers, New York. 1992. $155. ISBN 1-56375-013-9

This guide will attract anyone who is faced with emergency treatment of the multiply injured patient. Once one starts reading any of the 20 chapters that might be of particular interest, it is difficult to put the text down before reading it from cover to cover. In my experience of reviewing trauma texts over many years, this is one of the very best.

Multiple American authorities cover each of the subjects from the points of view of prehospital, emergency department and trauma specialists. Topics are covered thoroughly and concisely and are emphasized clearly with highlighted tables and illustrations. The subject matter is presented definitively, and where controversy exists, the schools of thought are explained. The pathophysiology of the mechanics of injury, respiratory failure and ventilatory support for both penetrating and blunt injury are clearly presented. Specific injuries to the face, neck, chest, abdomen and extremities are dealt with individually, and appropriate surgical exposure and techniques are described. Various organ injuries are classified by severity, and each classification of injury is separately described with regard to the most appropriate treatment. Pediatric trauma, various forms of nutrition, burn management and specific injuries to the face and hands are dealt with in detail. Each chapter is thoroughly referenced.

The organization of various levels of hospital trauma category are explained. This, I believe, is particularly important in Canada, where such great distances separate the major trauma centres. A thorough knowledge of the resource base of each hospital is extremely important so that undue delay in organizing transfer to a major trauma centre, where indicated, is avoided. The principles of advanced trauma life support (ATLS) are well covered, and, more importantly, the management beyond ATLS in resuscitation and specific treatment is appropriately explained.

I find it difficult to criticize this work because it is comprehensive and well done. However, some emphasis might have been directed toward the assessment of neurosurgical injury, indicating when further resuscitation is contraindicated. Similarly, the significance of certain orthopedic injuries such as the crushed, disrupted pelvis, which is frequently associated with blunt trauma to the colon and small bowel, and mesen-

continued on page 80

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THERAPEUTIC CLASSIFICATION

Analgesic Agent

ACTION

Toradol (ketorolac tromethamine) is a non-steroidal anti-inflammatory drug that exhibits analgesic activity. Its mode of action is to inhibit the cyclo-oxygenase enzyme system, thereby inhibiting the synthesis of prostaglandins, and is considered to be a peripherally acting analgesic. At analgesic doses it has minimal anti-inflammatory and antipyretic activity.

Ketorolac tromethamine is rapidly and completely absorbed when administered by both the oral and intramuscular routes, and pharmacokinetics are linear following single and multiple dosing.

Steady state plasma levels are attained after one day of Q.I.D. dosing. Based only on pharmacokinetic principles, a faster attainment of the steady state plasma level might be achieved with a loading dose of about twice the maintenance dose. This occurs when the dosing interval is approximately equal to the drug's half-life.

Following oral administration, peak plasma concentrations of 0.52 to 1.31 mcg/ml occurred 35 minutes after a single 10 mg dose. The terminal plasma elimination half-life ranged between 4.1 and 6.1 hours in healthy adults, while in elderly subjects (mean age: 72 years) it ranged between 3.0 and 6.1 hours. A high fat diet decreased the rate but not the extent of absorption of oral ketorolac tromethamine, while antacid had no effect.

Following intramuscular administration, peak plasma concentrations of 2.2 to 3.0 mcg/ml occurred an average of 50 minutes after a single 30 mg dose. The terminal plasma half-life ranged between 3.8 and 6.3 hours in young adults and between 4.4 and 8.6 hours in elderly subjects (mean age: 72).

The primary route of excretion of ketorolac tromethamine and its metabolites (conjugates and the p-hydroxy metabolite) is in the urine (91.4%) and the remainder is excreted in the feces.

More than 99% of the ketorolac in plasma is protein bound over a wide concentration range.

INDICATIONS

Orally administered Toradol (ketorolac tromethamine) is indicated for the short-term management of mild to moderately severe pain, including post-surgical pain (such as general, orthopedic and dental surgery), acute musculoskeletal trauma pain and post-partum uterine cramping pain.

Intramuscular injection of Toradol is indicated for the short-term management of moderate to severe pain, including pain following major abdominal, orthopedic and gynecological operative procedures.

CONTRAINDICATIONS

Toradol (ketorolac tromethamine) should not be used where there is a known or suspected hypersensitivity to the drug. Because of the possibility of cross-sensitivity, ketorolac tromethamine should not be used in patients in whom acetylsalicylic acid (ASA) or other non-steroidal anti-inflammatory agents induce acute asthmatic attacks, urticaria, rhinitis or other allergic manifestations. Fatal anaphylactoid reactions may occur in such individuals.

Toradol (ketorolac tromethamine) also should not be used in patients with peptic ulcer or active inflammatory disease of the gastrointestinal system.

WARNINGS

Long-term administration of ketorolac tromethamine oral formulation has shown that this drug shares the risks that other non-steroidal anti-inflammatory drugs pose to patients when taken chronically. Peptic ulceration, perforation and gastrointestinal bleeding, sometimes severe and occasionally fatal have been reported during therapy with non-steroidal anti-inflammatory drugs and may occur with ketorolac tromethamine, both in the presence or absence of previous symptoms. Elderly and debilitated individuals are most susceptible to these complications, the incidence of which increases with dose and duration of treatment. Close medical supervision is recommended in patients prone to gastrointestinal tract irritation, particularly those with a history of peptic ulcer, diverticulosis or other inflammatory disease of the gastrointestinal tract. In these cases the physician must weigh the benefits of treatment against the possible hazards.

Patients taking any non-steroidal anti-inflammatory drug including ketorolac tromethamine should be instructed to contact a physician immediately if they experience symptoms or signs suggestive of peptic ulceration or gastrointestinal bleeding. These reactions can occur at any time during the treatment. If peptic ulceration is suspected or confirmed, or if gastrointestinal bleeding occurs, ketorolac tromethamine should be discontinued and appropriate treatment instituted and the patient closely monitored.

Ketorolac tromethamine is not recommended for routine use with other non-steroidal anti-inflammatory drugs because of the potential for additive side effects.

Use in pregnancy, lactation and labour: The administration of ketorolac tromethamine is not recommended during pregnancy or lactation.

Ketorolac tromethamine is not recommended for use as an obstetrical preoperative medication or for obstetrical analgesia because of the known effects of non-steroidal anti-inflammatory drugs on uterine contraction and fetal circulation.

Use in children: Safety and efficacy in children have not been established. Therefore, Toradol is not recommended for use in children under age 16.

Use in the elderly: Because ketorolac is cleared somewhat more slowly by the elderly (See PHARMACOKINETICS) who are also more sensitive to the renal effects of non-steroidal anti-inflammatory drugs, extra caution and the lowest effective dose should be used.

PRECAUTIONS

Renal effects: As with other drugs that inhibit prostaglandin biosynthesis, elevations of blood urea nitrogen (BUN) and creatinine have been reported in clinical trials with ketorolac tromethamine. Since ketorolac tromethamine and its metabolites are excreted primarily by the kidney, patients with significant impairment of renal function (serum creatinine values greater than 5 mg/dL) should not receive ketorolac tromethamine unless the expected benefits outweigh the risks. In patients with moderately impaired renal function serum creatinine values ranging from 1.9 to 5.0 mg/dL, the rate of ketorolac clearance was reduced to approximately half of normal. The total daily dose of ketorolac tromethamine should be reduced by half in such patients. The disposition of ketorolac in dialysis patients has not been studied.

Patients who are volume depleted because of blood loss or severe dehydration may be dependent on renal prostaglandin production to maintain renal perfusion and therefore glomerular filtration rate. In such situations the use of drugs which inhibit prostaglandin synthesis might be expected to further decrease renal blood flow. Caution is advised if ketorolac tromethamine is used in such circumstances. Close monitoring of urine output, serum urea and serum creatinine is recommended until the patient is normovolemic.

Hepatic effects: Meaningful elevations (greater than 3 times normal) of serum transaminases (glutamate pyruvate (SGPT or ALT) and glutamic oxalacetic (SGOT or AST)) occurred in controlled clinical trials in less than 1% of patients. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), ketorolac tromethamine should be discontinued. Patients with impaired hepatic function from cirrhosis do not have any clinically important changes in ketorolac tromethamine clearance. Studies in patients with active hepatitis or cholestasis have not been performed.

Fluid and electrolyte balance: Fluid retention and edema have been observed in patients treated with Toradol. Therefore, as with many other non-steroidal anti-inflammatory drugs, the possibility of precipitating congestive heart failure in elderly patients or those with compromised cardiac function should be borne in mind. Toradol should be used with caution in patients with cardiac decompensation, hypertension or other conditions predisposing to fluid retention.

Hematologic effects: Ketorolac tromethamine inhibits platelet function and may prolong bleeding time. It does not affect platelet count, prothrombin time (PT) or partial thromboplastin time (PTT). Patients who have coagulation disorders or are receiving drug therapy that interferes with hemostasis should be carefully observed when ketorolac tromethamine is administered. Unlike the prolonged effects from aspirin, the inhibition of platelet function by ketorolac tromethamine is normalized within 24 to 48 hours after the drug is discontinued.

Blood dyscrasias associated with the use of non-steroidal anti-inflammatory drugs are rare, but could occur with severe consequences.

Infection: In common with other anti-inflammatory drugs, ketorolac tromethamine may mask the usual signs of infection.

Drug Interactions: Toradol (ketorolac tromethamine) is highly bound to human plasma protein (mean 99.2%) and binding is independent of concentration.

Prothrombin time should be carefully monitored in all patients receiving oral anticoagulant therapy concomitantly with ketorolac tromethamine.

Ketorolac tromethamine does not alter digoxin protein binding.

In vitro studies indicated that at therapeutic concentrations of salicylates (300 mcg/mL), the binding of ketorolac tromethamine was reduced from approximately 99.2% to 97.5%. Therapeutic concentrations of digoxin, warfarin, acetaminophen, phenytoin, tolbutamide and piroxicam did not alter ketorolac tromethamine protein binding. Since ketorolac tromethamine is a highly potent drug and present in low concentrations in plasma, it would not be expected to displace other protein-bound drugs significantly.

There is no evidence in animal or human studies that ketorolac tromethamine induces or inhibits the hepatic enzymes capable of metabolizing itself or other drugs. Hence, it would not be expected to alter the pharmacokinetics of other drugs due to enzyme induction or inhibition mechanisms.

Ketorolac tromethamine mildly reduces the diuretic response to furosemide in normovolemic subjects. Inhibition of renal lithium clearance leading to an increase in plasma lithium concentration and potential lithium toxicity has been reported with some non-steroidal anti-inflammatory drugs. The effect of ketorolac tromethamine on lithium plasma levels has not been studied.

Concomitant administration of methotrexate and some non-steroidal anti-inflammatory drugs have been reported to reduce the clearance of methotrexate, enhancing the toxicity of methotrexate. The effect of ketorolac tromethamine on methotrexate clearance has not been studied.

There is limited experience on concurrent administration with morphine. Available information shows no evidence of adverse interactions. The extent of a possible narcotic-sparing effect of ketorolac tromethamine is currently under investigation.

ADVERSE EFFECTS

Toradol tablets: The incidence of adverse reactions in approximately 600 patients and subjects receiving short-term oral therapy (less than 2 weeks) with Toradol (ketorolac tromethamine) are listed below. The most common adverse effects include: Gastrointestinal: dyspepsia (2%), gastrointestinal pain (2%), nausea (2%). Central nervous system: headache (2%), dizziness (2%).

The following adverse events are rare but have been reported (less than 1%): Gastrointestinal: flatulence, gastritis. Respiratory: dyspnea. Dermatologic: urticaria, rash, pruritus. Metabolism/nutritional: edema. Body as a whole: asthenia. Hemic and lymphatic: purpura. Musculoskeletal: myalgia.

Toradol IM: The adverse reactions listed below were reported to be probably related to Toradol IM in clinical trials in which patients received up to 20 doses of 30 mg of intramuscularly administered Toradol over a period of up to five days.

Incidence between 3 and 9%: Gastrointestinal: nausea, dyspepsia, gastrointestinal pain. Central nervous system: drowsiness.

Incidence between 1 and 3%: Gastrointestinal: diarrhea. Central nervous system: dizziness, headache, sweating. Body as a whole: edema. Injection site pain was reported by 2% of patients in multi-dose studies (vs. 5% for morphine control group).

Incidence 1% or less: Gastrointestinal: constipation, flatulence, gastrointestinal fullness, liver function abnormalities, melena, peptic ulcer, rectal bleeding, stomatitis, vomiting. Body as a whole: asthenia, myalgia. Cardiovascular: vasodilatation, pallor. Hemic and lymphatic: purpura. Nervous system: dry mouth, nervousness, paresthesia, abnormal thinking, depression, euphoria, excessive thirst, inability to concentrate, insomnia, stimulation, vertigo. Respiratory: dyspnea, asthma. Urogenital: increased urinary frequency, oliguria. Dermatologic: pruritus, urticaria. Special senses: abnormal taste, abnormal vision.

OVERDOSAGE

The absence of experience with acute overdosage precludes characterization of sequelae and assessment of antidotal efficacy at this time. In a gastroscopic study of healthy subjects, daily doses of 360 mg given over an 8-hour interval for each of five consecutive days (3 times the highest recommended dose) caused abdominal pain and peptic ulcers which recovered after discontinuation of dosing.

DOSAGE AND ADMINISTRATION

Adults: Dosage should be adjusted according to the severity of the pain and the response of the patient.

Oral: The usual oral dose of Toradol (ketorolac tromethamine) is 10 mg every 4 to 6 hours for pain as required. Doses exceeding 40 mg per day are not recommended.

Toradol is recommended for short-term use only i.e. for a maximum of a few weeks.

Parenteral: The recommended usual initial dose is 30 mg. Subsequent dosing may be 10 mg to 30 mg every 4-6 hours as needed to control pain. A lower initial dose may be suitable for patients under 50 kg in body weight, over age 65years and/or with less severe pain at baseline. In the initial post-operative period, more frequent dosing (e.g., every 2 hours) may be employed, but the total daily dose should not exceed 120 mg. Dose above 120 mg could cause drug toxicity (see Warnings & Precautions). If supplemental analgesia is required, a concomitant low dose of opiate can be used.

The administration of continuous multiple daily doses of Toradol IM should not exceed 5 days for Injection dosing. There has been limited experience with dosing for more than 5 days since the vast majority of patients have transferred to oral medication or no longer required analgesic therapy after this time.

Directions for use: Insert the plunger into the syringe barrel and thread it onto the screw. WITHOUT REMOVING THE NEEDLE GUARD, apply quick, firm pressure to the plunger to break the inner seal (you will feel it let go). Pull back on the plunger slightly to relieve pressure. Remove the needle guard by twisting as you pull. Use the unit as you would a normal syringe. Dispose of properly. Single use only. Discard unused portions.

CONVERSION FROM PARENTERAL TO ORAL THERAPY

Toradol tablets may be used either as monotherapy or as follow-on therapy to parenteral ketorolac. In the latter case, the total combined daily dose of ketorolac should not exceed 120 mg on the day the change of formulation is made, this includes a maximum of 4 of the 10 mg tablets.

Toradol (ketorolac tromethamine) is a Schedule F drug.

COMPOSITION

Toradol Tablets: Each Toradol tablet contains ketorolac tromethamine, the active ingredient, with microcrystalline cellulose, lactose and magnesium stearate. The coating suspension contains hydroxy-propyl-methylcellulose, titanium dioxide and polyethylene glycol.

Toradol IM: Toradol IM is available for intramuscular administration as: 15 mg in 1 mL (1.5%), or 30 mg in 1 mL (3%) of ketorolac tromethamine in sterile solution. The 15 mg/mL solution contains 10% (w/v) alcohol, USP, and 6.68 mg sodium chloride in sterile water. The 30 mg/mL solution contains 10% (w/v) alcohol, USP and 4.35 mg sodium chloride in sterile water. The pH is adjusted with sodium hydroxide or hydrochloric acid. The sterile solutions are clear and slightly yellow in colour.

STABILITY AND STORAGE RECOMMENDATIONS

Toradol Tablets: Store at room temperature. The blister package tablets should be protected from light.

Toradol IM: Store at room temperature with protection from light.

AVAILABILITY OF DOSAGE FORMS

Toradol (ketorolac tromethamine) is available as 10 mg white round film coated tablets with one side printed in red with TORADOL inside a bold T and the other side with Syntex. Toradol (ketorolac tromethamine) 10 mg tablets are available in bottles of 100 and 500 tablets.

Toradol IM is available in 1 mL syringes containing 15 or 30 mg/mL of ketorolac tromethamine.

Product Monograph available on request.

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Laparoscopic Gastrointestinal Anastomoses

Dawn L. Anderson, BSc(Med), MD; Patrick J. O'Regan, MB, BCh, BAO, FRCSC

In a preliminary study of laparoscopic gastrointestinal anastomosis, a gastric outlet obstruction was created under laparoscopic control in six domestic pigs, weighing an average of 25 kg. A simultaneous gastroenterostomy was formed with an end-stapling device. All animals recovered clinically, and good anastomotic healing was documented 1 week postoperatively. The authors suggest that an end-stapling device could be one method of creating a gastrointestinal anastomosis for humans that is safe and reliable, allows rapid recovery and decreases hospital stay.

Au cours d'une étude préliminaire portant sur l'anastomose gastro-intestinale laparoscopique, une obstruction de la sortie gastrique a été créée sous contrôle laparoscopique chez six porcs domestiques pesant, en moyenne, 25 kg. Concomitamment, une gastroentérostomie a été effectuée à l'aide d'une agrafeuse à alimentation par le bout. Tous les animaux ont récupéré cliniquement et le succès de de l'anastomose a été vérifié 1 semaine après l'opération. Les auteurs suggèrent qu'une agrafeuse à alimentation par le bout pourrait servir à créer une anastomose gastro-intestinale chez l'humain de façon sûre et fiable, tout en assurant une guérison rapide et en diminuant le temps d'hospitalisation.

Since the report in 1989 on laparoscopic cholecystectomy,[1] the age of videoendoscopic general surgery has been expanding at an explosive rate. Laparoscopic cholecystectomy and appendectomy are common,[2-4] and techniques for other procedures are being rapidly developed. In this paper we describe a technique of laparoscopic gastroduodenostomy in domestic pigs using an end-stapling device, and we discuss possible human applications.

Materials and Methods

Six domestic pigs weighing 25 kg each were used for this study. Under general anesthesia and with antibiotic coverage, a Veress needle was used to create a pneumoperitoneum with a Storz 9.9-L high-flow insufflator (Laparoflator 26012C; Karl Storz, Tuttlingen, Germany). A Storz ST-615C xenon light source, ST 599C flash generator, ST 9050 Supercam laparoscopic camera and a Sony Trinitron monitor (model PVM 1943 MD; Sony Corp., Tokyo, Japan) were used, all supplied on loan for research purposes by R. Laborie Surgical Ltd. (Brossard, Que.), as were all of the laparoscopic instruments. A forward-viewing laparoscope was inserted near the umbilicus, and three additional working ports made up the total of four punctures. Ampicillin and gentamicin were used perioperatively for antibiotic prophylaxis.

A gastric outlet obstruction was created by placement of a ligature of 0 Prolene around the proximal duodenum and tying it tight with a Roeder loop knot. The duodenum was chosen as the small-bowel segment to use in the anastomosis, because in the pig the duodenum is long, has an easily mobilized portion and is of similar diameter and wall thickness to human jejunum. This type of procedure performed in humans would most likely use the jejunum. A segment of duodenum distal to the obstruction was brought up to the anterior wall of the stomach where it was held by corner stay sutures placed directly through the abdominal wall. Openings were made in stomach and duodenum with cautery and scissors. An Endopath, single-loading end-stapling device (Figs. 1 and 2) applied on loan by Ethicon, Peterborough, Ont., was used to place 15 titanium staples individually along the back and front walls of a 2-cm diameter anastomosis. The animals were kept on intravenous hydration for 24 hours. Their diet was advanced over 3 days, and they were killed 1 week postoperatively. The site of gastroduodenostomy was examined with the organs intact, the stomach was then opened to allow inspection and measurement of the anastomosis. A probe was also inserted through the pylorus to confirm that the laparoscopically created gastric outlet obstruc-

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tion was complete. The appearance was recorded photographically.

Results

In terms of visual and manual examination, healing of the gastroduodenal anastomosis was virtually complete in all six animals at the time of sacrifice (Fig. 3). The anastomotic diameter was always between 15 and 20 mm. In every case the obstructing suture around the proximal duodenum was intact, confirming that the anastomosis was the sole route of gastric emptying.

One animal, the second in the series, showed signs of intermittent obstruction, manifested by vomiting after ingestion of large amounts of food or water. It tolerated frequent small liquid feeds, however. At autopsy it was found that, although the anastomosis itself was well healed and widely patent, the loop of duodenum used had been inadvertently twisted 360° intraoperatively, causing the short afferent limb to obstruct the efferent limb whenever the stomach was very distended.

Two animals appeared sick postoperatively, but the attending veterinarian diagnosed the source of their sepsis as pneumonia, and they were given appropriate antibiotics. In both animals, the diagnosis of respiratory infection, not intra-abdominal infection, was confirmed after sacrifice.

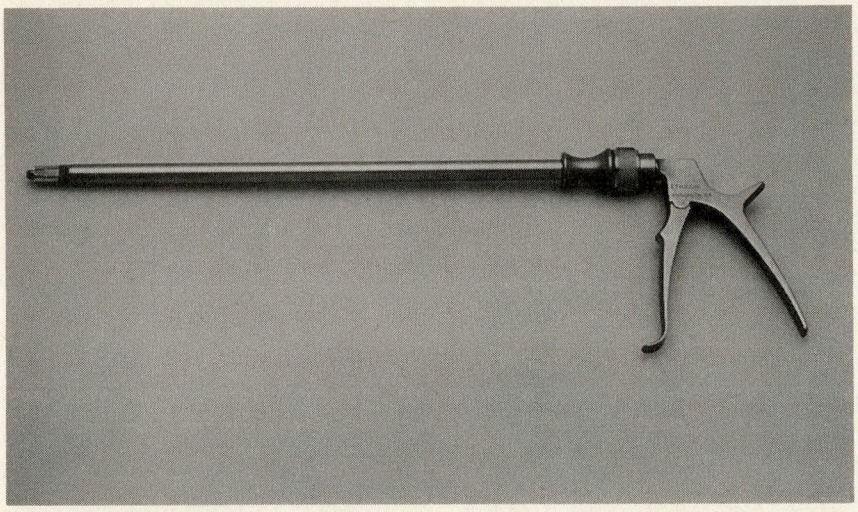

FIG. 1. Endopath (Ethicon, Peterborough, Ont.) end-stapling device.

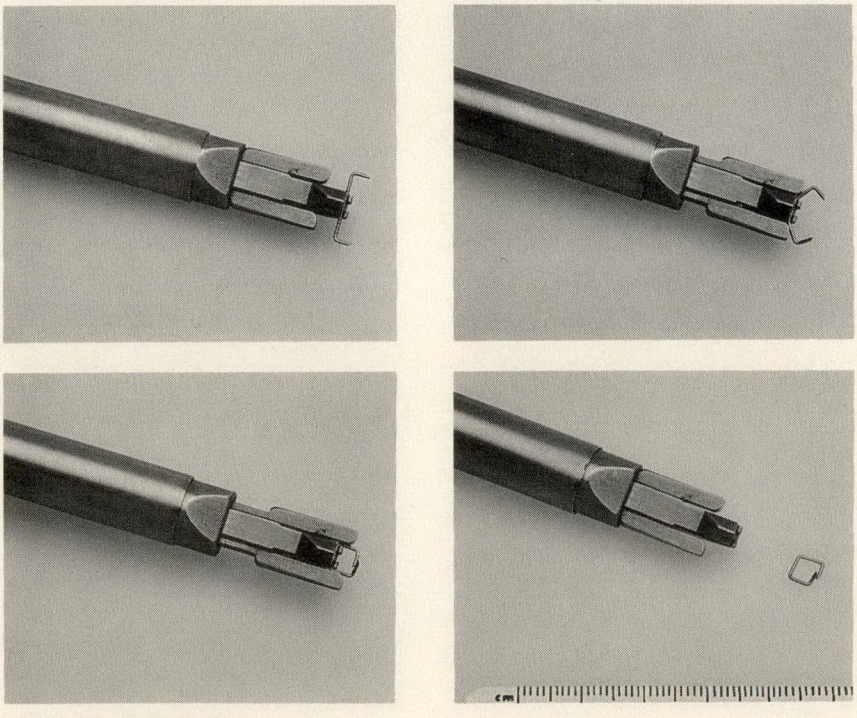

FIG. 2. Staple formation.

Discussion

The benefits of laparoscopic over traditional open general surgical techniques have only been well documented for a few procedures such as cholecystectomy and appendectomy.[5–7] However, extrapolation from the observed decrease in postoperative pain, length of hospitalization and rapidity of return to work has led many surgeons to explore the frontiers of this technology. Many reports are found in the literature of familiar common operations with well-established indications being performed under laparoscopic control, such as vagotomy, Nissen fundoplication, feeding jejunostomy and others.[8–11] There are many situations that require bypassing a segment of the gastrointestinal or biliary tract for established benign or malignant obstruction or for prophylaxis as with a vagotomy. A substantial benefit of decreased narcotic analgesics would be more rapid recovery of gastrointestinal function. For patients with malignant disease and reduced life-

span, the avoidance of a major laparotomy, especially for a palliative procedure, would certainly add to their quality of life. Thus, laparoscopic cholecystojejunostomy, with use of the end-stapling device, might be appropriate treatment in certain cases of obstructive jaundice due to carcinoma of the head of the pancreas.

Conclusions

The ability to perform a safe, reliable gastrointestinal anastomosis under laparoscopic control would allow a wide variety of patients the same benefits in terms of rapid recovery and decreased hospital stay currently enjoyed by patients who undergo laparoscopic cholecystectomy. The authors suggest that an end-stapling device is one method of creating a suitable anastomosis for humans. This technique could also be used to supplement other methods — to complete an endoscopic anastomosis, as an adjunct to other stapling devices or for suturing. An appropriate multifire instrument would reduce operating time.

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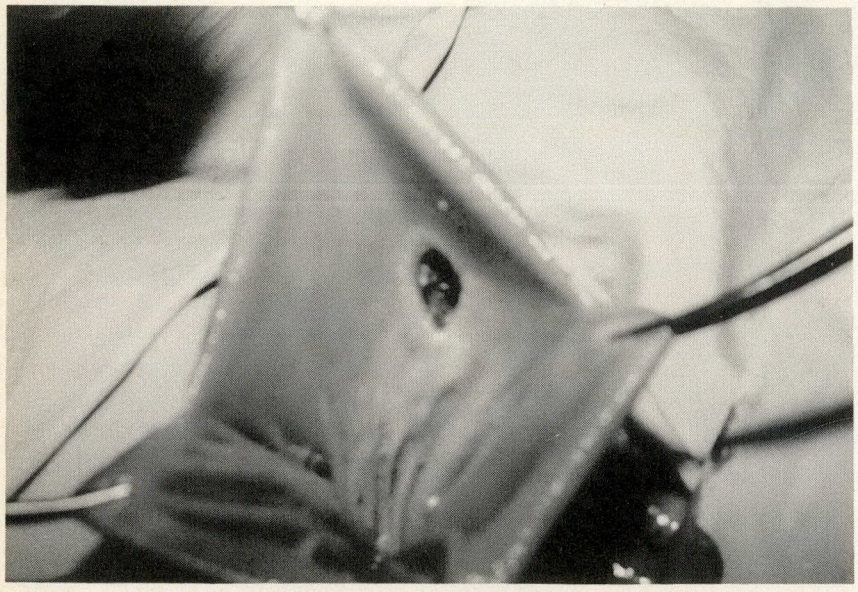

FIG. 3. Autopsy view of stomach with healing anastomosis.

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Open Cholecystectomy: Its Morbidity and Mortality as a Reference Standard

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In a retrospective study of 10 471 cholecystectomies, performed between 1971 and 1990, the incidence and causes of death and morbidity of cholecystectomy were analysed. There were 47 postoperative deaths (0.4%); 6 deaths occurred in 5841 patients less than 50 years old, 23 in 3898 patients between 50 and 70 years old and 18 in 732 patients more than 70 years old. Death rates in each group were, respectively, 0.1%, 0.6% and 2.5% ($p < 0.001$). The death rate in 9339 patients who had cholecystectomy alone was 0.3% and the death rate in 1132 patients who had a concomitant common bile duct exploration (CBDE) was 1.6% ($p < 0.001$). Cardiovascular complications were the main cause of death, and biliary, pulmonary and wound complications were the most common. There were 614 complications in 529 patients; 176 of these patients were less than 50 years old, 252 were between 50 and 70 years old and 101 were more than 70 years old. Complication rates were, respectively, 3.0%, 6.5% and 13.8% ($p < 0.001$). For patients with cholecystectomy alone the morbidity was 3.6% and for patients who had a concomitant CBDE the morbidity was 17% ($p < 0.001$). The mortality and morbidity of cholecystectomy increase significantly with age and a concomitant CBDE. However, patients who underwent cholecystectomy electively or for acute cholecystitis had comparable mortality and morbidity.

Dans une étude rétrospective portant sur 10 471 cholécystectomies effectuées entre 1971 et 1990, on a analysé la fréquence et les causes de la mortalité et de la morbidité. Quarante-sept décès postopératoires ont été enregistrés (0,4 %); 6 décès sont survenus chez 5841 patients de moins de 50 ans, 23 chez 3898 patients de 50 à 70 ans et 18 chez 732 patients de plus de 70 ans. La mortalité dans chaque groupe a été, respectivement, de 0,1 %, 0,6 % et 2,5 % ($p < 0,001$). La mortalité chez 9339 patients qui avaient subi une cholécystectomie simple a été de 0,3 %, alors qu'elle était de 1,6 % chez 1132 patients qui avaient eu, concurremment, une exploration du cholédoque (EC) ($p < 0,001$). Les complications cardiovasculaires représentent la principale cause de décès, alors que les complications biliaires, pulmonaires et de plaies ont été les plus fréquentes. Il y a eu 614 complications chez 529 patients (5 %); 176 patients avaient moins de 50 ans, 252 patients, entre 50 et 70 ans et 101, plus de 70 ans. Les taux de morbidité respectifs étaient de 3,0 %, 6,5 % et 13,8 % ($p < 0,001$). La morbidité chez les patients qui ont subi une cholécystectomie simple a été de 3,6 %, contre 17 % ($p < 0,001$) pour les patients qui ont eu une EC concurrente. La mortalité et la morbidité reliées à la cholécystectomie augmentent significativement avec l'âge et avec l'exécution d'une EC concomitante. Toutefois, la mortalité et la morbidité ont été comparables, que les patients aient subi une cholécystectomie non urgente ou pour une cholécystite aiguë.

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Cholecystectomy has been the standard therapy for patients with symptomatic gallstone disease for many decades and has proven to be a safe and effective procedure. The mortality and morbidity are low.[1-6] Long-term results are excellent, with most patients being asymptomatic after surgery.[5] Despite the good results with traditional cholecystectomy, the treatment of gallstones has undergone drastic changes in the past few years. Several alternative nonsurgical options for the management of biliary lithiasis have been introduced, including extracorporeal shockwave lithotripsy,[6] chemical dissolution[7] and endoscopic and percutaneous extraction.[8] More recently, laparoscopic cholecystectomy has emerged as a promising surgical alternative to traditional cholecystectomy,[9] We carried out a retrospective study of traditional cholecystectomy to analyse the incidence and causes of mortality and morbidity and to compare our experience with that of others.

Patients and Methods

The medical records of 10 501 patients who underwent cholecystectomy between April 1971 and April 1990 at Maisonneuve-Rosemont Hospital were reviewed. Excluded from the analysis were 30 patients who died after cholecystectomy but in whom the cause of death was unrelated to the procedure. Twenty-two of these patients died of complications secondary to

major surgery in which cholecystectomy was only incidental. The other eight patients died of serious diseases up to 90 days after cholecystectomy performed for acute cholecystitis, which complicated the course of their disease.

Among the remaining 10 471 patients, 6574 (63%) underwent cholecystectomy alone, 2765 (26%) underwent cholecystectomy with other concomitant non-biliary procedures (the most frequent being incidental appendectomy, hernia repair, tubal ligation and liver biopsy) and 1132 (11%) underwent cholecystectomy with common bile duct exploration (CBDE) for presumed choledocholithiasis.

Most of the operations were performed by a right subcostal incision. Cholecystectomy was usually performed from the porta hepatis to the fundus (anterograde) after identification of the anatomic structures at the porta hepatis. If it was impossible or unsafe to perform anterograde cholecystectomy, usually because of acute cholecystitis, cholecystectomy was then performed from the fundus downward to the porta hepatis (retrograde). Routine operative cholangiography was performed when technically possible. Cholecystitis was considered acute when inflammation and edema of the gallbladder were present at operation and confirmed histopathologically. Until 1976, the subhepatic space was drained in every case with a soft Penrose drain. After 1976, a drain was used less frequently, and since 1985 it has been used selectively in patients who had a cholecystectomy for acute cholecystitis or a cholecystectomy with CBDE. When choledochotomy was performed, the common duct was closed over a T tube.

Differences were analysed by the χ^2 test. Differences were considered statistically significant at $p < 0.05$.

Findings

Of the 10 471 patients, 7277 (69.5%) were female and 3194 (30.5%) were male. There were 5841 (55.8%) patients less than 50 years of age, 3898 (37.2%) between 50 and 70 years of age and 732 (7.0%) more than 70 years of age. The youngest patient was 7 years old and the oldest was 96 years old. Routine intraoperative cystic duct cholangiography was performed when technically possible, in approximately 90% of the patients. Histopathological examination of the gallbladder showed chronic calculous cholecystitis in 8484 (81.0%), chronic acalculous disease in 296 (2.8%), acute calculous cholecystitis in 1639 (15.7%) and acute acalculous cholecystitis in 52 (0.5%).

Deaths

Forty-seven patients died, for an overall mortality of 0.4%. Six (0.1%) were younger than 50 years, 23 (0.6%) were between 50 and 70 years and 18 (2.5%) were older than 70 years. The difference between each group is significant ($p < 0.001$). The indications for operation in those who died are shown in Table I. Twenty-two of them had either associated acute pancreatitis or jaundice, or both, at the time of surgery. Four had acute suppurative cholangitis.

The surgical procedures performed for chronic and acute cholecystitis and the death rates are depicted in Table II. Among the 8780 patients with chronic disease, 36 died (0.4%), while among the 1691 patients with acute cholecystitis, 11 died (0.6%). This difference is not significant, and patients with acute cholecystitis had a death rate comparable to that of patients who underwent elective cholecystectomy. The death rate in 9339 patients who had cholecystectomy alone was 0.3%, whereas in 1132 patients who had cholecystectomy with CBDE the death rate was 1.6% ($p < 0.001$). Death rates according to

Table I. Indications for Operation in Patients Who Died After Cholecystectomy

Indication	No. of patients	No. with associated disease	
		Acute pancreatitis	Jaundice
Chronic cholecystitis	36	7	8
With cholelithiasis	22	3	0
With choledocholithiasis	14	4	8
Acute cholecystitis	11	2	5
With cholelithiasis	7	2	1
With choledocholithiasis	4	0	4

Table II. Surgical Treatment for Acute and Chronic Cholecystitis

Treatment	Chronic cholecystitis			Acute cholecystitis		
	No. of patients	No. of deaths	%	No. of patients	No. of deaths	%
Cholecystectomy	7841	22	0.3	1498	7	0.5
Cholecystectomy with CBDE	939	14	1.5	193	4	2.1
Total	8780	36	0.4	1691	11	0.6

age and type of cholecystitis are shown in Table III. The only significant difference found was in patients with acute cholecystitis: in patients between 50 and 70 years of age the death rate was 0.4%, whereas in patients over 70 years of age the death rate was 4.0% ($p < 0.005$). The most frequent cause of postoperative hospital death was cardiovascular complications (Table IV), which accounted for 50% of the deaths. Among the 23 patients who died of cardiovascular complications, 10 had myocardial infarction, 4 had cardiac insufficiency, 3 had pulmonary embolism, 2 had mesenteric thrombosis, 2 had cerebrovascular thrombosis, 1 had endocarditis and 1 had a dissecting thoracic aneurysm. There were nine intra-abdominal extrahepatic deaths caused by perforated duodenal ulcer in three patients, abscess in three patients and gastrointestinal bleeding in two patients. The other patient died of a duodenal fistula with peritonitis after an emergency procedure for biliary ileus, during which a cholecystectomy with repair of a cholecystoduodenal fistula was also performed. Six of these patients had cholecystectomy with CBDE and had pancreatitis or jaundice, or both, at surgery.

Six patients died of hepatobiliary complications, five of them after cholecystectomy with CBDE. Three deaths were attributed to septicemia in patients with acute suppurative cholangitis at operation, and two deaths were caused by hepatic insufficiency. The other patient died of a prolonged biliary fistula with dehydration 4 months after a cholecystectomy with CBDE. The other causes of death were pulmonary (four patients) and renal (one patient) complications, infection from a fulminant necrosis of the abdominal wall (one patient) and undetermined causes (three patients).

Postoperative Complications

Postoperative complications were found in 529 patients (5.1%). Of these, 176 patients (3.0%) were less than 50 years old, 252 patients (6.5%) were between 50 and 70 years old and 101 patients (13.8%) were more than 70 years of age. The difference between each group is significant ($p < 0.001$). In those who underwent cholecystectomy alone, 121 patients less than 50 years old had complications (morbidity 2.3%), 169 patients between 50 and 70 years old had complications (morbidity 5.0%) and 47 patients more than 70 years old had complications (morbidity 9.2%) ($p < 0.01$). Among the 8742 patients with chronic disease, 403 (4.6%) had complications, whereas among the 1680 patients with acute cholecystitis, 126 (7.5%) had complications. The incidence of complications after cholecystectomy alone was 3.6% (3.1% for chronic cholecystitis and 6.1% for acute cholecystitis) whereas after cholecystectomy with CBDE the incidence was 17% (16% for chronic cholecystitis and 24% for acute cholecystitis) ($p < 0.001$).

In the 529 patients, 614 complications were seen, the most frequent being biliary, pulmonary and wound complications. There were 169 wound complications among which 126 were infected wounds. Pulmonary complications were seen in 140 patients. Among the 174 biliary complications, 75 were external biliary fistulas, 64 were residual stones and 5 were bile peritonitis. In addition, there were 30 in-

Table IV. Causes of Death

Cause	Procedure, no. of patients: Cholecystectomy	Cholecystectomy with CBDE	Total
Cardiovascular	17	6	23
Intra-abdominal (extra-hepatic)	3	6	9
Hepatobiliary	1	5	6
Pulmonary	3	1	4
Infectious	1	0	1
Renal	1	0	1
Undetermined	3	0	3
Total	29	18	47

Table III. Age-related Mortality and Type of Cholecystitis

Age, yr	Chronic cholecystitis: No. of patients	No. of deaths	%	Acute cholecystitis: No. of patients	No. of deaths	%	
< 50	5089	5	0.1	752	1	0.1	
50 – 70	3145	20	0.6	753	3	0.4	*
> 70	546	11	2.0	186	7	4.0	*
Total	8780	36	0.4	1691	11	0.6	

*$p < 0.005$

traoperative bile duct injuries (0.3%); 24 occurred in 9339 patients who had cholecystectomy alone: 17 were considered minor (small lacerations or punctiform wounds) and 7 were considered major (section or ligation). Eighteen bile duct injuries occurred during cholecystectomy for chronic cholecystitis and 6 during cholecystectomy for acute cholecystitis. There were 6 cases of trauma to the common or right hepatic duct, 12 in the area of the cystocholedochal junction, 5 in the common bile duct and 1 in a right accessory hepatic duct. Except for one, all these traumas were recognized at the initial operation and repaired. The only unrecognized trauma was a partial section of the common hepatic duct, which led to a prolonged postoperative biliary fistula and later bile duct stenosis. This stenosis was repaired 1 year later by a Roux-en-Y hepaticojejunostomy. Two other patients had reoperation for drainage of a bile collection.

Two of the six bile duct injuries that occurred during cholecystectomy with CBDE were major and four were minor. All were recognized and repaired at initial operation with no further problem.

The other complications that should be mentioned were intra- or postoperative hemorrhage in 20 patients, postoperative intra-abdominal abscesses in 21 patients and cardiovascular nonlethal complications in 26 patients.

Sixty-seven patients underwent a second procedure for complications 1 to 45 days after cholecystectomy, the most frequent being closure of wound dehiscence, drainage of an intra-abdominal abscess and control of postoperative bleeding (Table V).

Discussion

In general, three factors are alleged to increase the death rate in patients who undergo cholecystectomy: increasing age, the addition of a concomitant CBDE and the degree of inflammation of the gallbladder.[1,3,4]

A major risk factor is age. Of the 9339 patients who had cholecystectomy without CBDE, 5383 were less than 50 years of age, and there were four deaths in this group (death rate 0.07%). In the group of 3431 patients between the ages of 50 and 70 years, there were 12 postoperative deaths (death rate 0.3%); in the group of 525 patients over 70 years of age, there were 13 deaths (death rate 2.5%). Our experience confirms that the death rate increases significantly with age ($p < 0.001$), due primarily to associated medical conditions, particularly cardiovascular problems.

The addition of a concomitant CBDE also increases mortality. Although the death rate recorded for 9339 patients who had cholecystectomy alone was 0.3%, it increased fivefold to 1.6% in 1132 patients who had cholecystectomy with CBDE ($p < 0.001$). Although the addition of a CBDE is an important factor influencing the death rate of cholecystectomy, we believe that, rather than the choledochotomy *per se*, the main influencing factor is that CBDE is most often necessary in patients of advanced age with associated medical conditions. In addition, the increased likelihood of sepsis in many patients with common duct stones also influences the death rate. Not only does the death rate increase with the addition of a CBDE, but also the causes of death differ (Table IV). Whereas 17 (59%) of the 29 deaths after cholecystectomy alone were caused by cardiovascular complications, this was the cause of death in only 6 (33%) of the 18 deaths after cholecystectomy with CBDE. In this last group, the causes of death were more frequently related to the intra-abdominal condition at the time of surgery (pancreatitis or cholangitis) and to postoperative complications that developed secondary to the associated acute pancreatitis or cholangitis.

Many series have shown that the presence of acute cholecystitis is an important determinant of operative mortality related to cholecystectomy.[1,3,4] But our experience as well as that of Pickleman and Gonzalez[2] cannot confirm that the presence of acute cholecystitis increases the death rate significantly. In our series, as shown in Table II, the degree of inflammation of the gallbladder was not a significant determinant of operative mortality. Of 1691 patients with acute cholecystitis, 11 died (death rate 0.6%). Cholecystectomy without CBDE was performed in 1498 of these 1691 patients and 7 died (death rate 0.5%). In contrast, 8780 patients were operated on for chronic cholecystitis and 36 died (death rate

Table V. Indications for Reoperation

Indication	After cholecystectomy no. of patients	After cholecystectomy with CBDE, no. of patients	Total
Wound dehiscence	19	7	26
Intra-abdominal abscess	13	5	18
Intra-abdominal bleeding	7	3	10
Biliary fistula	3	3	6
Fixed Penrose drain	3	0	3
Small-bowel obstruction	2	0	2
Gastrointestinal bleeding	1	0	1
Hemobilia	1	0	1
Total	49	18	67

0.4%). Cholecystectomy without CBDE was performed in 7841 of these 8780 patients and 22 died (death rate 0.3%). Table III shows that the difference in mortality for patients with chronic or acute cholecystitis is not affected by age. Only patients more than 70 years old with acute cholecystitis have an increased death rate when compared with younger patients.

Acute pancreatitis or jaundice, or both, may also be considered as factors increasing mortality and morbidity. Of the 29 patients who died after cholecystectomy alone, 5 had pancreatitis at surgery. Of the 18 patients who died after cholecystectomy with CBDE, 4 had pancreatitis and 12 had jaundice at surgery. The high incidence of jaundice in patients who died tends to confirm the observation of others that it increases the risk of cholecystectomy with CBDE.[10]

There is much published data proving the safety of cholecystectomy. A study on biliary tract surgery appeared in 1970 and summarized the results of treatment in over 28 000 patients requiring cholecystectomy.[1] The overall death rate was 1.8%, with a rate of 1.5% for elective cholecystectomy and 3.5% for cholecystectomy for acute cholecystitis. More recent studies, however, have reported an operative death rate of less than 1% (Table VI[2-6]). These rates vary from 0% to 0.5% in elective cholecystectomy to 1.1% to 1.7% in urgent cholecystectomy.[2-6] One of the largest series reported showed that cholecystectomy alone performed in 10 749 patients was associated with an operative death rate of 0.6% (0.4% for chronic cholecystitis and 1.2% for acute cholecystitis); furthermore, in the last 1693 cholecystectomies performed, there were only three deaths for a mortality of 0.2%.[4] In addition, two series of patients who underwent elective cholecystectomy reported no deaths.[3,5]

Our overall death rate of 0.3% in elective cholecystectomy does not differ substantially from these series. But in this series the overall death rate of 0.5% for cholecystectomy in acute cholecystitis is much lower than that reported in other series.[4,6] This difference possibly can be explained by a more aggressive approach at the Maisonneuve-Rosemont Hospital where patients with acute cholecystitis are operated on as soon as the diagnosis is made. Another explanation is that the patients in this series were younger than those in other series. As to the death rate associated with cholecystectomy with CBDE, recent series reported a mortality between 0.7% and 4.4%,[3,4] whereas in the present series it was 1.6%.

As with mortality, the morbidity of cholecystectomy also increased with age and the addition of a CBDE. From 2.3% in those less than 50 years old it increased to 5.0% for those between 50 and 70 years old and 9.2% for those more than 70 years old ($p < 0.01$). Similarly, the addition of a concomitant CBDE increases the morbidity of cholecystectomy from 3.6% to 17.5% ($p < 0.001$). Contrary to the mortality, which has decreased since 1970, the morbidity has not changed substantially. In the Ohio report,[1] the incidence of complications was approximately 4%. In the more recent series, the incidence varied from 3.7% to 5.5%, being higher after operation for acute cholecystitis.[2,4,5] Our overall morbidity of 3.6% (3.1% in chronic cholecystitis and 6.1% in acute cholecystitis) does not differ significantly from the rates in these series.

We encountered 30 intraoperative iatrogenic bile duct injuries (0.3%). Twenty-four of these injuries occurred in the 9339 patients who had cholecystectomy alone, and 6 occurred in the 1132 patients who had cholecystectomy with CBDE. The incidence of bile duct injury during cholecystectomy usually reported in the literature varies between 0.1% and 0.3% but most often includes only major trauma.[11] In this series, we considered minor as well as major traumas. If only major traumas (section or ligation) had been included, the incidence would be 0.07% for cholecystectomy alone and 0.2% for cholecystectomy with CBDE.

In this review an attempt was made to analyse the mortality and morbidity in a large number of patients who had undergone cholecystectomy over the last two decades. The findings confirm that open cholecystectomy is a safe procedure that can be performed with low mortality and morbidity. Mortality and morbidity of cholecystectomy increase with advancing age and with the addition of a concomitant CBDE. The presence of acute cholecystitis at cholecystectomy does not increase mortality or morbidity significantly. Cardiovascular complications, especially myocardial infarction, are the main causes of death.

Because of its low mortality and

Table VI. Operative Mortality After Cholecystectomy

Series	Year	No. of patients	Mortality, %
Gallbladder Survey Committee[1]	1970	28 621	1.8
Pickleman and Gonzalez[2]	1986	389	0.8
Ganey and associates[3]	1986	1 024	0.5
McSherry[4]	1989	10 749	0.6
Gilliland and Traverso[5]	1990	671	0.0
Heberer and associates[6]	1990	898	0.4
Present series	1993	9 339	0.3

morbidity, traditional cholecystectomy is still the gold standard with which the numerous new nonoperative techniques for gallstone management as well as laparoscopic cholecystectomy must be compared.

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BOOK REVIEWS

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teric injury should have been stressed. These injuries are very difficult to diagnose because of associated abdominal physical signs, poor specificity by abdominal lavage and poor definition by plain radiography or computed tomography. Rectal injury is well emphasized; however, in my experience it is a far less common injury than the others.

At the Health Sciences Centre in Winnipeg, we follow the guidelines of a crash protocol in patients who have class IV hemorrhage on arrival at the hospital, have no blood pressure or exhibit no electromyographic activity or, finally, those who suffer cardiac arrest within minutes of entering the emergency department. In the young, otherwise-healthy patient, this is usually secondary to massive hemorrhage, so we quickly determine the site of bleeding by insertion of right and left thoracostomy tubes, abdominal lavage and pericardiocentesis, if indicated. Each cavity with massive bleeding is immediately explored in the operating room. The bleeding is controlled by compression or clamping, and resuscitation by other means is carried out in the operating room. Review of such cases in our experience has provided a 12% survival rate in cardiac arrest and myocardial activity categories and a 77% survival rate in class IV deteriorating shock. These principles are covered in the text of this book, but they are buried in the discussion of intra-abdominal injuries. As far as the chest is concerned, the author of that section recommends emergency thoracotomy and determination of the site of bleeding in the operating room. I would suggest that our principle of crash guidelines avoids the misadventure of performing an excellent surgical exercise and controlling hemorrhage in the chest, while the patient exsanguinates from intra-abdominal hemorrhage. Obviously, it is unfair to criticize something that is present, albeit hidden, in the text. However, I believe these guidelines and the principle of surgery as part of resuscitation should be emphasized. Otherwise those patients balancing between death at the accident scene and arrival in the emergency department in extremis will fall through the crack and die.

This text is a superb resource as a reference and basic teaching vehicle for those practising any form of trauma surgery and those practising as emergency physicians. I would recommend it for all hospital libraries, surgical programs and as a personal reference text.

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Endoscopic Retrograde Cholangiopancreatography in the Management of Choledocholithiasis With Laparoscopic Cholecystectomy

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With the advent of laparoscopic cholecystectomy, endoscopic retrograde cholangiopancreatography (ERCP) has an increasing role in perioperative management. To assess this role, the authors studied, retrospectively, 12 patients who underwent ERCP out of a series of 475 who had laparoscopic cholecystectomy. ERCP was indicated preoperatively for biliary colic in four patients, gallstone pancreatitis in two and common bile duct stone on ultrasonography in one. ERCP was performed postoperatively for jaundice in three patients, for cholangitis in one and for a positive intraoperative laparoscopic cholangiogram in one. Choledocholithiasis was diagnosed in six patients preoperatively and in three postoperatively. Only one patient had an unsuspected residual bile duct stone postoperatively. Of nine patients with stones, endoscopic sphincterotomy was performed in eight and stones were cleared in all with no complications; a stone passed spontaneously in the other patient. ERCP is indicated before laparoscopic cholecystectomy in cases of jaundice, gallstone pancreatitis, cholangitis, abnormal liver biochemistry suggesting cholestasis and ultrasonographic demonstration of either a common bile duct stone or a common bile duct greater than 8 mm in diameter. Operative laparoscopic cholangiography is indicated when the anatomy is unclear or the bile duct appears dilated. If choledocholithiasis is founded, the options include open or laparoscopic common bile duct exploration and intra- or postoperative endoscopic sphincterotomy.

Avec l'avènement de la cholécystectomie laparoscopique, la cholangiopancréatographie endoscopique rétrograde (CPER) joue un rôle de plus en plus important dans la démarche peropératoire. Afin d'évaluer ce rôle, les auteurs ont étudié, en rétrospective, 12 patients qui avaient subi une CPER d'un groupe de 475 patients qui avaient subi une cholécystectomie laparoscopique. L'indication préopératoire de la CPER fut une colique biliaire chez quatre patients, une pancréatite lithiasique chez deux et une cholédocholithiase identifiée à l'échographie chez un. Une CPER postopératoire fut pratiquée pour ictère chez trois patients, pour cholangite chez un et pour un cholangiogramme laparoscopique positif en cours d'intervention chez un. Une cholédocholithiase fut diagnostiquée en préopératoire chez six patients et en postopératoire, chez trois. Un seul patient présenta un calcul biliaire résiduel insoupçonné après l'intervention. Sur neuf patients présentent des calculs, une sphinctérotomie endoscopique fut pratiquée chez huit patients et les calculs furent éliminés dans tous les cas, sans complications; un calcul fut éliminé spontanément chez l'autre patient. Une CPER préopératoire est indiquée avant la cholécystectomie laparoscopique dans les cas d'ictères, de pancréatite lithiasique ou de cholangite, quand les enzymes hépatiques anormaux suggèrent une cholestase ou que l'échographie démontre soit un calcul dans le cholédoque, soit un cholédoque de diamètre supérieur à 8 mm. La cholangiographie laparoscopique opératoire est indiquée quand l'anatomie demeure obscure ou que le canal biliaire paraît dilaté. Quand une cholédocholithiase est confirmée, les options comprennent l'exploration ouverte ou laparoscopique du cholédoque et la sphinctérotomie endoscopique intra ou postopératoire.

Since the early reports of Dubois and associates,[1] Perissat, Collet and Belliard[2] and Reddick and Olsen,[3] laparoscopic cholecystectomy has revolutionized the management of gallstones by shortening hospital stay to 2 days and allowing an earlier return to normal activity, in 7 to 15 days. Laparoscopic cholecystectomy has become the procedure of choice in managing symptomatic gallstones.[4–6]

With the advent of laparoscopic cholecystectomy, there is an increasing role for endoscopic retrograde cholangiopancreatography (ERCP) perioperatively.[7,8] In this paper, we review our experience with ERCP and endoscopic sphincterotomy (ES) in 12 patients who underwent laparoscopic cholecystectomy, and we discuss the evolving role of ERCP.

Patients and Methods

Between January and September 1991, 475 patients underwent laparoscopic cholecystectomy at University Hospital, London, Ont., and three referral hospitals. Among this

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group of patients, ERCP was performed pre- or postoperatively in the 12 patients (10 women, 2 men). The mean age of the patients was 43 years (range from 28 to 86 years). All patients were treated initially as outpatients. Seven were hospitalized for 24 hours after undergoing ES. Two other patients were hospitalized for 4 days after undergoing percutaneous transhepatic cholangiography (PTC).

Findings

Among the 12 patients (2.5% of the study population) who needed ERCP at some point in their investigation or treatment, ERCP disclosed a stone (9 patients) and a lesion (1 patient) in 83% of them (10 of 12) and was successful in clearing the bile duct of stones in 78% of patients (7 of 9). By combining PTC with ERCP, the stone clearance rate was 100% (nine of nine). No complications related to ERCP or ES occurred. Eight of nine patients who had stones needed ES for their extraction. In the ninth patient a stone passed spontaneously.

Preoperative ERCP

The indications for ERCP preoperatively were jaundice associated with biliary colic and increased liver enzymes (four), gallstone pancreatitis (two) and common bile duct (CBD) stones on ultrasonography (one) (Table I).

Preoperative ERCP revealed CBD stones in five patients and a normal bile duct in two (Table I). Among the five cases of choledocholithiasis, one was diagnosed by ERCP, but cannulation with the sphincterotome was unsuccessful. PTC was performed 3 days later and was normal. The stone passed spontaneously during the delay. One patient who had a normal ERCP underwent a liver biopsy that showed drug-related hepatitis. The second patient with a normal ERCP underwent this investigation because of a gallstone pancreatitis.

Postoperative ERCP

The indications for ERCP postoperatively were jaundice with an increased alkaline phosphatase level (three), cholangitis (one) and positive laparoscopic cholangiography (one) (Table I).

Postoperative ERCP revealed choledocholithiasis in four patients and CBD injury in one (Table I). In one patient with choledocholithiasis, cannulation with the sphincterotome was unsuccessful. PTC with insertion of a no. 8 French ring biliary catheter and ES by a combined approach as previously described[9] were performed. The bile duct injury was caused by a hemoclip misplaced while attempting to control intraoperative bleeding. A Roux-en-Y hepaticojejunostomy bile duct reconstruction was performed 3 weeks later. Only one patient had a residual stone that was not identified from the clinical history and preoperative work-up, resulting in an incidence of 0.2% (1 in 475). The patient presented 8 months postoperatively and cholangitis was diagnosed.

Discussion

At present, like many others, we favour a selective approach to the perioperative assessment of patients who undergo laparoscopic cholecystectomy.[5,10–13] All patients should undergo liver function testing (serum aspartase transaminase [AST], serum alanine transaminase [ALT], serum bilirubin and serum alkaline phosphatase measurements) and abdominal ultrasonography in addition to routine history-taking and physical examination.[14] Patients with jaundice, cholangitis, gallstone pancreatitis, biochemical abnormalities on liver function testing, a CBD greater than 8 mm or ultrasonographic evidence of choledocholi-

Table I. Course of 12 Patients Who Underwent Laparoscopic Cholecystectomy and Endoscopic Retrograde Cholangiopancreatography (ERCP)

Patient no.	Timing of ERCP	Indication for ERCP	Diagnosis	Treatment
1	Preop	Jaundice, high enzymes	Normal	Liver biopsy
2	Preop	CBD stone on ultrasonography	CBD stone	ES
3	Preop	Jaundice, high enzymes	CBD stone Failed ES	PTC normal
4	Preop	Pancreatitis	Normal	
5	Preop	Jaundice, high enzymes	CBD stone	ES
6	Preop	Jaundice, high enzymes	CBD stone	ES
7	Preop	Pancreatitis	CBD stone	ES
8	Postop	Cholangitis	CBD stone	ES
9	Postop	Jaundice, fever	CBD stone Failed ES	PTC, ES
10	Postop	Positive cholangiogram	CBD stone	ES
11	Postop	Jaundice	CBD stone	ES
12	Postop	Jaundice	CBD injury	Roux-en-Y reconstruction

CBD = common bile duct, ES = endoscopic sphincterotomy, PTC = percutaneous transhepatic cholangiography

thiasis should undergo ERCP preoperatively (Table II).[14,15] If ERCP is unsuccessful, the CBD can usually be cannulated with the aid of PTC and insertion of a biliary catheter.[9] Intravenous cholangiography with computed tomography is used commonly for CBD assessment before laparoscopic cholecystectomy. We consider it neither routinely necessary nor justified. In a recent report from Ireland,[16] every patient who had a choledocholithiasis shown on a preoperative intravenous cholangiogram also had abnormal liver function, justifying a preoperative ERCP.

ERCP with sphincterotomy preoperatively is contrary to the findings of Neoptolemos, Carr-Locke and Fossard[17] and Neoptolemos, Shaw and Carr-Locke[18] in their studies on CBD stones and standard open cholecystectomy. However, open CBD exploration would negate the advantage to the patient of laparoscopic over open cholecystectomy. It is therefore advantageous to the patient to have ERCP preoperatively with ES instead of an open bile duct exploration when there is a CBD stone. When a diagnostic ERCP is performed, a morbidity as low as 0.8% and a mortality as low as 0.05% can be attained. If ERCP with ES is executed for choledocholithiasis, morbidity less than 5% and mortality less than 1% can be achieved. Bleeding (1.4%), infections (0.9%) and perforations (0.5%) are the most serious complications.[19,20] Those numbers are comparable to, if not better than, the reported morbidity of 16% and mortality of 3.8% associated with open CBD exploration.[21]

Table II. Indication for ERCP Related to Laparoscopic Cholecystectomy

Preoperative ERCP
Jaundice
Gallstone pancreatitis
Abnormal liver function test results (serum transaminases, bilirubin, alkaline phosphastase)
Abdominal ultrasonography
common bile duct > 8 mm
common bile duct stone
Postoperative ERCP
Positive operative cholangiography
Jaundice
Biliary fistula/biloma
Abnormal liver function test results (serum transaminases, bilirubin, alkaline phosphatase)

With selective preoperative ERCP, operative cholangiography through the gallbladder or cystic duct is necessary only when the dissection is complex, the anatomy is distorted by inflammation, there is a dilated bile duct or the preoperative ERCP is unsuccessful.[14] When an operative laparoscopic cholangiogram shows a CBD stone, a transcystic duct drain may be inserted for draining the bile duct of an impacted stone and for introducing a guide wire if postoperative ERCP and ES are not successful (10% to 20% of cases).[22] The other options are open or laparoscopic bile duct exploration and intraoperative ERCP.

With selective preoperative ERCP and intraoperative laparoscopic cholangiography, a 2% to 3% (0.9% to 6.3%) incidence of residual bile duct stones is expected.[7,23–25] Most retained stones will never cause problems or will pass spontaneously into the gut.[26] Only 0.2% to 0.5% of patients will eventually need treatment for a symptomatic residual CBD stone.[11,27,28]

Routine laparoscopic cholangiography can be performed, with a success rate of 70% to 95%.[10] However, routine operative cholangiography has never been proved to have a positive risk–benefit ratio. Disavantages include an increased cost (estimated $299 US), radiation exposure and problems related to false-positive diagnoses.[18,27,29] A false-positive cholangiogram (10% to 25%),[30] leading to an unnecessary negative CBD exploration would increase the morbidity and mortality of the procedure. Operative cholangiography has not decreased the incidence of bile duct injury.[31] Finally, it is difficult to justify a test that benefits only 0.21% of the patients, those who will eventually present with a symptomatic residual CBD stone.

Laparoscopic CBD exploration performed via the cystic duct or a choledochotomy has been reported but does not appear as a practical approach.[5,28,32,33] It is a time-consuming (up to 6 hours), complicated, experimental procedure with a low success rate.[34] It should be reserved for the experienced laparoscopist. Most surgeons cannot hope to reach and maintain sufficient skill to match the low morbidity, the success rate and the efficacy of ERCP and ES.[19]

Intraoperative ERCP has recently emerged as a treatment for choledocholithiasis. It has been used previously in the management of pancreatic trauma discovered intraoperatively.[35] It would be indicated when an unsuspected stone is demonstrated intraoperatively. The safety of this approach is unknown; one case of pancreatitis with a pseudocyst has been reported.[36]

The perioperative management of choledocholithiasis for patients undergoing laparoscopic cholecystectomy can now be added to the pre-existing roles of ERCP. Various indications for diagnostic as well as therapeutic ERCP exist with laparoscopic cholecystectomy as well as with standard open cholecystectomy (Table II).[28,37]

Conclusions

We consider that ERCP should be performed preoperatively when choledocholithiasis is suspected, based on the patient's history and the findings on physical examination, abdominal ultrasonography

and biochemical investigations. We do not advocate routine operative cholangiography or laparoscopic CBD exploration. Intraoperative ERCP may have a limited role for choledocholithiasis diagnosed by laparoscopic cholangiography when performed because of a dilated bile duct discovered during surgery. Prospective studies need to be done to establish the best possible approach to the management of patients who undergo laparoscopic cholecystectomy. It would have to define the role of ERCP and operative cholangiography as well as the best sequence of execution based on the morbidity and mortality of the procedures.

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Anterior Cervical Corpectomy for the Treatment of Complex Cervical Lesions

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Instability and stenosis of the cervical spine have been treated by posterior decompression and anterior decompression with fusion. In this study the authors evaluate the results obtained in 31 patients who underwent anterior cervical corpectomy for compressive or unstable lesions of the cervical spine. Operative level, preoperative and postoperative symptoms and physical findings were assessed. Twenty-seven patients had preoperative neurologic symptoms and signs, including alterations in sensation, motor findings and reflexes. The average follow-up was 12 months, average number of disc spaces excised was 2.5 and average number of vertebral bodies excised was 1.6. With respect to relief of pain, results were good or excellent in 27 patients. All patients but one had union of the bone graft. No neurologic deterioration occurred. The authors believe that patients with compressive lesions of the cervical spine can benefit from anterior cervical corpectomy with fusion and that complications are minimal.

La sténose et l'instabilité de la colonne cervicale ont, jusqu'à maintenant, été traitées par décompression postérieure ou par décompression antérieure avec fusion. On a évalué dans la présente étude, les résultats obtenus par corpectomie cervicale antérieure chez 31 patients opérés pour des lésions compressives ou instables de la colonne cervicale. Le niveau opératoire, les symptômes pré et postopératoires, ainsi que les observations physiques ont été évalués. Vingt-sept patients présentaient des symptômes et signes neurologiques préopératoires comprenant l'émoussement des sensations et une diminution du tonus moteur et des réflexes. La surveillance moyenne des suites thérapeutiques est de 12 mois; on a excisé en moyenne 2,5 espaces interdiscaux et 1,6 corps vertébral. En ce qui a trait au soulagement de la douleur, on a obtenu de bons ou d'excellents résultats chez 27 patients. Sauf pour un cas, il y a eu fusion du greffon osseux chez tous les malades. Aucune détérioration neurologique n'a été observée. Les auteurs croient que les patients souffrant de lésions compressives de la colonne cervicale peuvent bénéficier d'une corpectomie cervicale antérieure avec fusion, tout en éprouvant un minimum de complications.

Stenosis of the cervical spinal canal has been treated with a variety of techniques. Controversy exists as to whether an anterior or posterior approach should be used and whether stabilization is required. Instability of the spine often occurs after posterior surgical intervention,[1-4] and as a result of degenerative or traumatic conditions. Proponents of posterior decompressive methods such as laminectomy and laminaplasty[5,6] believe that morbidity is minimal and recovery of neurologic function satisfactory. Postoperative instability is not considered serious provided the facet joints have not been damaged. Proponents of anterior decompression and fusion report good results for return of neurologic function and stability.[7-11] The goal of this paper is to describe the technique and results of anterior vertebral corpectomy for symptomatic cervical stenosis and instability.

Patients and Methods

A consecutive series of 31 patients who underwent anterior cervical corpectomy at MetroHealth Medical Centre, Cleveland, were reviewed retrospectively. All patients had surgery performed by one of the authors (R.G.W.). Follow-up included a review of the outpatient clinic notes and radiographs. Indications for surgery included compressive conditions with myelopathic or radicular symptoms, instability after posterior decompressive surgery and nonunion of segments previously operated on.

Patients were assessed preoperatively by history taking and physical examination. Particular attention was paid to symptoms of pain in the cervical spine, to motor deficits and to signs of myelopathy, including abnormal reflexes and weakness. Radiologic assessment included an-

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teroposterior and lateral radiographs of the cervical spine (Fig. 1). Magnetic resonance imaging (MRI) followed by computed tomography (CT) with intrathecal contrast medium was performed to confirm the clinical diagnosis and help determine proposed levels of decompression and fusion (Fig. 2). The level of decompression used was based on the symptomatic radicular level with confirmatory motor deficit distal to the lesion and on the compressive levels on MRI and CT as demonstrated by loss of subarachnoid cerebrospinal fluid surrounding the spinal cord. Atrophy or deformation of the cord was considered a sign of substantial compression.

Surgical Procedure

Patients were positioned supine on the operating table with a small roll beneath the shoulders to allow slight extension of the cervical spine. Somatosensory-evoked potentials were used intraoperatively (Pathfinder; Nicolet, Inc., Madison, Wis.). Shoulder traction was maintained with adhesive tape to allow satisfactory intraoperative radiologic visualization of the entire cervical spine. The head was turned to the contralateral side, allowing an anterolateral approach to the cervical spine. With the aid of self-retaining cervical retractors, the longus colli muscle was bluntly dissected from the anterolateral aspect of the vertebral bodies. Segmental vessels were coagulated with diathermy. A lateral radiograph and a spinal needle in the disc spaces allowed identification of upper and lower disc spaces for proposed decompression. Routine discectomies were then performed and decompression to the posterior longitudinal ligament (PLL) was done. Further decompression of vertebral bodies was carried to a depth corresponding with the disc space. A power burr was used to remove the rest of the vertebral body. Once the posterior cortical surface was reached, the burr was changed to a diamond-tipped one to allow more gentle removal of the posterior cortex of the bodies. Angled and straight curettes were used to pull forward fragments that were adherent to the PLL. Adequate posterolateral decompression of the vertebral body must be done by undermining the vertebral body and the disc space with the diamond-tipped burr or the curettes.

Preparation of the end plates for acceptance of bone graft was then done with a keystone-type technique.[12] The superficial margin of the trough for bone graft is narrower than the deeper portions, thus allowing a shaped graft to lock into place once inserted (Fig. 3). Bone graft was obtained from the ipsilateral iliac crest if two or fewer vertebral bodies were removed. If more than two bodies were removed a fibular strut graft was used. The bone was harvested from the ipsilateral extremity. Postoperatively, the patients were maintained in a rigid cervical thoracic orthosis if fewer than three levels were fused. If more than three levels were fused, patients were placed into a Halovest (Bremer Corp., Jacksonville, Fla.).

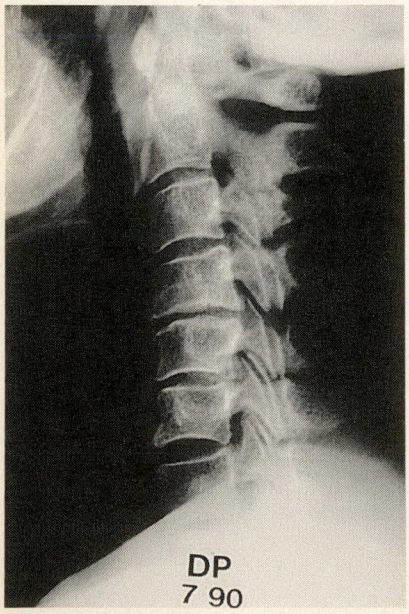

FIG. 1. Lateral radiograph of cervical spine demonstrating area of spondylosis with disc-space narrowing and osteophytes.

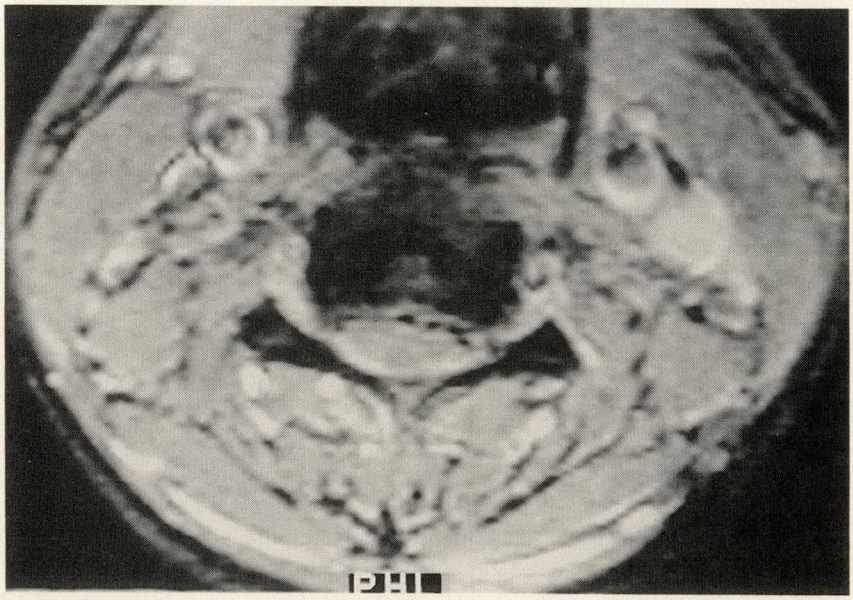

FIG. 2. Axial magnetic resonance image shows loss of cerebrospinal fluid anterior to spinal cord and cord compression.

Patients with more than than three levels of decompression were kept in the intensive care unit with endotracheal intubation for approximately 36 to 48 hours because of the potential for obstruction of the airway secondary to edema in the neck.

Follow-up

Postoperative follow-up and assessment were performed at 6 weeks, 3 months, 6 months and 1 year after surgery. Patients were assessed for pain, sensory and motor signs and myelopathic signs. Pain and neurologic findings were assigned a numeric grade. Pain was graded from 0 to 3 as follows: 0, a poor result, showing continuous pain with no improvement from preoperative levels; 1, a fair result, some improvement; 2, a good result, marked improvement with minimal pain; and 3, excellent or no pain. Postoperative neurologic status was graded similarly as follows: 0, no improvement; 1, minimal improvement; 2, substantial improvement in motor findings; and 3, normal motor strength.

Bony union was assessed from flexion and extension lateral radiographs.

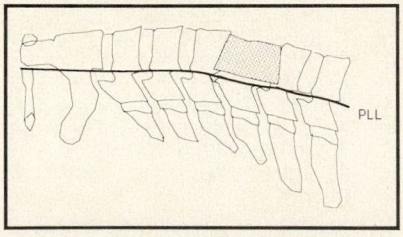

FIG. 3. Diagram demonstrating keystone shape of prepared trough with fitted graft in place. PLL = posterior longitudinal ligament.

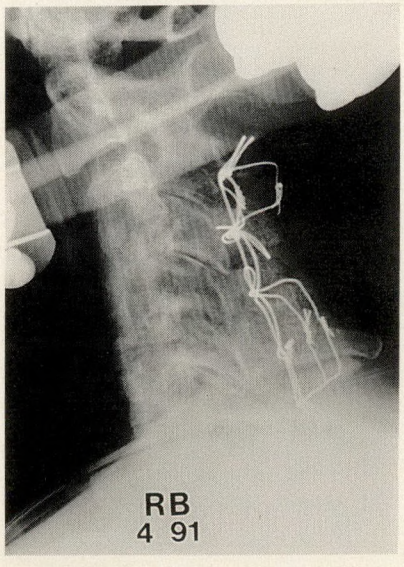

FIG. 4. Nonunion of fibular graft treated with posterior multilevel wiring and fusion.

Results

Thirty-one patients were reviewed. The indications for surgery included cervical stenosis or cord compression (17 patients), nonunion from previous surgery (6 patients), an ossified PLL (5 patients) and cervical kyphosis after previous posterior decompression (3 patients). There were 19 men and 12 women in whom the average age was 52.9 years (range from 23 to 77 years). Average time to follow-up was 12 months (range from 10 to 42 months). Preoperative neurologic findings included sensory deficit in 27 patients, motor weakness in 24 patients and myelopathy in 17 patients. The average number of discs excised was 2.5 with a mode of 3. Four patients had one disc excised, 11 patients had 2 discs excised, 12 patients had 3 discs excised and 4 patients had four discs excised. An average of 1.6 vertebral bodies were excised with the mode being one. Sixteen patients had one vertebral body excised, 11 patients had two vertebral bodies excised and 4 patients had three vertebral bodies excised.

An iliac-crest bone graft was used in 27 patients and a fibular strut graft was used in 4 patients.

Twenty-seven patients had good or excellent (grades 2 and 3) results on assessment of pain relief. Four patients had poor or fair results. For patients with pre-existing neurologic findings, 16 had good (grade 2) results and 11 had excellent (grade 3) results. There was a slight negative correlation between number of vertebral bodies excised and neurologic result ($r = 0.6$).

All patients with iliac-crest grafts had bony union. One of four patients with a fibular strut graft had nonunion (Fig. 4).

Complications

Six patients had complications. One patient required re-exploration. After three-level anterior decompression there was improvement from the preoperative levels, but neurologic recovery plateaued with continued weakness of the right arm. CT with intrathecal contrast medium demonstrated inadequate decompression of the right posterolateral vertebral body. Re-exploration resulted in neurologic improvement. One patient experienced nonunion of a fibular graft and subsequently underwent posterior fusion with wiring of the spinous process and bone grafting. One patient had a sterile seroma of the incision, and one had loosening of the halo pin. Two patients had persistent pain at the graft site. There were no neurologic complications and no other cases of nonunion.

Discussion

Cervical corpectomy is useful in the treatment of complex compressive diseases of the cervical spine. Alternatives include multilevel anterior cervical discectomy with or

without fusion,[2,7,10-15] cervical laminectomy[2,13] and cervical laminaplasty.[5,6]

Multilevel discectomy has been shown to be useful; however, completeness of decompression and the limited visibility make this a more technically demanding procedure. A more complete decompression is possible with corpectomy, and osteophytes may be removed safely without potential damage to the spinal cord.[8,9,12] With multilevel discectomy, the number of interfaces that are required for fusion increase, and this will increase the incidence of nonunion. With corpectomy, only two surfaces are presented for fusion with fewer chances for nonunion. Laminectomy as a treatment method for multilevel stenosis should be discouraged. Long-term results have proven that neurologic progression is the rule rather than the exception and that instability will occur producing cervical kyphosis.[2-4,13] Biomechanical testing confirms the instability of the spine after laminectomy.[16] Laminaplasty is commonly practised in the Far East where multilevel ossified PLL is common. It is considered that laminaplasty will maintain biomechanical stability while enabling decompression of the central canal. This approach may not be useful in patients who have radicular symptoms.

Postoperatively, 27 of the 31 patients in our study showed satisfactory neurologic improvement and 27 had satisfactory pain relief. The number of vertebral bodies excised seems to have a negative correlation with neurologic results; that is, patients with greater numbers of vertebral bodies excised will have the poorer neurologic scores postoperatively. This is not unexpected because patients requiring decompression of larger numbers of vertebral bodies have more severe symptoms and findings preoperatively. No patient in this series experienced neurologic deterioration.

The choice of graft material depends upon the number of levels being decompressed. Autogenous graft material is less prone to nonunion than xenograft or allograft material. With more than two vertebral bodies being removed, iliac-crest graft is not straight enough to provide a strong bicortical strut that will fit within the trough created by corpectomy. Fibula will fit, but the rate of nonunion is higher with this type of grafting.[17] One patient experienced nonunion of his fibular graft and required posterior fusion, which resolved his symptoms.[17] Graft dislodgement did not occur in this series but is a complication of corpectomy.[18] Patients with more than three bodies excised, with cervical lordosis or with posterior instability following laminectomy are prone to dislodgement and require halo immobilization postoperatively.[4] Airway obstruction is life threatening, and our patients with three-level corpectomy or high cervical corpectomies remain intubated in the intensive care unit for 36 to 48 hours postoperatively. Other complications in this series have not been serious and have been managed easily.

Conclusions

Cervical corpectomy is a safe and effective treatment for complex compressive lesions of the cervical spinal cord. With appropriate preoperative planning, intraoperative technique and postoperative care optimal results can be achieved.

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Carcinoma of the Prostate: Case Report

Padraig Warde, MB, MRCPI, FRCPC; Mary Gospodarowicz, MD, FRCPC

The authors report a case of carcinoma of the prostate with an unusual presentation. The patient, an 80-year-old man, had swelling of the right buttock and right side of the lower abdomen, diffuse bony pain and increasing weakness of both lower limbs. He responded well to therapy. Aggressive management of previously untreated carcinoma is warranted even in elderly patients with metastatic disease.

Les auteurs décrivent un cas de carcinome prostatique ayant présenté un tableau clinique inhabituel. Le patient, un homme de 80 ans, montrait une enflure de la fesse droite et du côté droit de l'abdomen inférieur, une douleur osseuse diffuse et une faiblesse croissante des membres inférieurs. Il répondit bien à la thérapie. Un traitement agressif d'un cancer préalablement non traité est de mise, même chez les patients âgés qui montrent un envahissement métastatique.

Adenocarcinoma of the prostate is the second commonest cause of cancer death in men in the United States. There, in 1991, it was estimated that 122 000 cases of the disease would be diagnosed, of which approximately 20% would be metastatic.[1] We report on a patient with an unusual presentation of metastatic adenocarcinoma of the prostate and a gratifying response to therapy.

Case Report

An 80-year-old man was first seen in June 1986. He gave a 2-year history of swelling of the right buttock and right side of the lower abdomen, a 3-month history of diffuse bony pain of increasing severity and a 2-week history of increasing weakness of both lower limbs. He was admitted to a community hospital with acute urinary retention and paraplegia.

At the time of admission his performance status was estimated at 40% on the Karnofsky scale. He had a distended abdomen with a large nontender mass in the right iliac fossa, measuring 12 cm in diameter. A second mass in the right buttock measured approximately 15 cm in diameter, and a third mass in the medial left groin measured 10 cm in diameter. He had a urinary catheter in situ, and on rectal examination anal tone was normal. He had a moderately enlarged hard prostate, which was clinically consistent with malignancy.

Neurologic examination of his lower limbs showed virtually absent power in all muscle groups. Muscle tone and sensation were decreased bilaterally, plantar responses were normal, but both ankle and knee jerks were absent bilaterally.

Biochemical screening revealed a 10-fold elevation in the serum acid phosphatase level. Computed tomography (CT) of the pelvis and abdomen (Fig. 1) showed a large mass in the right side of the pelvis, with destruction of the right iliac bone. The mass, anterior to the iliac wing, measured 11 cm in diameter; the mass posteriorly measured 11.5 cm in diameter. A left pelvic sidewall mass and a third palpable mass were present in the medial region of the left thigh, extending from the level of the mid-femur to the pubic ramus.

Initially, the patient refused to consent to any invasive investigations, but he agreed to a biopsy of the right buttock mass under local anesthesia. This showed a moderately differentiated adenocarcinoma consistent with a primary carcinoma of the prostate (prostate-specific-antigen staining was positive). Bilateral orchiectomy was recommended, but the patient refused and was started on stilbestrol, 1 mg three times daily. He returned to the referring hospital.

When seen again 6 weeks later the patient had no pain and was able to walk with some assistance. Repeat CT showed a marked decrease in the size of the previously noted masses; however, some disease was still present (Fig. 2). The

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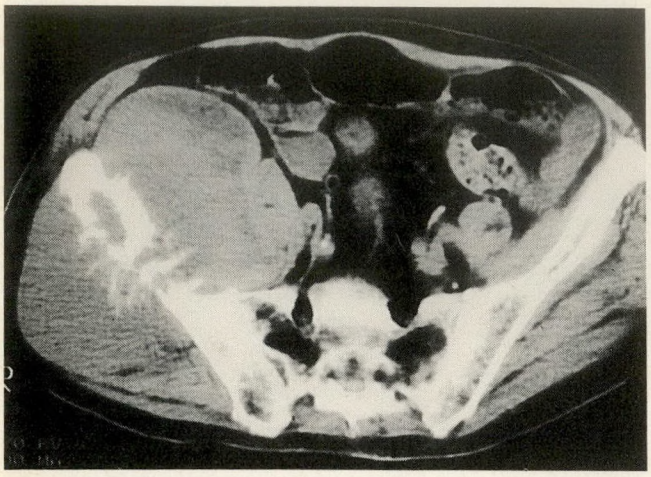

FIG. 1. Computed tomography (CT) scan of pelvis at presentation.

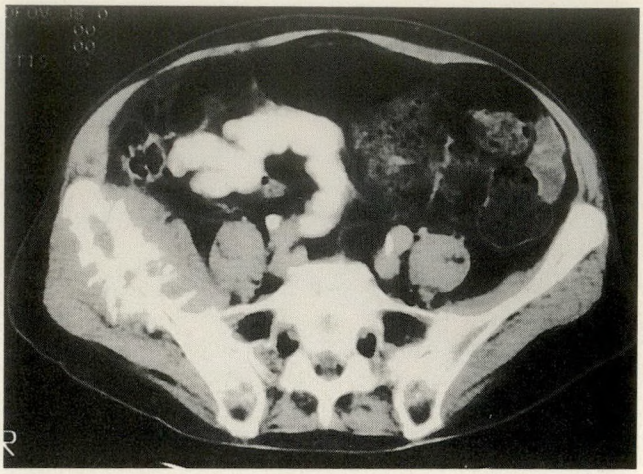

FIG. 2. CT scan of pelvis 6 weeks after start of stilbestrol therapy, showing marked improvement.

serum acid phosphatase level had returned to the normal range. The urinary catheter was removed, and stilbestrol was discontinued because of concern regarding cardiovascular complications. The patient continued to refuse orchiectomy and was started on 1 mg leuprolide daily.

The patient has been followed up in the clinic at regular intervals for 5 years since diagnosis. On the last follow-up examination he was fully ambulant and pain free with a Karnofsky performance status of 90%. Bladder control was normal. On physical examination he had no palpable masses, and digital rectal examination revealed a soft, somewhat enlarged prostate. Neurologically his lower limbs were normal. A recent CT scan of the pelvis showed an enlarged prostate but no other abnormality. His acid phosphatase level was normal, and his prostate-specific-antigen level was only moderately elevated. He continues to have daily leuprolide injections and to refuse orchiectomy.

Discussion

Soft issue metastases as a presenting feature of metastatic carcinoma of the prostate are very unusual. When we first examined this patient it was our opinion that, although he likely had metastatic carcinoma of the prostate, he might have another malignant tumour, perhaps a soft tissue sarcoma.

We emphasise that aggressive management of previously untreated carcinoma of the prostate is warranted, even in elderly patients with metastatic disease. The extent of disease does not accurately predict response to hormonal therapy; indeed there are no absolute predictors of hormonal sensitivity.[2]

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The Spectrum of Surgery in Ethiopia

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Ethiopia's need for surgical services is assessed from on-site reviews of operating-room records in various hospitals and compared with data from other countries. Information on surgical manpower and total operations for the country were obtained from the Ministry of Health of Ethiopia. In Ethiopia the ratio of surgeons to population is very low (0.32 surgeons per 100 000 population) and inadequate numbers of essential operations (e.g., cesarean section and inguinal-hernia repair) are performed. The average age of the surgical patient is young (37 years), and men are operated on twice as frequently as women.

Of the 9422 operations performed during 6 months in the central, regional and rural hospitals surveyed, 7037 (75%) could be performed by a general practitioner or a paramedic specially trained for the procedure and would not require a fully trained general surgeon. The implications for surgical manpower training are discussed.

Les besoins éthiopiens en services chirurgicaux ont été évalués par une étude sur place des dossiers chirurgicaux de divers hôpitaux et une comparaison avec les données d'autres pays. L'information sur les effectifs chirurgicaux et sur le total des interventions chirurgicales pratiquées dans ce pays ont été obtenus du ministère de la santé de l'Ethiopie. En Ethiopie, le rapport du nombre de chirurgiens à la population est très faible (0,32 par 100 000 de population) et un nombre insuffisant d'opérations essentielles (par exemple, césarienne ou réparation de hernie inguinale) est pratiqué. L'âge moyen des opérés est bas (37 ans) et les hommes sont opérés deux fois plus souvent que les femmes.

Des 9422 opérations effectuées en 6 mois dans les hôpitaux centraux, régionaux et ruraux ayant fait l'objet de l'enquête, 7037 (75 %) auraient pu être pratiquées par un médecin généraliste ou par un infirmier paramédical formé spécialement pour ces interventions, sans avoir à recourir à un chirurgien général. On commente les implications de ces résultats quant à la formation des effectifs chirurgicaux.

Published data on surgery in developing countries is scarce. From observation it appears that surgeons are few, that many people die of treatable surgical conditions and that the quality of surgical service is often low.

To develop a rational approach to improve this situation, it is important to have data on what surgery is currently performed and on the current state of surgical manpower. This study was undertaken to identify the number of surgeons and the type and complexity of surgical conditions commonly treated at the different levels of the health system in Ethiopia.

Methods

Information on the numbers of surgeons, surgical beds and operations performed throughout the country was obtained from the Ethiopian Comprehensive Health Services Directories for 1983–1984 and 1986–1987.[1,2] Additional information on specific types of operations (groin-hernia repair, cesarean section and appendectomy) was gathered from all the hospitals in Addis Ababa and from three regional hospitals (Jimma, Bahar Dar and Gondar) for the period September 1988 to February 1989 inclusive. From this information, we calculated the annual rate of these operations per 100 000 population.

The spectrum of surgery was based on a review of the operating-room log books and outpatient records of minor operations for the 6-month period September 1988 to February 1989 for the following institutions: two central teaching hospitals in Addis Ababa; the three regional hospitals already mentioned, all of which were located more than 350 km from Addis Ababa; two rural hospitals; and five health centres.

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Although the rural and regional hospitals and the health centres were selected largely on the basis of accessibility, from personal experience they seem to be representative of these types of health institutions in Ethiopia. An important exception is health institutions in areas of active fighting due to the civil war. These areas were not accessible to the authors.

All operations were grouped into four categories (A, B, C and D) in ascending order of complexity, as recommended by Watters and Bayley.[3] These categories are defined as follows.

- Group A — operations that should be within the competence of any qualified doctor or suitably trained paramedic.
- Group B — operations that could be performed by a doctor or paramedic specially trained for the procedure.
- Group C — operations that normally could be performed by someone with higher qualifications and surgical training appropriate for developing countries.
- Group D — operations that require subspecialty training beyond the scope of the average general surgeon.

Sex and age of the surgical patients were assessed for the two central teaching hospitals.

To assess seasonal variations, data were reviewed from one each of the central, regional and rural hospitals for an entire year, and compared with the 6-month findings.

Findings

The population of Ethiopia was approximately 42 million according to the 1983–1984 census. With an estimated growth rate of 2.9% per year, the 1988–1989 population is estimated to be 49 million.

In 1986–1987 in Ethiopia there were 170 surgeons, including all general surgeons, orthopedic surgeons, urologists, otorhinolaryngologists and obstetrician-gynecologists. Only 50 of these were Ethiopians. In total 67 982 operations were performed. The rate of operations was 148 per 100 000 population, and there were nine surgical beds per 100 000 population.

Table I compares the rates of operations and surgeons per 100 000 population in Ethiopia with those in other countries.[4–6]

In an attempt to contrast the need for surgery with the surgery performed in Ethiopia, population-based data on cesarean sections, groin-hernia repairs and appendectomies were compared with the need for surgery in East African countries as estimated by Nordberg[7] (Table II[5,7,8]).

The seven hospitals and five health centres from which data were drawn ranged in size from 30 to 448 beds. The two central hospitals accounted for 873 beds (27.5% of all beds in Addis Ababa), the three regional hospitals for 625 beds (60.5% of all beds in the regions studied) and the two rural hospitals for 150 beds. All seven hospitals had qualified general surgeons, and all but one had a qualified gynecologist during the period for which the operations were determined. Expatriate surgeons represented 50% of surgeons in teaching hospitals and 100% of the surgeons in the other hospitals.

Tables III to VI show the type and number of operations performed at the three levels of hospitals in the various groups (A to D). Table VII shows the number and percentage of the different categories of surgery performed in the three levels of hospitals. Overall, 75% of the operations performed at all hospitals fell into groups A and

Table I. Rates of Operations and Surgeons per 100 000 Population in Various Countries

Country	Operations	Surgeons
Ethiopia, 1983 – 1984	163	0.32
Pakistan, 1983[4]	124	0.36
England and Wales, 1976[5]*	1314	1.8
United States, 1978[6]	9200	38

*Includes general surgeons and general surgery cases only

Table II. Number of Cesarean Sections, Groin-Hernia Repairs and Appendectomies Performed in Ethiopia and Other Countries Compared With the Need for These Operations in East Africa as Estimated by Nordberg[7]*

Area/country	Cesarean section	Groin-hernia repair	Appendectomy
Addis Ababa†	66	8.7	26
Regional hospitals‡	9.2	2.5	3
England and Wales[5]	—	129.6	143.5
Canada (1977)[8]	184	219	163
Nordberg[7]§	4 – 62	2 – 100	—
Need as estimated by Nordberg[7] for East African countries	225	175	—

*Numbers per 100 000 population
†Includes all hospitals performing surgery
‡Jimma, Bahar Dar and Gondar. Although these are regional hospitals, the town population was used as the denominator to calculate the rates, because few patients actually come from outside the town. If the regional population was used as the denominator, the rates would, of course, be much lower.
§Data are from various East African countries, including Ethiopia.

B, and these two groups accounted for 64% of all general surgery cases, 70% of urology cases, 59% of orthopedic cases and 89% of obstetric and gynecologic cases. The three levels of hospitals had similar proportions of the different groups of surgery.

When the operations were grouped according to subspecialty, operative obstetrics and gynecology accounted for 44% of the total operations, general surgery accounted for 34% of operations, orthopedics accounted for 15% of operations and urology accounted for 7% of operations.

The 10 most commonly performed major operations were similar in the three levels of hospitals (Table VIII). A similar distribution was also found for the most common minor operations, with dilatation and curettage being the most common.

General surgical emergencies accounted for 31%, 43% and 52% of all general surgical cases at the central, regional and rural hospitals respectively.

When sex was assessed, excluding obstetric and gynecologic cases, the male-to-female ratio was 2:1, and the average age, excluding pediatric patients 12 years of age or younger, was 38 years for males and 34 years for females.

The average hospital stay on the surgical wards was 14 days for the two rural hospitals but over 20 days for all others, and up to 51 days for one of the regional hospitals.

Comparison of 6-month data versus 1-year data in the selected hospitals showed no important differences.

Of the 1650 patients with surgical conditions who were seen at the five health centres in 6 months, 90% had suffered trauma or had general surgical emergencies. The majority had lacerations, bites and closed fractures that were managed at the health centre. Patients with acute abdominal and obstetrical emergencies and elective conditions were advised to go to the closest hospital.

Table III. Number of Operations of Group A* Performed at the Three Levels of Hospitals in Ethiopia

	Level of hospital		
Procedure	**Central**	**Regional**	**Rural**
Simple biopsy	367	12	—
Wound repair	224	169	91
Foreign-body removal	137	50	25
Incision and drainage of abscess	87	79	27
Chest-tube insertion	33	25	8
Miscellaneous (cutdown, catheterization, dressing)	47	—	2
Total	895	335	153

*Operations within the competence of any qualified doctor or suitably trained paramedic

Table IV. Number of Operations of Group B* Performed at the Three Levels of Hospitals in Ethiopia

	Level of hospital		
Procedure	**Central**	**Regional**	**Rural**
Skin grafting	109	24	1
Perianal surgery	74	51	27
Excision of lump	187	27	60
Groin-hernia repair	53	31	13
Appendectomy	111	40	14
Burr holes	10	1	—
Sigmoidoscopy	51	—	—
Circumcision	91	6	61
Scrotal operations	85	27	9
Amputation	92	41	13
Débridement/ sequestrectomy	249	107	6
Bouginage	118	5	—
Minor testicular operations	20	14	1
Cystostomy	9	11	1
Fracture: closed reduction	NA†	63	39
Dilatation and curettage	2654	314	90
Cesarean section	301	116	30
Minor gynecologic procedures	81	90	26
Total	4295	968	391

*Operations that could be performed by a doctor or paramedic specially trained for the procedure.
†NA = not available

Discussion

A study such as this one, which merely records what is done, does not provide data on what operations should or should not have been performed. For this, population-based information is needed. Also we cannot comment on the outcome of these operations, clearly a factor of major interest and worthy of future study.

It seems clear that the operations being performed in Ethiopia vary little between teaching and rural hospitals, with the exception of proportionally more general surgical emergencies (52% v. 31%) being done in rural as opposed to teach-

ing hospitals. This difference may be a reflection of the more limited resources in peripheral hospitals, where beds and supplies are used for emergency conditions, and not enough are left for elective cases.

Like Watters and Bayley,[3] we have found that the majority of cases (75%) were not complex.

Without information on the complexity of individual cases, it is difficult to comment on the appropriateness of the relatively long average stay for surgical patients. However, personal experience in central hospitals suggests that much of it is unnecessary, and in a significant proportion of patients is due to long pre- and postoperative stays for elective procedures.

That the unmet surgical needs in most parts of East Africa are great is not disputed. Nordberg[7] estimated that only 15% of needed operations are carried out, and for some areas this rate is much lower. We found that the regional hospitals performed only 4% of the needed cesarean sections and 1.4% of the needed hernia repairs. Many conditions requiring surgery affect men and women during the most productive years of their life, when they may be the primary breadwinners. This finding is supported by the relatively young age of surgical patients (38 years for men, 34 years for women). The high ratio of men to women on the surgical wards suggests that women are probably underserved.

Although most surgeons (71%) in Ethiopia are expatriates and the aim is to replace them with nationals, it will take some time to replace them, because the only training program for surgeons in the country follows a standard 4-year curriculum.[8] Therefore, serious consideration should be given to assessing and improving the surgical skills of general practitioners, especially those in rural areas. This could be done through a short training program in which the practitioners can learn how to manage the commonly encountered surgical and obstetric conditions seen in the rural hospital or health centre. Specifically, they

Table V. Number of Operations of Group C* Performed at the Three Levels of Hospitals in Ethiopia

	Level of hospital		
Procedure	**Central**	**Regional**	**Rural**
Elective laparotomy	46	18	5
Colorectal operations	41	7	3
Colostomy	24	7	1
Gastroduodenal operations	77	8	—
Gallbladder operations	112	—	1
Mastectomy	27	10	—
Thyroidectomy	50	17	1
Bronchoscopy	30	8	—
Tracheostomy	21	4	—
Incisional-hernia repair	25	18	5
Operation for intestinal obstruction	58	51	33
Operation for peritonitis	81	81	32
Intestinal fistula	10	8	—
Varicose-vein surgery	26	3	—
Prostatectomy	39	9	—
Kidney operations	30	2	1
Bladder operations	12	4	—
Cystoscopy	91	—	1
Hypospadias repair	9	—	1
Fracture fixation	296	128	9
Hysterectomy and other major gynecologic procedures	291	110	40
Total	1396	493	133

*Operations that normally could be performed by someone with higher qualifications and surgical training appropriate for developing countries.

Table VI. Number of Operations of Group D* Performed at the Three Levels of Hospitals in Ethiopia

	Level of hospital		
Procedure	**Central**	**Regional**	**Rural**
Plastic surgery	121	19	5
Orthopedics†	122	13	12
General surgery‡	51	19	1
Total	294	51	18

*Operations that require subspecialty training beyond the scope of the average general surgeon.
†Includes operations such as tendon transfers, hip replacement and laminectomy.
‡Includes thoracic, vascular, head-and-neck tumour surgery and anal atresia surgery.

Table VII. Total Number (%) of the Four Groups of Operation Performed at the Three Levels of Hospitals in Ethiopia

	Level of hospital			
Group	**Central**	**Regional**	**Rural**	**Total**
A	895 (13)	335 (18)	153 (22)	1383 (15)
B	4295 (62)	968 (52)	391 (56)	5654 (60)
C	1396 (20)	493 (27)	133 (19)	2022 (21)
D	294 (4)	51 (3)	18 (3)	363 (4)
Total	6880 (100)	1847 (100)	695 (100)	9422 (100)

need to be able to perform all operations in groups A and B. These trained practitioners should be visited regularly by a fully trained surgeon to help maintain morale and quality control and to provide continuing medical education.[9]

Ideally, these procedures should be in the repertoire of finishing interns. However, in Ethiopia the relatively high ratio of students, interns and residents to patients in teaching hospitals means that opportunities for students and interns to perform the operations are limited.

Three areas are of particular interest for further research. The first, mentioned above, is the outcome of the operations performed. The second is to know, before training general practitioners further in surgical skills, how many health centres and hospitals in Ethiopia actually have functioning equipment and staff that would allow surgery to be performed. The third area for research is health centres. In Ethiopia in 1988 and 1989, there were 156 health centres and 88 hospitals. Thus, more people have access to health centres than hospitals. The referral system here is essentially nonfunctional and it is likely that, for reasons of logistics, many who present to health centres with acute surgical problems will never get to a hospital. Thus, it is important to know what surgical services health centres can and should provide.

Table VIII. Ten Most Frequently Performed Major Operations by Level of Hospital in Ethiopia

	Level of hospital		
Frequency	**Central**	**Regional**	**Rural**
1	Cesarean section	Fracture fixation	Hysterectomy
2	Fracture fixation	Cesarean section	Relief of intestinal obstruction
3	Hysterectomy	Hysterectomy	Operation for peritonitis
4	Débridement/ sequestrectomy	Débridement/ sequestrectomy	Cesarean section
5	Plastic surgery	Operation for peritonitis	Plastic surgery and tendon transfers
6	Gallbladder	Relief of intestinal obstruction	Appendectomy
7	Appendectomy	Amputation	Amputation
8	Amputation	Appendectomy	Groin-hernia repair
9	Operation for peritonitis	Groin-hernia repair	Fracture fixation
10	Gastroduodenal operations	Plastic surgery	Débridement/ sequestrectomy

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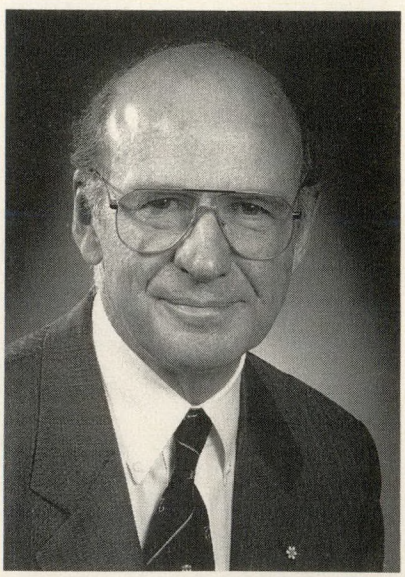
Special Announcement

The Editorial Board of the *Canadian Journal of Surgery* was delighted to learn of the news, announced at the 78th Annual Clinical Congress of the American College of Surgeons in New Orleans in October 1992, that Dr. Lloyd D. MacLean has been elected to the office of president elect of the American College of Surgeons. Dr. MacLean will take office as president of the College in October 1993, during the Clinical Congress in San Francisco. This honour is richly deserved by Dr. MacLean who has served the American College of Surgeons throughout his illustrious surgical career. He has been an international representative of the Canadian surgical community and is held in highest regard by many national organizations, as recognized by election to this prestigious office.



Lloyd D. MacLean, OC, MD, PhD, FACS, FRCSC

The success of the Clinical Congress of the American College of Surgeons is due primarily to its highly organized and broadly ranging scientific program. The chairman of the Program Committee is Dr. MacLean, in whose honour the 1991 Surgical Forum was dedicated. The Editorial Board and readers of the Journal applaud Dr. MacLean.

Canadian Association of General Surgeons

1992–1993 Executive

President: Dr. Marvin J. Wexler
Past president: Dr. Frank W. Turner
President elect: Dr. Frederic G. Inglis
Secretary: Dr. Roger G. Keith
Treasurer: Dr. Marshall C. Hunting

1993 Annual Meeting

The 1993 annual meeting of the Canadian Association of General Surgeons (CAGS) will be held in conjunction with the annual meeting of the Royal College of Physicians and Surgeons of Canada in Vancouver, in September. The preliminary program under the chair of Dr. John Macfarlane is very exciting. The first postgraduate course will be held on the Thursday and will feature laparoscopic surgery. A second postgraduate course to be held on the following Monday will be on surgical oncology with a focus on colorectal cancer. The CAGS Lecture will be presented by Mr. R.J. Heald from Basingstoke, England. He will speak on rectal cancer. The Ghent Lecture will be presented by Dr. Ernest Moore of Denver. The Langer Lecture will be presented by Professor Alfred Cuschieri from Dundee, Scotland, who will speak on the place of laparoscopic surgery. The 3 days of paper sessions will feature the CAGS CME Day on Saturday and a combined paper/poster session with the Canadian Association of Gastroenterology on Sunday.

Other Forthcoming Meetings

The CAGS Research Conference will be held in June 1993 in Banff, Alta. General surgery program directors are reminded to encourage submission of resident research abstracts in response to forthcoming announcements.

The 1993 spring meeting of the American College of Surgeons will be held in Montreal from Apr. 25 to 28. This meeting has become a focus for general

surgery and will feature four postgraduate courses, on cancer management, ambulatory surgery, vascular surgery and trauma. Dr. Jonathan Meakins will present a named lecture entitled "Determinants of sepsis in surgical patients."

Royal College Maintenance of Competence (MOCOMP) Program

Over 700 CAGS members have enrolled in the Royal College's MOCOMP Pilot Program aimed at developing a comprehensive strategy for motivating specialists to continuously update their clinical practice. This pilot project will end in 1 year, and the formal program will be initiated by the Royal College thereafter.

Core Training Program in Surgery

The Royal College Specialty Committee in General Surgery has approved the 2-year program for core training in surgery and has developed guidelines to integrate this within the full 5 years of general surgery resident training. Most Canadian general surgery programs are integrating the combined programs with changes that have developed with the replacement of rotating internship by a basic clinical training year. Reduction in provincial funding for postgraduate training is concurrent with these changes in most provinces.

CAGS Coat of Arms

The CAGS has approved the preparation of a formal coat of arms for the Association. Gratitude is directed to Dr. Bob Thorlakson for his leadership and contributions to this project. The coat of arms will subsequently be displayed in the new Royal College headquarters and will be incorporated in the Association's stationery and materials.

Merck Frosst Awards

At the 1992 annual meeting, the CAGS Merck Frosst Awards for Teaching Excellence were presented to the successful resident from each Canadian university, general surgery program. The following residents were honoured: University of British Columbia — Dr. Gary W. Kingston; University of Calgary — Dr. Doug Johnson; University of Alberta — Dr. Douglas May; University of Saskatchewan — Dr. Richard Bigsby; University of Manitoba — Dr. Donald Clark; University of Western Ontario — Dr. Edward Davis; McMaster University — Dr. Adrian Park; University of Toronto — Dr. George Azzie; Queen's University — Dr. John Drover; University of Ottawa — Dr. Sully Garba; McGill University — Dr. Andrew Hill; Université de Montréal — Dr. Lucie Bilodeau; Université de Sherbrooke — Dr. Jean-Jacques Klopenstein; Université Laval — Dr. Regent St. George; Dalhousie University — Dr. Russell Gowan; Memorial University — Dr. Barry Fleming.

General surgery program directors are reminded to submit nominations for the 1993 CAGS Merck Frosst Awards by the end of May 1993.

Canadian Orthopaedic Association

1992–1993 Executive

President: Dr. Maurice Duhaime
Past president: Dr. Marvin Tile
President elect: Dr. R. Mervyn Letts
Secretary: Dr. Robert F. Martin
Treasurer: Dr. Robert M. Hollinshead

Forthcoming Meetings

The Canadian Orthopaedic Association wishes to announce the following forthcoming meetings for the spring of 1993. Information on these programs may be obtained by contacting the Canadian Orthopaedic Association Secretariat in Montreal (phone: [514] 874-9003):

Apr. 14 to 16, 1993. The 6th Sainte-Justine Pediatric-Orthopedic Review Course, Montreal, Que.

Apr. 23 and 24, 1993. The 24th Annual Meeting of the Quebec Scoliosis Society, Montreal, Que.

June 10 to 18, 1993. The University of British Columbia Orthopedic Update Course, Vancouver, BC.

Canadian Society for Vascular Surgery

1992–1993 Executive

President: Dr. Adrien Bouchard

Past president: Dr. William G. Jamieson
President elect: Dr. Neil V. McPhail
Secretary: Dr. Kenneth A. Harris
Treasurer: Dr. Kenneth C. Grant

1993 Annual Meeting

The 15th annual meeting of the Canadian Society for Vascular Surgery (CSVS) will be held in Vancouver, Sept. 10 to 12, 1993, in conjunction with the annual meeting of the Royal College of Physicians and Surgeons of Canada. To accommodate those wishing to catch the Sunday flight "back east," the format of the meeting has been changed. Seminars will begin Friday afternoon, concluding on Sunday morning. This year the CSVS Lecture will be delivered by Dr. Jonathan Towne from Milwaukee. The topic of the Saturday afternoon symposium is "Controversies in the Management of Cerebral Vascular Disease." This symposium will provide an update on many of the recently completed or ongoing trials and will include presentations by such distinguished speakers as Dr. Thomas Riles from New York.

Abstract forms were distributed in the December 1992 issue of *Annals of the Royal College of Physicians and Surgeons of Canada*. They are also available from the Secretary of the Society. Surgeons are encouraged to submit papers or case reports. Cases should illustrate principles of vascular surgery or describe unusual conditions or abnormalities and include a review of the literature.

Dr. David Taylor and the local arrangement committees are promising an excellent social program to complement the scientific menu. We hope to have a record turnout in Vancouver.

Course on Venous Thromboembolism

McMaster University will be conducting a course entitled "Clinical Advances in Venous Thromboembolism — A Practical Approach" from May 14 to 16, 1993, at Niagara-on-the-Lake, Ont. Further information may be obtained from the Continuing Education Office, McMaster University, Hamilton, Ont.; phone: (416) 521–7966 or (416) 389–4224.

Small Aneurysm Treatment Trial (SATT)

This study, randomizing patients with abdominal aortic aneurysms measuring 4.5 to 5.4 cm in greatest diameter, continues to recruit patients from around the world. The study is funded by the Medical Research Council of Canada, with Dr. William Cole of Ottawa as the principal investigator. Many centres in Canada, the United States and Great Britain are participating in this study, and it is hoped that enrolment will reach over 400 patients in the next 2 years. The study design compares operative treatment and follow-up with ultrasonography of patients with appropriate sized aneurysms. Follow-up is over a 4-year period. The information gained should be useful to all vascular surgeons making decisions about treating infrarenal abdominal aortic aneurysms.

Membership

The CSVS accepts membership applications on three different levels. Active members are surgeons with an interest in vascular surgery who hold a Certificate of Special Competence in Vascular Surgery or its equivalent. Associate members are those with an interest in vascular surgery or vascular diseases. Associate (candidate) members are those enrolled in a vascular training program in Canada or the United States.

Application forms may be obtained from the Office of the Secretary of CSVS.

Luke Award

The Luke Award is given to the best paper presented at the CSVS annual meeting. The selection committee consists of the CSVS lecturer, the society president and the chairman of the program committee. The 1992 selection committee comprised Drs. T. O'Donnell, W. Jamieson and A. Salvian. The 1992 prize was awarded to Dr. Joseph Sladen of Vancouver for his paper entitled "Superficial femoral vein: a useful alternative arterial conduit."

Useful Addresses

The President of the CSVS is Dr. Adrien Bouchard who can be reached at the Ottawa General Hospital, 501 Smyth Rd., Ottawa, ON K1H 8L6; phone: (613) 737–8539. The Secretary, Dr. Kenneth A. Harris, can be reached at Victoria Hospital, 375 South St., London, ON N6A 4G5; phone: (519) 667–6780.

Canadian Society of Cardiovascular and Thoracic Surgeons

1992–1993 Executive

President: Dr. F. Neil McKenzie
Vice president: Dr. Elliot T. Gelfand
Secretary: Dr. W.R. Eric Jamieson
Treasurer: Dr. Edward F. Busse

Meetings

The Canadian Society of Cardiovascular and Thoracic Surgeons (CSCTS) meets annually with the Royal College of Physicians and Surgeons of Canada. Highlights of the 1992 meeting were a symposium entitled "Further Directions in the Management of Myocardial Infarction — Modern Interventional Therapies" and the Wilfred Bigelow Lecture, presented by Dr. Hermes Grillo of Harvard Medical School and entitled "Modern concepts in tracheal surgery."

In 1993, the CSCTS will conduct joint symposia — one symposium on transplantation with the Canadian Thoracic Society and another symposium on thoracoscopic surgery with the Canadian Society of Endoscopic and Laparoscopic Surgery.

In July 1994, the Society will cosponsor, with the International Scientific Committee for the Advancement of Cardiac Bioprostheses, the VIth International Symposium on Cardiac Bioprostheses in Vancouver. The deadline for submission of abstracts for this meeting is Dec. 1, 1993. The Canadian organizing committee comprises Drs. Eric Jamieson (chairman), Tirone David, Conrad Pelletier and Lawrence Burr.

Royal College Task Force

The Royal College of Physicians and Surgeons of Canada is formulating a task force on training requirements in cardiothoracic and thoracic surgery. This task force will incorporate the nucleus members of the specialty committees in thoracic and cardiothoracic surgery. The CSCTS and membership will have an opportunity to participate in the process.

Canadian Society of Surgical Oncology

1992–1993 Executive

President: Dr. Walley J. Temple
Past president: Dr. Henry R. Shibata
Secretary/treasurer: Dr. David R. McCready

2nd Annual Scientific Meeting

The Canadian Society of Surgical Oncology (CSSO) will hold its 2nd annual scientific meeting on Saturday, Apr. 17, 1993 at the Queen Elizabeth Hotel, Montreal. The meeting will take place in conjunction with the National Cancer Institute of Canada (NCIC) spring meeting from Apr. 17 to 20, 1993.

We encourage all interested members of the CAGS to attend.

Further details about the meeting may be obtained from: Dr. Walley J. Temple, President, CSSO, Tom Baker Cancer Centre, 1331 – 29th St. NW, Calgary AB T2N 4N2; phone: (403) 670–1914; fax: (403) 283–1651.

Membership

The CSSO, a young and developing Canadian society, has joined the group of societies/associations sponsoring the *Canadian Journal of Surgery*. A mission of the Society is to stimulate the development of surgical participation in regional and national clinical trials. There is a continuing need for increasing involvement of surgical oncologists with the programs of the NCIC. The Executive of the CSSO welcomes membership applications from enthusiastic surgeons with a dedicated interest in the fields of surgical oncology. We also invite all members of the CAGS with a training in cancer and those with a practice of at least 50% oncology from all surgical disciplines to become members. For further information contact Dr. Walley Temple in Calgary (phone: [403] 670–1914).

Instructions for Authors

The *Canadian Journal of Surgery* will consider manuscripts of original articles, clinical research, surgical technique, clinical reviews, history of surgery, a limited number of case reports, editorials and letters. Four copies of manuscripts, in English or French, should be submitted to Dr. Roger G. Keith, *Canadian Journal of Surgery,* Department of Surgery, Royal University Hospital, 103 Hospital Dr., Saskatoon, SK S7N 4J9.

A covering letter, signed by all the authors, should state that the manuscript has not been published previously and is not under consideration by any other journal. The authors should include a signed letter of permission from people identified in the acknowledgements or identifiable in illustrative material as well as from the copyright holder of previously published material (e.g., tables, illustrations and long quotations) that is being reproduced, with or without modification, in the submitted article. The authors must disclose the source of any financial or material support, any commercial interest they may have in the subject of the study and any affiliation or involvement with an organization that has a financial interest in the research materials used or the topic.

Manuscript Preparation

The style of the submission should be compatible with "Uniform requirements for manuscripts submitted to biomedical journals" (*Can Med Assoc J* 1992; 146: 861–868).

The authors' names should appear on the title page and the back of each set of illustrations. All acknowledgements should be placed on a separate unnumbered page after the list of references.

To facilitate editing and electronic scanning, all pages (title page, abstract and key words [MeSH terms if possible], text, references and figure legends) must be double-spaced, in 10-cpi, letter-quality type, without right justification or proportional spacing.

For all manuscripts, authors should submit an original and three high-quality photocopies or additional printouts of the text and tables, and four camera-ready copies of the figures.

In writing a case report it is not necessary to give a detailed patient history and results of physical examination in the standard clinical format. Negative findings and normal results of laboratory tests need be included only if they are essential for ruling out a possible diagnosis. It is enough to establish the reasons for the diagnosis and the management. The clinical course should be described briefly and the significant observation or event described in sufficient detail to establish its credibility. Reference to the literature should be confined to supporting the principal point being made about the event or observation.

Abstracts are required for original, review and history articles and for case reports, but not for articles on surgical technique and editorials. A structured abstract should be provided for original and review articles (see October 1992 issue, pages 473 to 475). Abstracts for history articles and case reports should be brief, but detailed (from 60 to 150 words long).

References should be cited in numerical order of their appearance in the text. References cited in tables should be numbered according to where the table is first cited in the text. The style for references should be that used in this issue of the Journal.

Other Considerations

Colour figures can be reproduced only at the author's expense. Authors should submit a positive transparency and three colour prints of each figure.

If the manuscript has been prepared on a computer-based word-processing system, authors must specify the software program used. We edit manuscripts with an IBM-compatible word-processing system and cannot edit from diskettes that are not IBM-compatible. Authors should indicate if they are willing to send us a diskette when their manuscript has been accepted.

The process of initial consideration, peer review and editorial decision making of the manuscript usually takes about 8 weeks. The original copy of a rejected manuscript will be returned to the authors; all other copies will be destroyed.

Accepted manuscripts will be edited not only to conform with *Canadian Journal of Surgery* style and for correctness of grammar, syntax and punctuation but also for clarity. The corresponding author will receive a copy of the edited manuscript *or* a galley proof before publication and is responsible for obtaining coauthors' approval of the changes.

Authors will be expected to sign a document transferring copyright to the *Canadian Journal of Surgery.* All accepted manuscripts become the permanent property of the Canadian Medical Association and may not be published elsewhere, in whole or in part, without written permission of the publisher. Reprints will be available for purchase and may be distributed as the author desires.■

Directives aux auteurs

Le *Journal canadien de chirurgie* étudiera les manuscrits d'articles originaux, de recherche clinique, de technique chirurgicale ou d'histoire de la chirurgie, un nombre restreint d'études de cas, des éditoriaux et des lettres. Quatre exemplaires des manuscrits, en français ou en anglais, doivent être adressés au Dr Roger G. Keith, *Journal canadien de chirurgie*, Département de chirurgie, Hôpital Royal University, 103 Hospital Dr, Saskatoon, SK S7N 4J9.

La lettre de présentation, signée par tous les auteurs, doit confirmer que le manuscrit n'a jamais été publié et n'a été soumis à aucun autre journal. Les auteurs divent y joindre une autorisation signée par les personnes citées sous la rubrique des remerciements ou identifiable dans le matériel d'illustration ainsi que de tout détenteur de droits d'auteur de matériel déjà publié (p.ex., tableaux, illustrations et longues citations) et qui est reproduit, avec ou sans modification, dans l'article soumis. Les auteurs doivent indiquer la source de toute aide financière ou matérielle, tout intérêt commercial qui les aurait motivé en ce qui concerne le sujet à l'étude ainsi que toute affiliation ou travail avec un organisme qui a un intérêt financier dans le matériel de recherche utilisé ou dans le sujet lui-même.

Préparation du manuscrit

Le style doit se conformer aux «Exigences uniformes pour les manuscrits présentés aux revues biomédicales» (*Can Med Assoc J* 1992; 146 : 871–878).

Les noms des auteurs doivent paraître sur la page titre, de même qu'à l'endos de chaque jeu d'illustrations. Les remerciements doivent figurer sur un feuillet séparé, non paginé, à la suite de la bibliographie.

Toutes les pages (page titre, résumé et mots clefs [termes MeSH si possible], textes, références, tableaux et légendes de figures) doivent être dactylographiées à double interligne, à 10 caractères au pouce, sans justification à droite ni espacement proportionnel, et imprimé en «qualité lettre» afin de faciliter la révision et la lecture électronique.

Pour tout manuscrit, les auteurs doivent soumettre un original et trois photocopies de bonne qualité, ou trois impressions supplémentaires de texte et des tableaux, et quatre copies des figures prêtes à la reproduction photographique.

Pour les études de cas, il n'est par nécessaire de rapporter une anamnèse détaillée avec les résultats de l'examen physique dans le format clinique normal. Les résultats négatifs ou normaux d'examens de laboratoire ne doivent être mentionnés que s'ils sont essentiels à l'exclusion d'un diagnostic possible. Il suffit d'établir les raisons qui ont contribué au diagnostic ou au traitement. L'évolution clinique doit être décrite succinctement et les observations ou évènements importants doivent être rapportés avec suffisamment de détails pour en établir la crédibilité. La bibliographie doit se limiter au soutien du point que l'on veut faire ressortir quant à l'évènement ou à l'observation.

Des résumés sont exigés pour les articles originaux, historique ou de revue ainsi que pour les études de cas; ils ne sont pas requis pour les articles sur les techniques chirurgicales ou pour les éditoriaux. Un résumé structuré doit être fourni pour les articles originaux et de revue (voici le numéro d'octobre 1992, pages 473 à 475). Les résumés pour les articles historiques et les études de cas doivent être brefs mais, détaillés (de 60 à 150 mots).

La bibliographie doit être établie numériquement, selon l'ordre d'apparition dans le texte. Les références citées dans les tableaux doivent être numérotées d'après l'ordre de la première mention du tableau dans le texte. Le style adopté pour la bibliographie est celui qui est utilisé dans ce numéro du Journal.

Autres considérations

Les figures en couleur sont à la charge de l'auteur. Il lui faudra fournir une diapositive et trois épreuves en couleur pour chaque figure. Les auteurs sont priés de nous préciser, le cas échéant, le logiciel ayant servi à préparer le manuscrit. Nous révisons les manuscrits avec un système de traitement de texte compatible avec le système IBM. Nous ne pouvons pas réviser à partir de disquettes qui ne sont pas compatibles avec le système IBM. Les auteurs doivent nous indiquer s'ils sont disposés à nous faire parvenir une disquette quand leur texte est acceptée.

Le processus relatif à l'étude préliminaire de l'article, à la révue critique et à la prise de décision de la rédaction peut durer à peu près 8 semaines. La copie original de tout manuscrit refusé est retournée à ses auteurs et toutes les autres copies sont détruites.

Tout manuscrit accepté est révisé non seulement pour le rendre conforme au style du *Journal canadien de chirurgie* et pour corriger les fautes de grammaire, de syntaxe et de ponctuation, mais aussi pour en assurer la clarté et la concision. L'auteur de l'article recevra une copie révisée *ou* les épreuves en placard avant la publication et doit obtenir l'approbation des coauteurs pour les changements apportés.

Avant la publication, tous les auteurs doivent signer un document par lequel les droits d'auteurs sont transférés au *Journal canadien de chirurgie*. Tout manuscrit accepté devient propriété permanente de l'Association des médecins du Canada et ne peut être publié ailleurs, en entier ou en partie, sans la permission écrite. Les tirés à part sont disponibles sur demande et peuvent être distribués selon les désirs de l'auteur.■

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Veuillez faire parvenir les réponses aux numéros de boîtes à l'adresse suivante : Boîte . . . , *Journal canadien de chirurgie,* CP 8650, Ottawa, ON K1G 0G8.

GFT – GENERAL SURGEON: MB – The Department of Surgery, Faculty of Medicine, University of Manitoba and the Health Sciences Centre are seeking a contingent geographical full-time general surgeon. Specific responsibilities in gastrointestinal surgery. Candidates must be eligible for registration with the College of Physicians and Surgeons of Manitoba. Certification in general surgery by the Royal College of Physicians and Surgeons of Canada is required. Additional specific requirements include the following: extensive clinical experience in gastrointestinal surgery including major hepatic and pancreatic resections and laparoscopic surgery; skills and extensive experience in endoscopic retrograde cholangiopancreatography and other G.I. endoscopy; and training and experience in research with publication success. Salary and academic rank will be at the entry level in the department of surgery. The University of Manitoba encourages applications from qualified women and men, including members of visible minorities, aboriginal people, and persons with disabilities. The university provides a smoke-free environment, save for specially designated areas. In accordance with Canadian immigration requirements, this advertisement is directed to Canadian citizens and permanent residents. Closing date for receipt of applications is Feb. 28, 1993. Interested candidates should apply, enclosing a curriculum vitae in writing, to: **Dr. R.J.W. Blanchard, Professor and Head, Department of Surgery, Health Sciences Centre, GC 411-820 Sherbrook St., Winnipeg, MB R3A 1R9.** –S93-137

SURGICAL ONCOLOGY FELLOWSHIP: ON – The Division of General Surgery at the University of Toronto is offering a 1-year clinical fellowship available July 1, 1993. The fellowship is intended for individuals who have completed an accredited North American university general surgical residency and are eligible for certification. Preference will be given to applicants eligible for Canadian licensure. Applicants should submit a current curriculum vitae with the names of three referees to: **Lorne E. Rotstein, MD, Director, General Surgical Oncology Postgraduate Education, Toronto General Hospital, Eaton Wing, 7th Floor, 200 Elizabeth St., Toronto, ON Canada M5G 2C4.** –S92-131

GENERAL SURGEON: ON – Well-established group practice is looking to replace a retiring partner/surgeon to serve a community of 30 000 + located 25 minutes west of London. Town population 10 000 +. Fully computerized, modern clinic adjacent to a fully accredited, well-equipped hospital using 116 acute care beds. Busy emergency department. Preference will be given to orthopedics/gynecology. Essentials include laparoscopy skills and fellowship status. One-in-three on-call schedule for this pleasant community. Large referral base guaranteed. Associate to full partnership attainable. Please contact or send CV to: **Steven Wong, c/o Strathroy Medical Clinic, 376 Carrie St., Strathroy, ON N7G 3E3; tel: (519) 245-0430.** –S92-128

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MSI currently has 311 outstanding practice opportunities in solo, group, clinic and HMO settings throughout the U.S. These include coastal and southeastern areas. We want to present these practices to you and be a problem solver. There is no charge to you for this service.

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–S93-143

FELLOWSHIP IN ENDOUROLOGY AND ESWL

This 1-year postgraduate fellowship offers a wide range of clinical experience in endourology including percutaneous surgery, ureteroscopy, ESWL and laparoscopic surgery in urology. Aproximately 50% of the fellow's time will be spent in the laboratory participating in projects related to endourologic and shock wave lithotripsy research. Salary will commensurate with the level of training.
Please reply with curriculum vitae to:

Dr. John Denstedt
Chief of Urology
St. Joseph's Health Centre
268 Grosvenor St.
London, ON
N6A 4V2

–S92-130

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GENERAL PRACTITIONER/SURGEON: BC – Souris Health District. Three physicians require a general practitioner/surgeon. Associate would enter into active surgical/endoscopic practice. The community of 1700 residents has a modern, 30-acute-bed facility, serving the district of approximately 7000 people. Located 30 minutes from Brandon (population 40 000), a university centre. Contact: **Mr. J. Woodmass, Administrator, or Dr. D. Cram, Chief of Staff, PO Box 10, Souris, MB R0K 2C0; tel (204) 483-2121.**
–S93-145

B/C ORTHOPEDIC SURGEONS AND OTHER SPECIALTIES: NEW YORK, US – Needed for a non-treatment disability evaluation centre in Buffalo, New York. For further information please reply with CV to: **Sam H. Stedman, 620 Erie Blvd. W, Ste. 208, Syracuse, NY, USA 13204; or tel (315) 475-3926.**
–S93-138

RESEARCH FELLOWSHIP SPINE SURGERY – Orthopaedic Hospital Spine Center in Los Angeles, California is offering a 1-year spine research fellowship starting July 1, 1993. Fellowship training will include laboratory and clinical research with exposure to clinical orthopedic surgery and academic conferences. Submit CV with references to: **Santi Rao, MD, Director, Orthopaedic Hospital Spine Center, 2300 S Flower St., Ste. 200, Los Angeles, CA 90007; tel (213) 741-0800, fax (213) 747-1716.**
–S93-144

GENERAL SURGEON

Second general surgeon required for the town of Milton in southern Ontario. This 103-bed hospital serves a population of 35 000 with a large catchment area; 16 general practitioners, an internist, radiologist, obstetrician and one other general surgeon comprise the active medical staff. Several other surgical subspecialties available. State-of-the-art laparoscopic equipment available. Milton is located within easy access to two university medical centres and provides great recreational opportunities.

Applications to:

Dr. L. Robinson
Chair, Manpower Committee
Milton District Hospital
30 Derry Rd. E
Milton, ON L9T 2X5
Tel (416) 878-2383
Fax (416) 878-0498.
—S93-146

CLINICAL FELLOWSHIP AVAILABLE
IN CARDIOVASCULAR SURGERY BEGINNING JULY 1, 1993

There is an opportunity for considerable surgical experience with a busy adult cardiac surgical team (650 pumps/year). Ideal for surgeon awaiting a position or between residencies. Eligibility for Ontario general or educational licence necessary. Salary according to experience or fee for service if applicable.

Replies to:

Dr. Bernard S. Goldman
Head, Cardiovascular Surgery
Sunnybrook Health Science Centre
2075 Bayview Ave., Ste. H410
Toronto, ON
M4N 3M5
Tel (416) 480-6070
Fax (416) 480-6072
–S93-136

CLINICAL FELLOWSHIP IN KNEE AND SHOULDER SURGERY IN SPORT MEDICINE

Applications are now being accepted for a 6-month sport medicine fellowship starting July 1, 1993 emphasizing arthroscopic and open treatment of knee and shoulder injury and disease.

Applicants must be eligible for licensure in the province of Alberta and preferably will have completed their FRCSC in orthopedic surgery.

Address enquiries to:

Caroline Eagles, Program Secretary
Department of Surgery, Room D6-012
Calgary General Hospital, BVC
841 Centre Avenue East
Calgary, Alberta
T2E 0A1
—S93-140

University of Ottawa • Faculty of Medicine

Chair of Surgery

The University of Ottawa invites applications for the position of chairperson of the university department of surgery.

Applicants must be eligible to practise in Ontario and hold certification of the Royal College of Physicians and Surgeons of Canada in surgery. The faculty is seeking an individual with a track record of clinical and academic excellence, leadership skills and potential to develop a strong research program in surgery.

The department is responsible for directing both undergraduate teaching and postgraduate programs in surgery in the Ottawa Civic Hospital and Ottawa General Hospital and Children's Hospital of Eastern Ontario. The successful candidate will hold a joint appointment as chair of the university department of surgery and head at one of the affiliated teaching hospitals.

The faculty is seeking an individual who will hold a full-time university appointment. Salary and fringe benefits are commensurate with qualifications and experience, and are in accordance with existing scales at the University of Ottawa.

Priority will be given to Canadian citizens and permanent residents of Canada in accordance with Canadian immigration requirements. Employment equity is university policy.

A working knowledge of both English and French is desirable and a commitment to support bilingualism within the faculty is essential.

Applicants are requested to forward their curriculum vitae and the names of three referees prior to Apr. 15, 1993.

John F. Seely, MD
Dean, Faculty of Medicine
University of Ottawa
451 Smyth Rd.
Ottawa, ON
K1H 8M5

Université d'Ottawa • Faculté de médecine

Chaire de chirurgie

L'Université d'Ottawa accueille les candidatures à la direction de sa chaire de chirurgie.

Les candidats et candidates doivent être admissibles à exercer la profession en Ontario et posséder l'agrément à titre de spécialiste du Collège royal des médecins et chirurgiens du Canada, tout en faisant preuve de réalisations et d'expérience en chirurgie clinique et universitaire. Le poste comporte un rôle de direction dans les milieux universitaire, hospitalier et communautaire et la préférence sera accordée à une personne compétente qui s'est engagée dans la voie de l'excellence universitaire en enseignement et en recherche.

Le département à la responsabilité de fournir un enseignement de qualité au niveau prédiplomé et postdoctoral dans les hôpitaux affiliés offrant une formation en chirurgie soit l'Hôpital Civic d'Ottawa, l'Hôpital Général d'Ottawa et l'Hopital pour enfants de l'Est de l'Ontario. La personne retenue assumera une double affectation à la direction de la chaire de chirurgie de l'université et à la direction de chirurgie dans un des hôpitaux d'enseignement mentionnés.

La faculté est à la recherche d'une personne pour combler un poste à temps complet. Le traitement et les avantages sont fonction de la formation et de l'expérience, conformément à l'échelle en vigueur à l'Université d'Ottawa.

En vertu des exigences canadiennes relatives á l'immigration, la priorité est accordée aux personnes de citoyenneté canadienne et de résidence permanente au Canada. L'université a une politique d'égalité en matière d'emploi.

Une connaissance de l'anglais et du francais est désirable. Un engagement à promouvoir le bilinguisme au sein de la faculté est essentiel.

Prière d'envoyer les demandes, accompagnées d'un curriculum vitae et du nom de trois répondants, à l'adresse ci-dessous avant le 15 avr. 1993.

John F. Seely, MD
Doyen, Faculté de médecine
Université d'Ottawa
451, chemin Smyth
Ottawa, ON
K1H 8M5
S93-139

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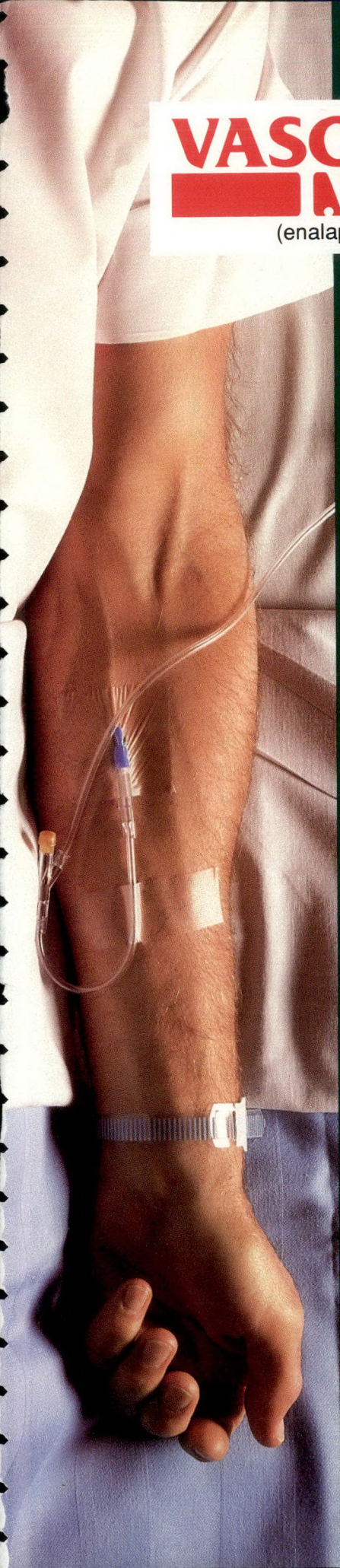

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