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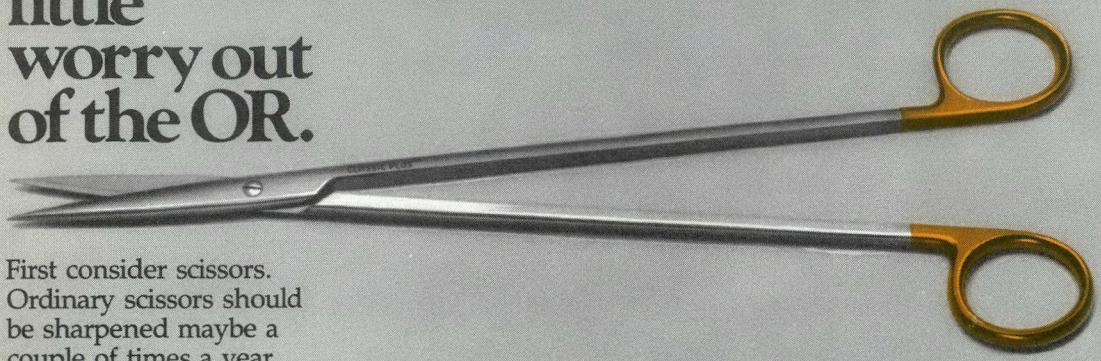
QUILL ON SCALPEL

Take a little worry out of the OR.



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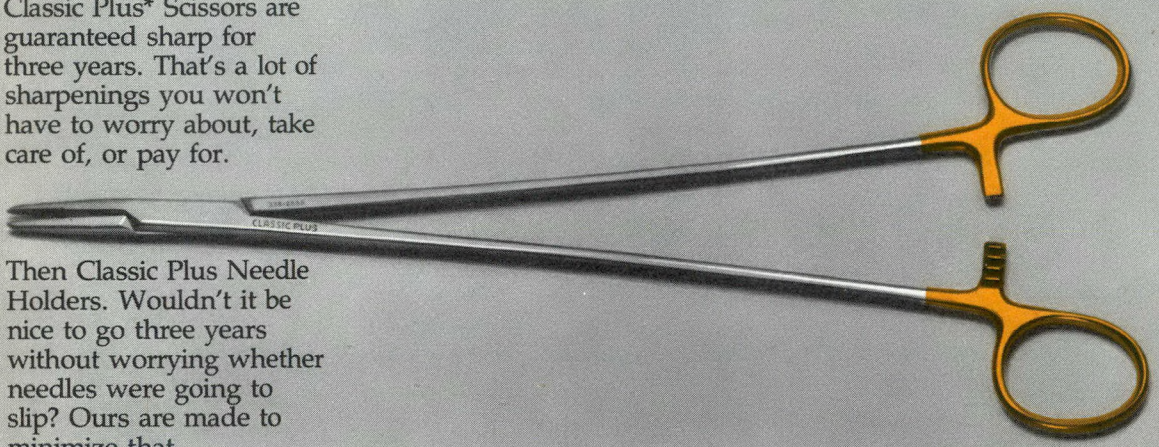

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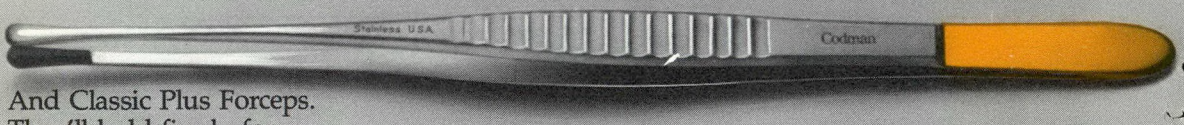

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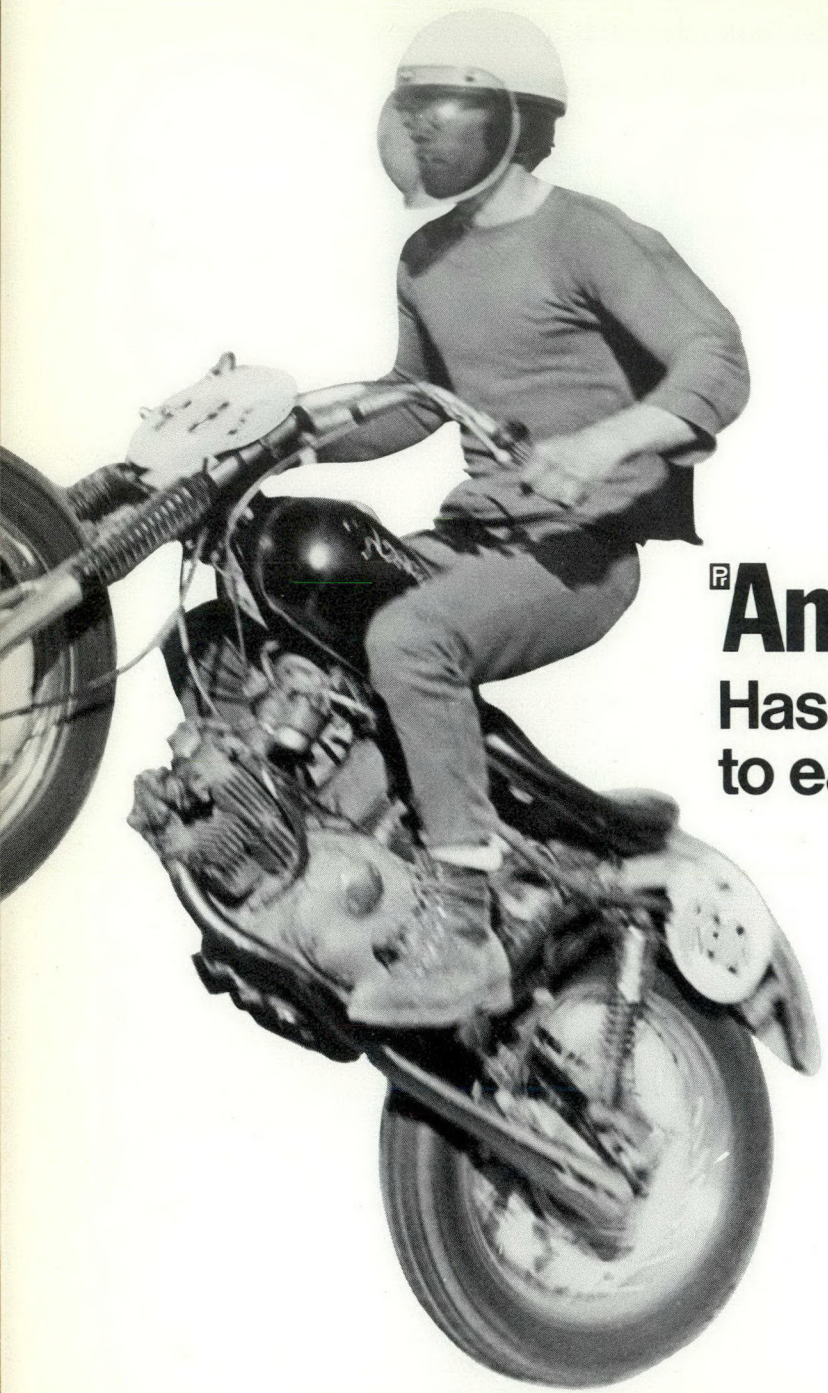

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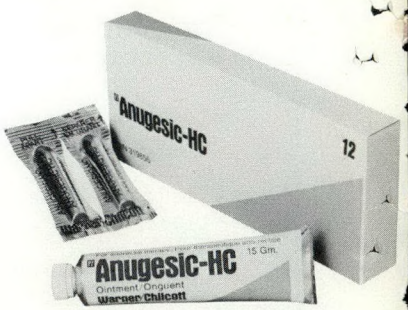

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An abstract, not exceeding 125 words in length, should accompany each article, on a separate page.

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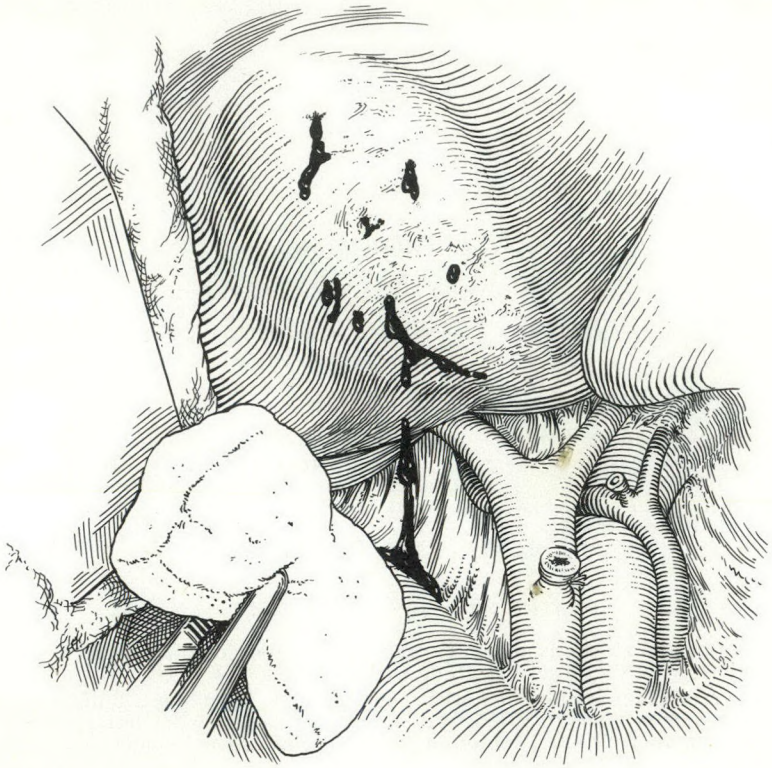

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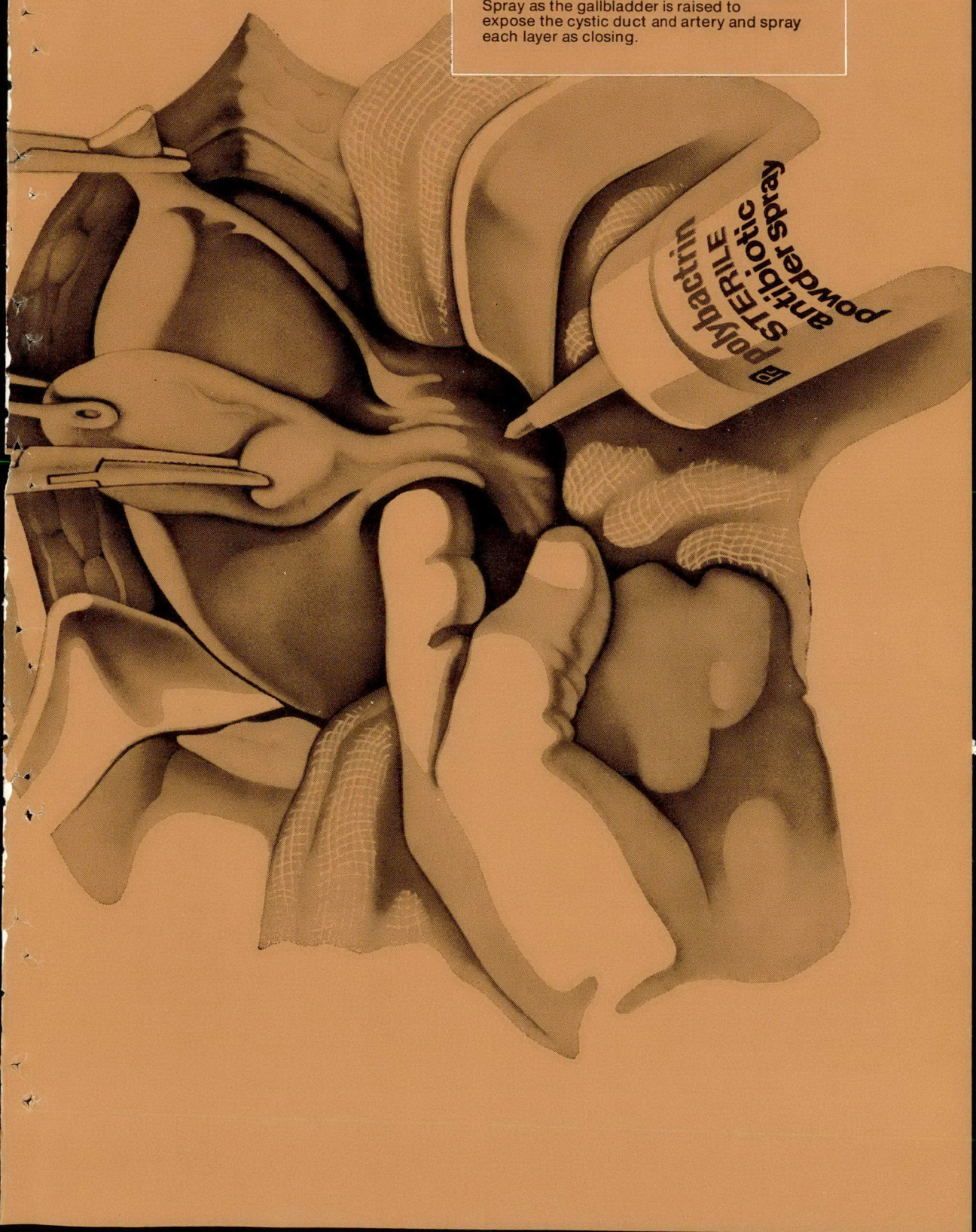

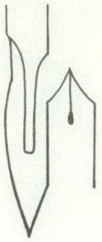

QUILL ON SCALPEL This section provides a medium through which Canadian surgeons can declare themselves, briefly and informally, on the day-to-day affairs of surgery.

PUS BONUM ET LAUDABILE OR ANTIBIOTICS?

Semmelweiss and Lister changed surgical wards from putrid smelling, frightening areas to clean places with the pervading smell of carbolic acid. They also drastically reduced postoperative mortality due to surgical wound infections. The discoveries of Louis Pasteur changed operating room procedures from antiseptic to aseptic surgical techniques, and this change led to a further reduction in the incidence of postoperative infectious complications. It also had the effect of changing the commanding presence of the surgeon operating in his morning coat or evening dress into the surgeon working in the present gleaming operating room suites populated by shrouded mummies.

A second Listerian period started with the discovery of antibiotics. Their effectiveness in killing bacteria tempted the surgeons to use them indiscriminately as a panacea to prevent postoperative infections. In fact, there were some nonfacetious suggestions of reinstituting Lister's spray loaded with antibiotics and using this in the operating rooms. Antibiotics were mixed into toothpaste and chewing gum, used for food preservation and added to animal fodder until it was recognized, almost too late, that this leads to the emergence of highly resistant microorganisms. The over-reliance on antibiotics led to slips in well-established aseptic techniques in the operating rooms. The danger of indiscriminate use of antibiotic was recognized and newer, more rational approaches were recommended. The results of prospective studies on the use of prophylactic antibiotics in surgery and the emerging recommendations are discussed in this issue by L. D. MacLean (page 243). Special areas of antibiotic prophylaxis became recognized: for example, antibiotic prophylaxis prior to instrumentation of the bacteriuric patient.

One area in which the value of antibiotic prophylaxis at the moment is not clearly established is the implantation of prostheses during clean surgical operations. Although some forms of antibiotic prophylaxis are practised by many surgeons, the lack of well-defined prospective studies leaves some questions. The appearance of infected prosthetic heart valves caused by *Staphyloccoccus epidermidis,* an unusual pathogen of low invasiveness, underlines the need for further studies.

The response of the host against invading microorganisms is probably the single most important factor in determining the postoperative fate of injured tissues. No antibacterial agent can even approach the efficiency of the concerted antibacterial effect of host response. The role of these factors is discussed by J. L. Meakins (page 259). Manipulation of these defence mechanisms in adaptation of the host to an allograft became everyday practice for transplant surgeons, who are highly skilled in navigating a sea of potential infections in the immunosuppressed host. In spite of our sophistication in managing infections, the ultimate fate of a transplant recipient is more dependent on the outcome of infections than on the adequate functioning of the transplanted organ. Although the genetically determined absence of defence mechanisms is rather rare, the iatrogenic or acquired immunodeficiencies are becoming more common. The surgical management and rational antibiotic therapy in such patients is becoming the everyday concern of surgeons. Laboratory tests that can establish the degree of immunologic deficiencies of a patient are at the moment difficult and lack accuracy. They are being developed rapidly and they will, in the not too distant future, become available to sur-

geons who wish to predict the state of cellular defences of their patients. When this time comes, the surgeon will resemble the careful general who will spy on all defence installations first, before attacking.

None of these developments will be satisfactory if we neglect the improvement of the operating theatre. Our society is technologically capable of placing several thousand tons of hardware on the surface of the moon, and having two astronauts emerge from a spaceship to drive around and set up sophisticated scientific equipment without spreading a single live microorganism. We have to find ways of acquiring the means to apply some of these technologic sophistications to provide an operating room environment that will diminish the risk of exposing the wounds to bacteria. Hospitals do not have the budgets that can approach the range of space spectacles, but some of the available budgets can be better spent. To convince those who control these budgets, we have to acquire the vocabulary and methodology of a cost accountant and start prospective studies to prove that the money spent on improvement of operating rooms would reduce hospital stay and postoperative costs.

STEPHEN I. VAS, MD, PhD, FRCP[C]

Microbiologist-in-chief,
Department of Microbiology and Immunology,
Royal Victoria Hospital and McGill University,
Montreal, Qué.

AMPUTATION IN ISCHEMIC FOOT DISEASE

The paper by Hunter in this issue of the Journal (page 273) reports the experience of the Toronto teaching hospitals with limited amputation of the foot as an acceptable solution for patients with gangrene of the foot complicated by diabetes or arteriosclerosis. In all of the patients studied foot pulses were absent.

Foot problems in the elderly have become prevalent and debilitating. Successful management of this problem is not measured by length of hospital stay, nor is it generally amenable to statistical criteria, such as are frequently presented in hospital statistics. The loss of a limb in the elderly has results that are measured in terms of social and family disruption, employability, and limited activity, and it is the avoidance of these effects that characterizes a successful outcome. Limb amputation in the middle-aged and younger individuals, although a major disability, allows some hope for successful rehabilitation. Amputation is a disablement of such magnitude that any effort that can possibly save an extremity useful for walking is justified.

The limb is jeopardized by a superimposed infection that usually begins at the edge of toenails, in the web spaces or as plantar surface ulcers — infections made more virulent by the presence of diabetes or arteriosclerosis, or both. Hunter makes the point that in the Toronto experience the diabetics were no different in their response to foot infections and subsequent treatment from nondiabetics, and that therefore diabetes itself should not be considered a *major* problem. Hunter's paper focuses attention on the role of impaired blood supply as the condition that is critical in the body's inability to respond adequately to the infection and heal the surgical wound, so the support of blood supply becomes a crucial factor in management. Hunter brings into focus the surgeon's obligation to examine the blood supply carefully and to determine appropriately the nature and cause of impairment, including adequate arteriography when indicated and peripheral vascular repair whenever possible.

The author emphasizes operations in the region of the foot. In a retrospective study, he is not permitted to view at first hand the nature of the infection, its treatment and subsequent wound management at the amputation site, and the possible impact that appropriate wound management may have had on the successful outcome. Surgical wounds of this nature are always contaminated to some degree, and careful treatment of the wound can exclude the postoperative infection that necessitates a higher amputation. The results reported are related more to the pulses than to the nature of the

wounds, and most of the comparative results from other series reported in this paper are related to the presence or absence of pulses. Hunter has clearly demonstrated that in some feet, even in the absence of distal pulses, there are collaterals with blood supply that is adequate for wound healing if the management is meticulous, since the Toronto series is composed solely of patients with peripheral vascular disease and no palpable foot pulses.

The tables in this paper present statistical comparisons between several reported series of operations. These tables permit one to conclude than an operation should be tailored to the condition of the foot, and when this is done a moderate degree of salvage may be obtained. The tables do not demonstrate the superiority of one procedure over another, because the groups subjected to the various procedures were not identical in their initial presentation.

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THE WORD, "SURGERY"

Words are slippery creatures that are, in the natural course of events, subject to a process of mutation. And these mutations may be for good or ill. The very word "surgery" is an example of the way word usage is often slipshod, as Ernst in a recent editorial notes (Surg Gynecol Obstet *140: 608, 1975). Some will ask, "Does abuse of such a word matter?", but a majority, one hopes, will object to abuse of the word, and for pragmatic reasons. Ernst objects to expressions such as "doing surgery on a patient" for two reasons: first, such expressions demean the discipline, because "surgery" denotes work that encompasses much more than technical expertise; and, second, such expressions fail to convey to colleagues that "surgery is much more than cutting". Ernst's editorial, framed and hung, might appropriately be seen in many operating rooms—and even some editorial offices.*

VILLOUS ADENOMA OF THE CECUM

SURENDAR K. KILAM, MB, BS, FRCS[C],* LAMBROSE B. COSTOPOULOS, MD† and WALTER W. YAKIMETS, MD, FRCS[C], FACS‡

Summary: Villous adenoma of the cecum developed in a 49-year-old man; the diagnosis was confirmed at operation. The pathologic and radiologic features of villous tumour in this location differ from those of tumours situated in the sigmoid colon and rectum. Signs and symptoms are vague; bleeding per rectum may not occur. Right hemicolectomy is recommended because of the high malignant potential of this tumour.

Résumé: Nous présentons ici le cas d'un adénome villeux du caecum qui s'est développé chez un homme de 49 ans. L'opération a confirmé le diagnostic. Les caractères pathologiques et radiologiques de cette tumeur diffèrent des tumeurs localisées dans le colon sigmoïde et le rectum. Les signes et symptômes restent vagues: l'hémorragie rectale n'est pas obligatoire. Nous conseillons une hémicolectomie, en raison du potentiel élevé de malignité de la tumeur villeuse du caecum.

VILLOUS adenomas are common in the rectum and sigmoid colon but rare in the cecum. In reviewing papillary tumours of the colon and rectum, Bacon, Lowell and Trimpi[1] and Swinton, Meissner and Soland[2] each reported one tumour in the transverse colon, and Fisher and Castro[3] found one in the ascending colon. In the Ochsner Clinic series,[4] in 163 cases only two villous adenomas arose in the cecum and one in the appendix.

Villous adenomas are usually sessile, consisting of projecting mucosal villi piled on one another; grossly, the clefts between the villi give them an irregular appearance. The mode of presentation and the clinical features vary, depending on the site and size of the tumour. Sigmoid tumours are occasionally associated with diarrhea and fluid and electrolyte imbalances, as a result of the large losses of electrolyte-rich colonic mucus,[5] but such symptoms have not been reported in cases of villous adenomas in the cecum. Radiologic appearances are usually typical; they are best seen in the postevacuation film or by double-contrast studies.

The clinical and radiologic features of villous adenomas of the cecum are illustrated in the following case report.

CASE REPORT

A 49-year-old man had a history of crampy right lower quadrant pain of 1 year's duration. The pain was associated with headache, flushing of the face and sweating; usually it started 2 hours after a meal. In between these cramps, he had a persistent dull ache in the same area. The frequency of bowel movements had increased from one to two each day. For 2 months before admission, the patient had been taking Maalox, which relieved the right lower quadrant pain. He also noted that ingestion of beer caused increased pain and the appearance of bright red blood in the stools.

The main physical findings were as follows: His height was 160 cm and his weight, 78 kg. He was in no acute distress, but the right lower quadrant of the abdomen was tender on palpation. Other findings, including those on rectal and sigmoidoscopic examination, were normal.

Laboratory investigation revealed a normal complete blood count, erythrocyte sedimentation rate, blood urea nitrogen concentration and serum electrolyte concentrations. The result of the screening test for carcinoid tumour was negative. Occult blood was detected in the stools. Fluoroscopy and air-contrast studies of the barium-filled colon showed that there was no reflux of barium into the terminal ileum, but a large, lobulated filling defect (Fig. 1) (dimensions, 4 cm x 4 cm) was seen in the cecum, with the base of the lesion in its lateral wall; the filling defect was persistent and apparent after evacuation of the barium and clearance of air contrast. The appendix was filled with barium and was unremarkable. The suggested radiologic diagnosis of this filling defect was a polypoid adenocarcinoma.

An exploratory laparotomy was performed

*Department of surgery, Memorial University of Newfoundland, St. John's, Nfld.

†Department of radiology, University of Alberta Hospital, Edmonton, Alta.

‡Department of surgery, University of Alberta Hospital.

Reprint requests to: Dr. S. K. Kilam, Department of surgery, Memorial University of Newfoundland, St. John's, Nfld. A1C 5S7.

through a right paramedian incision. A soft polypoid mass was palpated in the cecum. The remainder of the gastrointestinal tract and the liver felt normal. A cecotomy was performed because the cecal lesion did not feel like a carcinoma and because the tumour was broad-based. Frozen-section biopsy of a specimen of tumour tissue revealed evidence of a villous adenoma. A limited right hemicolectomy was performed after closure of the cecotomy. Microscopic examination of the tissue showed histologic features of a villous papilloma with no evidence of malignancy. Sections of regional lymph nodes were negative.

Discussion

The majority of villous adenomas are found in the rectosigmoid region although they have been noted in the duodenum, stomach and gallbladder. In one series of 1032 cases of villous adenomas, only 1.3% (13) of adenomas arose in the cecum.[6] In another, of more than 50 villous adenomas, 83% were either palpable or visible through the sigmoidoscope; and although 17% were located proximal to the sigmoid colon none arose from the right side of the colon.[7]

The radiologic features of villous tumours are often sufficiently typical to suggest the correct diagnosis. Double-contrast examination of the colon usually shows a bulky intraluminal mass with irregular contour (Fig. 2). After evacuation, the villous tumour changes size and configuration and shows a reticulated pattern produced by barium caught within the collapsed mass. The colonic segment harbouring a villous adenoma shows preserved haustral markings, good distensibility and a bubbly mucosal pattern.

Differentiation between benign and malignant tumours of the cecum is not always possible before operation. Striking changes on follow-up examination such as fixation, luminal narrowing, destruction of the adjacent haustral markings and ulceration of the mass may suggest the probability of malignant degeneration. When the bowel wall is involved in a superficial spreading manner, in appearance the lesion may be confused with retained stool; the diagnosis is established by proper colonic pre-

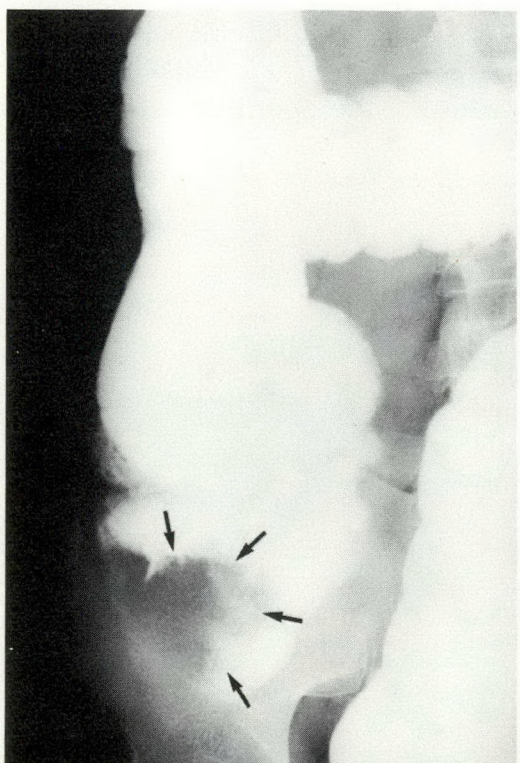

Fig. 1.—Demonstration of villous adenoma of cecum as large filling defect by fluoroscopy with air contrast.

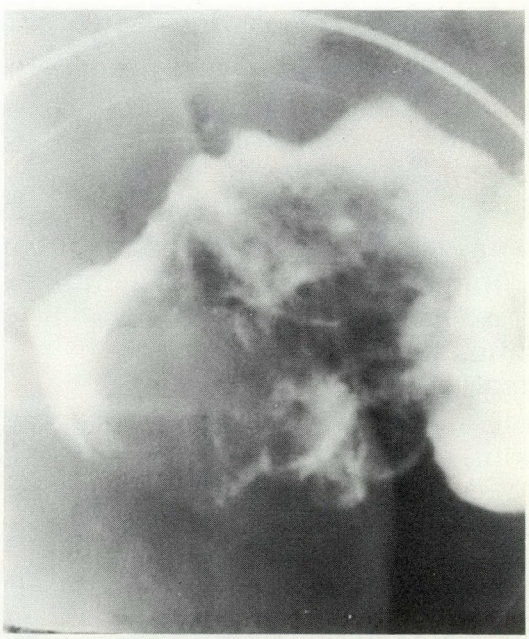

Fig. 2.—Irregular contour of bulky intraluminal mass revealed by double-contrast examination.

The Effect of Trasylol® in Acute Pancreatitis

*** Results**

Course of illness	Group A (Trasylol)		Group B (Placebo)	
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Moderate	13	24.5	9	17.3
Severe	6	11.3	8	15.4
Died	4	7.5	13	25.0
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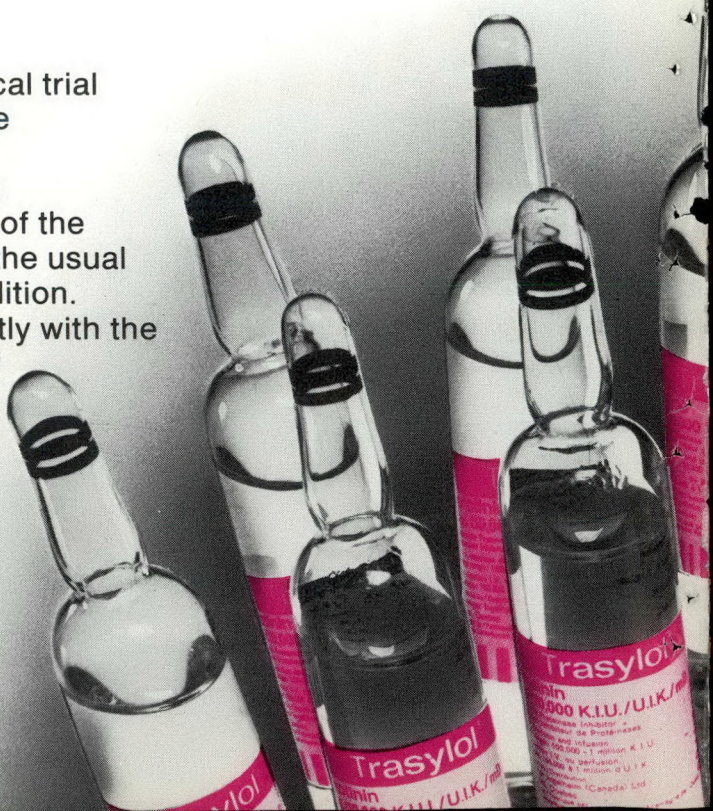
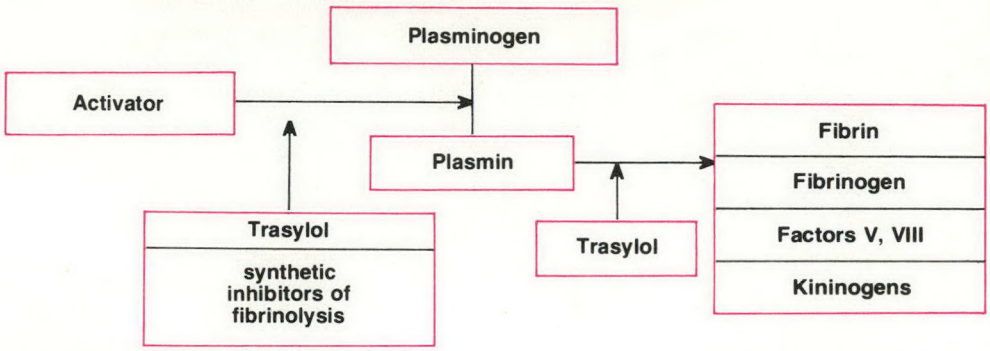


*Trapnell, J.E. et al, British J. Surg., March 1974.

The Effect of Trasylol® in Hyperfibrinolytic Hemorrhages



Trasylol, in its role as an antifibrinolytic agent, inhibits both plasmin and the plasminogen activator.

Synthetic antifibrinolytic agents inhibit only the plasminogen activator.

Trasylol is indicated for primary and generalized, secondary hyperfibrinolytic hemorrhages with and without the shock syndrome. Secondary hyperfibrinolysis following intravascular clotting may require heparin and/or fibrinogen replacement in addition to Trasylol. With Trasylol, the antifibrinolytic agent with simultaneous anti-coagulant (anti-thromboplastic) effect, there will not be a dangerous shift in the equilibrium between the clotting and the lysis system in favour of coagulation. Synthetic antifibrinolytics are contraindicated if there is evidence of active intravascular coagulation. Trasylol is indicated in all cases of hyperfibrinolysis, whether a differential diagnosis has been made or not.

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paration and further examination. Intramural soft polypoid lesions (e.g. lipoma) should not be confused with villous tumours.

The incidence of malignancy and of associated colonic lesions is high in cases of villous adenoma of the cecum.[8, 9] Olson and Davis[10] found a clear relationship between the size of the lesion and the incidence of malignancy: in lesions smaller than 2 cm in diameter, the incidence of malignancy was 24.4% and in lesions larger than 5 cm in diameter the incidence of malignancy was 80%.

Most discussions regarding the therapy of villous tumours relate to the rectosigmoid lesions and have little application to adenomas situated in the cecum. For villous adenomas in this region, right hemicolectomy is recommended because of the high malignant potential of these tumours.

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IMPEDANCE PHLEBOGRAPHY: ACCURACY OF DIAGNOSIS IN DEEP VEIN THROMBOSIS*

JACQUES E. NADEAU, MD, ROBERT DEMERS, PhD, BERNARD SKINNER, MD, FRCP[C] and LLOYD D. MacLEAN, MD, FRCS[C]

Summary: In an evaluation of the diagnostic accuracy of impedance phlebography for the diagnosis of deep vein thrombosis, 51 limbs in 32 patients were examined simultaneously by impedance phlebography and by venography. The impedance diagnosis was accurate in 47 limbs, erroneous in 2 and inconclusive in 2; the overall accuracy was 92%. Simultaneous clinical diagnosis yielded an accuracy of 53%.

The method requires full cooperation by the patient and meticulous attention to the details of the test by the physician or technician performing the examination.

Résumé: Pour nous permettre d'évaluer le degré de précision de la phlébographie sous impédance dans le diagnostic de thrombose des veines profondes, nous avons examiné 51 membres chez 32 malades, simultanément par phlébographie sous impédance et par phlébographie simple. Le premier type d'examen s'est révélé exact dans 47 membres, erroné dans 2 autres et n'a pas permis de conclure dans les 2 derniers cas. Le degré de précision atteignait 92%. Un diagnostic clinique simultané n'a été exact que dans 53% des cas.

Pour être efficace, cette méthode exige une coopération étroite du malade et, de la part du médecin ou du technicien qui pratique l'examen, une attention méticuleuse des détails.

IMPEDANCE phlebography, as described in 1970 by Mullick, Wheeler and Songster,[1] initially promised to be a useful method of making the early diagnosis of deep vein thrombosis. Together with suitable prophylactic measures, it also promised to aid in the prevention of pulmonary embolism. Results of more recent studies, however, contradicted those of the initial work.[2-4]

Wheeler and his associates obtained diagnostic accuracy of 97%, using venography[5] as the absolute reference, and Gazzaniga, cited by Wheeler,[5] achieved an accuracy of 100% in a group of normal volunteers. Studying the limb in a different position, so that the limb was under tension rather than relaxed, Dmochowski, Adams and Couch[4] reported an overall accuracy of 53%; they recorded false-positive results in 47% but still considered the method useful because of the low incidence (23%) of false-negative results. In contrast, Steer's group[2] found an incidence of false-negative results of 39% but no false-positive results; moreover, 20% of the recordings were nondiagnostic and 20% of the patients seen were not technically suitable for the test. Finally, Deuvaert, Dmochowski and Couch[3] studying the leg in different positions, as well as that described by Wheeler and that by Dmochowski, obtained an overall accuracy of 68% with 38% false-positive and 16% negative results.

This report summarizes our own attempt to evaluate the method and to determine the possible causes for the discrepancy in results by others reporting on the technique. In particular, we have examined artifacts in the impedance wave forms caused by different respiratory maneuvers.

MATERIAL AND METHODS

We did not specifically select the patients for this study. Patients were referred usually because of the clinical possibility of venous thrombosis.

Calf impedance was measured with a battery-operated impedance meter (Codman & Shurtleff, model IPG-100) originally described by Mullick, Wheeler and Songster[1] and by Wheeler and Mullick.[6] A constant current of less than 1 mA is applied to a pair of circumferential electrodes. The circumferential electrodes were applied 10 cm apart in the widest part of the calf, and voltage proportional to the calf impedance is detected by a second inner electrode pair. The output of the meter is a measure of the percentage change from the baseline im-

*From the departments of surgery and diagnostic radiology, the Royal Victoria Hospital and McGill University, Montréal, Qué.

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Reprint requests to: Dr. L. D. MacLean, Surgeon-in-Chief, Royal Victoria Hospital, 687 Pine Ave. W., Montréal, Qué. H3A 1A1.

pedance; a calibrated, 0.2% impedance step change is built in for adjustment of recorder sensitivity.

Respiratory movements, consisting of a deep thoracic inspiration and a passive expiration, were monitored by a simple pneumatometer constructed of a segment of corrugated tubing, which was placed around the chest and connected to a pressure transducer. Both the impedance and the respiratory transducer signals were registered on a two-channel direct-writing recorder.

Adequate relaxation of patients before any recordings were made was important. All patients were studied in the recumbent position; the leg to be studied was externally rotated and flexed between 30 and 45° at the hip and the knee, and was supported on a small pillow for maximal comfort and relaxation.

In all patients, the limb thought to be normal was studied first. After several reproducible recordings of adequate technical quality had been obtained for the normal limb, the limb thought to be affected by venous thrombosis was then studied. This approach ensured the best possible technique for each patient, with reference to position of the limb, respiratory movement and relaxation. Interpretation was made according to the maximum impedance variation, and for this series Wheeler's criteria were adopted. Patency of the venous system was signified by changes in baseline impedance exceeding 0.2%. Occlusion was indicated by variations of less than 0.15% whereas values in between were considered of uncertain diagnostic accuracy or borderline. Venograms were performed within 48 hours of the impedance recordings to verify findings with respect to both clinical diagnosis and impedance phlebography.

Results

In all, 51 limbs in 32 patients were studied at intervals of from 4 hours to 6 months after the onset of symptoms. In 28 instances thrombophlebitis had been diagnosed or suspected, and in 10 other instances pulmonary embolism had been diagnosed or suspected. Vena caval ligation had been performed in one patient in whom both legs were studied. In the other 11 instances the limbs studied were believed to be normal.

The impedance diagnosis was confirmed in 47 limbs by venography (accuracy, 92%): for 2 other limbs (4%) the impedance values were erroneous, and for 2 others (4%) the findings were inconclusive (Fig. 1).

Fig. 1 also indicates that impedance phlebography usually gave distinctly positive or negative findings, with a small borderline group. Moreover, the accuracy of the method was unchanged in a survey of all eight patients in whom the venogram revealed abundant collateral circulation.

The clinical diagnosis was correct in 53% of cases. In five cases false-positive results were obtained and in four, false-negative results; in all of these cases impedance phlebography yielded an accurate diagnosis.

Venography revealed the distribution of thrombosis along the deep venous system; there was widespread disease from the tibialis vessels to the vena cava (Table I).

Three case histories illustrate the accuracy of the method in different clinical situations.

Case 1.—A 50-year-old woman with diabetes had a 7-year history of bilateral calf tenderness and ankle and calf swelling with dependency. She had had deep vein thrombophlebitis of both legs 4 years before admission. A clinical diagnosis of bilateral postphlebitis limb disease was made. Her symptoms were alleviated by elevation and use of elastic stockings. Impedance phlebography yielded an impedance variation of 0.42% in the right leg

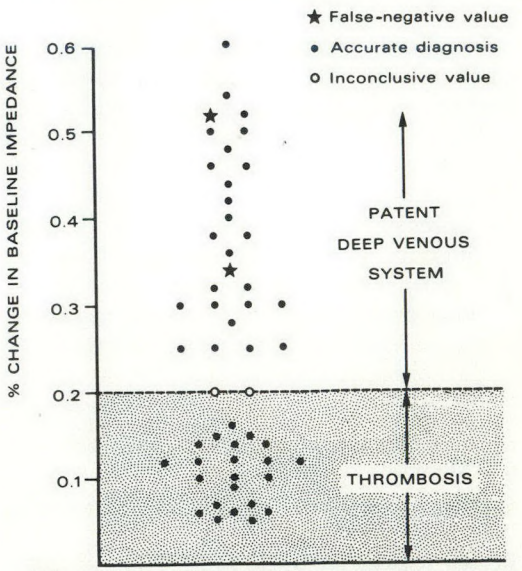

Fig. 1.—Results of impedance phlebography in 51 limbs.

and of 0.46% in the left leg; bilateral venography showed that the deep veins were entirely normal, with no evidence of old or recent phlebitis of the venous system (Fig. 2).

In this case impedance phlebography had good reliability in a patient whose legs were edematous and painful owing to a lesion other than deep venous occlusion.

Case 2.—A 77-year-old woman sustained a pathologic fracture of the left femur secondary to a metastatic breast lesion. Internal fixation was performed and a course of radiation therapy was given. Massive painless edema of the left leg from the upper thigh to the foot developed 1 week after the completion of radiation therapy. Impedance phlebography yielded an impedance variation of 0.12%. A venogram revealed the presence of clot in the thigh and calf, and complete occlusion of the deep venous system at the common femoral vein (Fig. 3). The patient was treated with intravenous heparin and over the following week the swelling resolved completely.

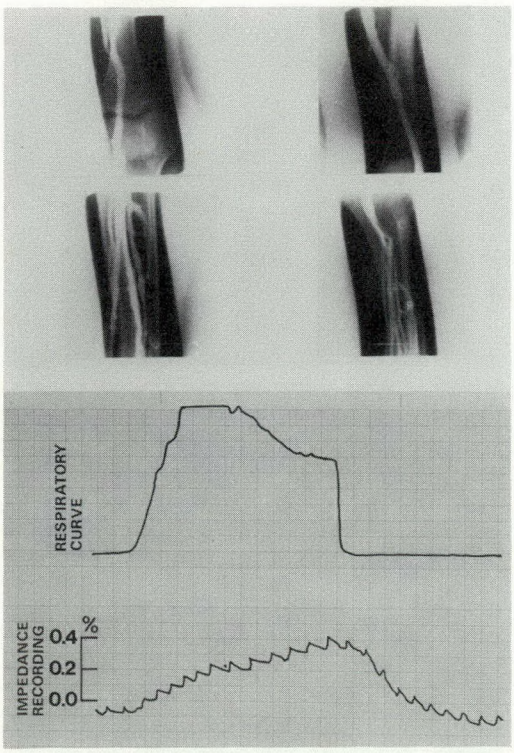

Fig. 2.—Impedance phlebogram, respiratory curve and venograms for left leg (case 1). Venogram shows that deep veins of leg are free of thrombosis, and impedance change is well within normal range. (Respiratory curve and venograms are aligned with time on horizontal axis; respiratory curve does not quantitate respiratory maneuver.)

Case 3.—A 77-year-old woman with longstanding, chronic, renal failure was admitted for investigation of a swollen and tender left calf; the presumptive diagnosis was of deep thrombophlebitis. On admission the right leg was entirely normal. Bilateral impedance phlebography yielded an impedance variation of 0.05% for both the right and left legs. Venography demonstrated complete occlusion of the left deep venous system and on the right, occlusion of the right superficial femoral vein with recanalization in the mid-thigh and occlusion of the right common femoral vein at the inguinal ligament level (Fig. 4).

Discussion

Our results support the value of impedance phlebography reported by Mullick, Wheeler and Songster,[1] and by Wheeler.[5, 7] Our findings included a few "borderline" results (0.16 to 0.24%) (Fig. 1), in contrast to the findings of Steer and associates,[2] who reported a 20% incidence of such results. It is also possible that the "borderline" area is narrower than that suggested by Wheeler and his colleagues.[5]

The discrepancy in results among reporters is probably explained by differences in technique. In the present study three aspects were emphasized: (a) the position of the limb, (b) the respiratory maneuver, and (c) the reproducibility obtained before the test and the precise interpretation of the recordings.

The position of the limb at the time of

TABLE I.—Localization of Occlusions or Thrombi by Venography

Site (vein)	*No. of patients*
Vena cava	2
Common iliac	4
Common iliac and external iliac	1
External iliac and common femoral	4
Common and superficial femoral	1
Deep femoral	1
Superficial femoral	2
Superficial femoral and popliteal	3
Superficial femoral, popliteal and trifurcation	1
Trifurcation	3
Entire deep venous system (external iliac to tibialis)	2
Total	24

the study is important; an ideal position will prevent undue compression on the venous system from the surrounding tissue that can produce false-positive results. This ideal position is found by first testing the clinically normal limb; otherwise, bias in the technician's mind leads him to obtain a position and an adequate respiratory maneuver that will give a normal tracing. This position, though varying slightly from patient to patient, has been within 30 to 45° of flexion of hip and knee with external rotation in all cases. It is comparable to the one proposed by Wheeler.[5] After reviewing Dmochowski's results[4], which did not support the accuracy of the method and which were obtained with a different position, Wheeler used both positions in the same group of patients and showed that the accuracy of the method was dependent on the position.[5]

The respiratory maneuver leading to the observed maximal impedance variation demands even greater attention to technique. Lack of relaxation of the patient or undue straining during the test can produce false-positive results. Forceful expiration will cause additional intra-abdominal pressure with either delay of the return to baseline or a new peak in the impedance deflection before return to baseline, leading to confusion in the calculation of the "true" deflection. For similar reasons, a Valsalva maneuver, instead of the deep and sustained inspiration, will cause a greater obstruction to venous outflow and, therefore, false-negative interpretations.

To obtain a reproducible recording we have found it necessary to train the patient to perform a maneuver properly. In order to recognize an optimal respiratory maneuver and to estimate more accurately the maximum impedance variation, a pneumatometer is useful. We found that its deflection permitted a better correlation of changes observed in the impedance recording with the pattern of the respiratory curve; it usually permits one to differentiate artifactual deflection caused by movement rather than inspiration, and precise knowledge of the

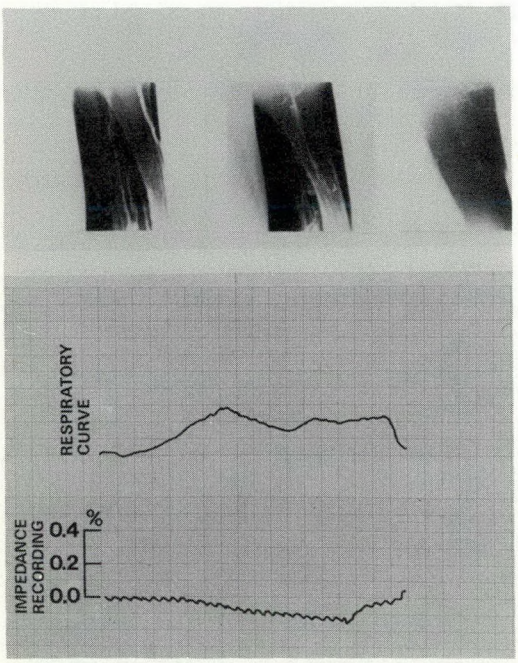

Fig. 3.—Impedance phlebogram, respiratory curve and venograms of left leg (case 2). Flattened impedance curve corresponds on venogram (from left to right) to numerous filling defects in calf veins and near absence of venous system in thigh.

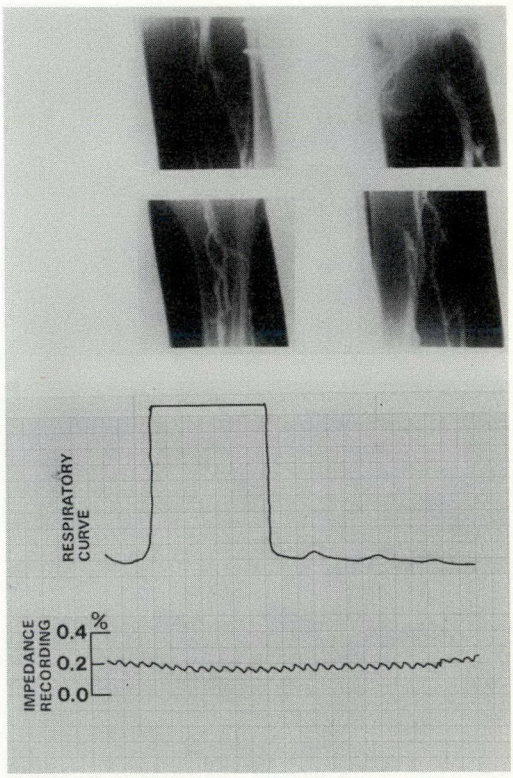

Fig. 4.—Impedance phlebogram, respiratory curve and venograms of right leg (case 3). Filling defects along superficial and common femoral veins with collateral circulation, and positive impedance test performed during respiratory maneuver.

onset, true peak and depth of inspiration—and therefore a more accurate measurement of the impedance deflection produced.

Summary and Conclusions

The technique of impedance phlebography we have described has been useful in detecting thrombi in large veins from the tibialis vessels to the vena cava. The method is noninvasive and appears equally applicable to the detection of old or recently formed thrombi. Its main limitation is the need for good cooperation by the patient and for time-consuming attention to detail. The test is not suited to patients who are agitated, confused, unconscious, or severely dyspneic, or to patients with limbs in plaster or in traction. Nevertheless, many patients remain accessible to study, and impedance phlebography should be explored further as a diagnostic measure in symptomatic as well as asymptomatic patients at risk. The technique does detect thrombi proximal to the inguinal ligament, which was the site of thrombosis in many of the patients herein reported.

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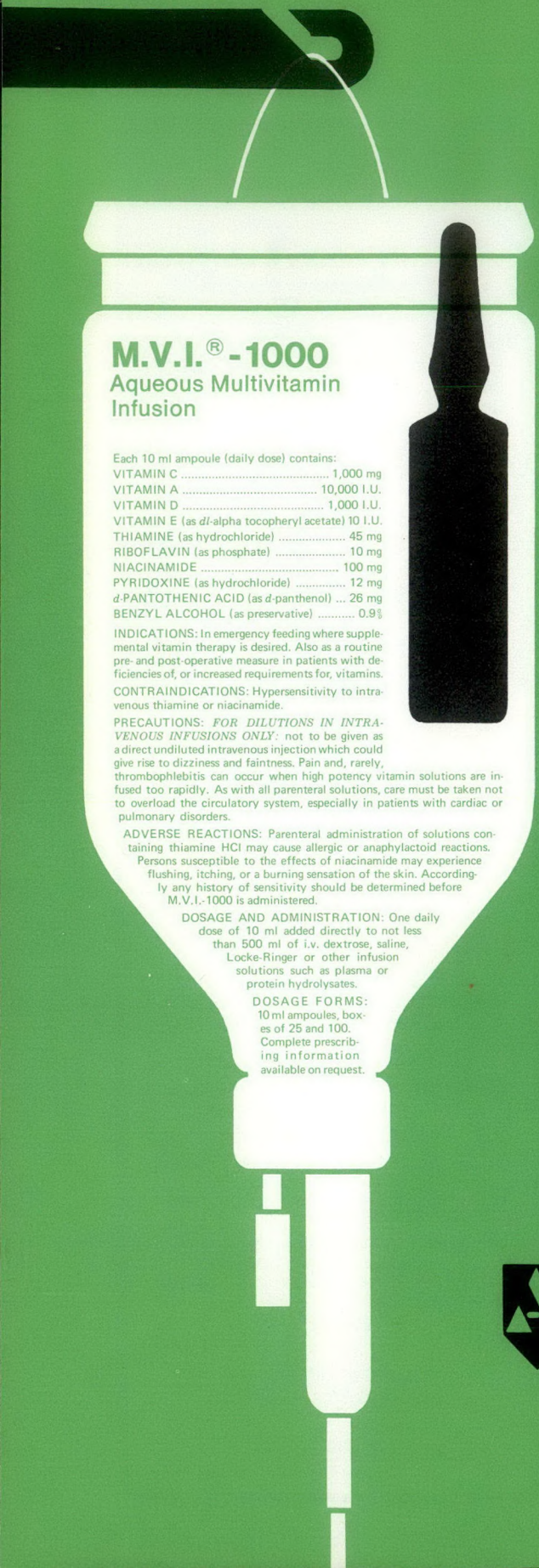

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CORRELATION BETWEEN HEMODYNAMIC CHANGES AND THE PRESENCE, SIZE, AND SITE OF MYOCARDIAL INFARCTION*

C. EDWIN KINLEY, MD, FRCS[C], ALLAN E. MARBLE, MEng, PEng, ALLAN S. MacDONALD, MD, FRCS[C] and VICTORIA L. MASLAND, BSc

Summary: Values for eight measured and calculated hemodynamic variables were recorded in 12 dogs before and after experimental anterior myocardial infarction. Changes were noted in stroke work and stroke power only; the changes in stroke work and stroke power were closely correlated with the presence of the infarct, whereas the changes in the other six dynamic variables were unpredictable and uncorrelated. The degree of correlation between the stroke work and power, and the size and site of the infarction, however, suggested that none of the eight variables would be an adequate indicator of all three characteristics of the infarction.

Résumé: Chez 12 chiens ayant subi un infarctus antérieur du myocarde, nous avons enregistré les valeurs des huit variables hémodynamiques, tant qu'avant qu'après l'infarctus expérimental. Nous n'avons noté de modifications que dans le travail systolique et la puissance de la contractilité ventriculaire. Ces changements révélaient une corrélation étroite avec la présence de l'infarctus. D'autre part, les changements observés dans les six autres variables de l'hémodynamique étaient imprévisibles et dénués de corrélation avec l'accident du myocarde. Par contre, le degré de la corrélation existant entre le travail systolique et la puissance de la contractilité ventriculaire d'une part, et, d'autre part, la dimension et le siège de l'infarctus permet de croire qu'aucune des huit variables puisse constituer un indicateur valable des trois caractéristiques de l'infarctus du myocarde.

THERE are several methods for the detection of the presence, site, size, and associated asynergy of myocardial infarction.[1] However, none of the methods used independently is adequate for a proper diagnosis of all aspects of infarction. Whereas a method may be quite reliable in predicting the presence of an infarct, it may convey little information regarding its size, site, and associated asynergy. There are three main approaches to this problem: indirect, qualitative and quantitative. Most methods provide either an indirect assessment of the presence of the infarction (i.e. electrocardiogram, enzymes, systolic time intervals, or maximal velocity of contraction), or qualitative information regarding its site or asynergy (i.e. ventriculography, apexcardiography and echocardiography). Also of interest is the quantitative assessment of the performance of the heart, for the patient's survival depends on the simultaneous maintenance of an adequate cardiac output and an adequate aortic pressure, and consequently an appropriate supply of oxygen to the tissues. A combination of the information obtained from the three approaches could provide a better means of diagnosing and assessing the treatment of myocardial infarction.

The quantitative approach to assessment has been somewhat overshadowed by the indirect and qualitative approaches. This has resulted from the difficulty in continuously measuring cardiac output in the intact patient, and it has meant that there is little information on the correlation between hemodynamic changes accompanying myocardial infarction and the presence, size, and site of the infarct. This problem of measurement has been overcome by the recent development of the catheter type of electromagnetic flow probe.[2] It is now possible to measure all hemodynamic variables associated with the heart accurately and safely.

The purpose of this paper is to present results from a controlled study on dogs of

*From the departments of surgery and anatomy, faculty of medicine, Dalhousie University, and the department of electrical engineering, Nova Scotia Technical College, Halifax, NS.

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Reprint requests to: Professor A. E. Marble, Department of surgery, 13K - Tupper Building, Dalhousie University, Halifax, NS B3H 4H7.

the correlations between alterations in the state of the myocardium and the resultant hemodynamic changes. The main objective of the study was to determine which hemodynamic parameters best reflect the change in the state of the myocardium.

Methods

Twelve mongrel dogs (weight range, 20 to 32 kg) were anesthetized with sodium thiopental (1 ml/kg body weight) and a uniform dose of succinylcholine (40 mg/ml). Ventilation was maintained with a Bird respirator connected to a cuffed endotracheal tube. After induction of anesthesia a Teflon catheter (USCI no. 7) was advanced in the femoral artery to a point near the aortic arch for the recording of ascending aortic pressure (Hewlett Packard 7858A recorder with a Hewlett Packard 1280B transducer and a Hewlett Packard 8801A preamplifier). Thoracotomy was then performed through an incision in the fourth interspace anteriorly. The ascending aorta was exposed, and a Statham electromagnetic flow probe (internal diameter, usually 18 mm) was attached for measurement of the blood flow rate in the ascending aorta; this probe was used in conjunction with a Statham SP2001 nonocclusive, zero blood-flow flowmeter. Left ventricular pressure was obtained by means of a no. 7F Teflon catheter advanced through the left atrial appendage into the ventricle via the mitral valve; the derivative of left ventricular pressure was obtained continuously (Hewlett Packard derivative computer). Heart rate and electrocardiogram (lead II) were also recorded continuously (Hewlett Packard bioelectric amplifier 8811A and Hewlett Packard 7858A eight-channel recorder). Control recordings of the variables were then obtained for all animals prior to infarction.

Infarction was induced by ligating the anterior descending artery just distal to the main septal artery. Continuous recordings of all variables were then taken for 30 minutes after creation of the infarct. When these measurements had been completed, the circumflex artery was injected with Micropaque (Damancy & Co. Ltd., Slough, England) at a pressure not exceeding 150 mm Hg. The heart was then removed, cooled and fixed in formalin for 24 hours. Each heart was weighed and the net weight obtained by subtracting the weight of the Micropaque injected. The fixed specimens were sliced from base to apex in 2-mm sections and contact angiograms made.[3] The cross-sectional area of the left ventricular myocardium (including the septum), as well as the area of the infarct, was calculated for each slice. This technique of specimen preparation makes it possible to distinguish the infarcted myocardium from the noninfarcted myocardium (Fig. 1). The areas, and consequently the volumes, of infarcted myocardium and overall left ventricular myocardium were established by superimposing a transparent grid of 0.25-cm (0.1-in) squares over each slice.

Stroke volume was calculated by dividing cardiac output by heart rate. Stroke power (the rate at which the heart is performing external work) was determined by multiplying the mean ascending aortic pressure during systole by cardiac output.[4, 5] Mean aortic pressure during systole was calculated by using the approach suggested by Walker and colleagues.[6] Stroke work was calculated by dividing stroke power by heart rate. Total peripheral resistance was determined by dividing mean ascending aorta pressure by cardiac output.

Results

These studies illustrate the alteration in hemodynamics that accompanies anterior in-

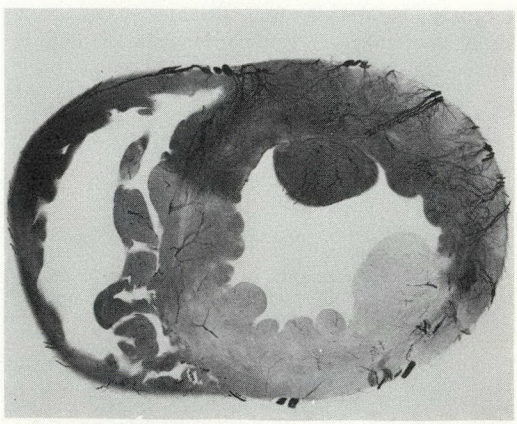

Fig. 1.—Typical slice of infarcted canine heart from which area and volume calculations were made. (Experiment no. 193; other data for this dog are given in Tables I and II.)

farction of 35 to 45% of the left ventricular myocardium. Tables I and II present data relating to the hemodynamic parameters, before and after infarction.

A statistical analysis of the percentage changes in cardiovascular dynamics accompanying infarction is shown in Table III. The correlation coefficients relating infarct size to percentage changes in the two most consistent changes (stroke power and stroke work) were 0.22 and 0.45, respectively (Fig. 2). Fig. 3 shows the site of the infarction relative to the apex and base of the heart.

Discussion

The cardiovascular variables we studied are not the only dynamic variables that have been studied in the assessment of myocardial infarction. Central venous pressure is sometimes used to indicate left ventricular filling pressure but it is not a reliable index because of the possibility of associated pul-

TABLE I.—Preinfarct Values of Measured and Calculated Hemodynamics* for Individual Dogs and Mean and Standard Deviation Values for all 12 Dogs

Experiment no.	*Weight (kg)*	*AP (mm Hg)*	*CO (l/min)*	*HR (beats/min)*	*SV (ml)*	*SP (watts)*	*SW (joules x 10^{-3})*	*TPR (mm Hg/ml · min)*
171	30	120	1.68	140	12.0	0.46	3.27	0.075
173	24	146	2.19	188	11.7	0.73	3.88	0.071
177	26	133	2.24	136	16.4	0.68	5.00	0.060
178	26	146	2.97	150	20.0	0.99	6.60	0.050
179	32	93	3.18	188	17.0	0.68	3.60	0.030
180	27	84	2.86	144	19.9	0.55	3.80	0.030
182	25	160	1.50	176	8.5	0.54	3.06	0.108
193	22	157	2.10	167	12.6	0.75	4.50	0.075
194	22	125	2.25	131	17.2	0.64	4.73	0.055
195	22	130	2.50	150	16.6	0.74	4.95	0.052
186	20	136	2.60	136	19.1	0.81	5.95	0.052
198	20	146	2.75	150	18.3	0.92	6.10	0.053
Mean	24.7	131	2.40	154.7	15.8	0.71	4.62	0.059
SD	± 3.8	± 23.4	±0.50	± 20.2	± 3.7	±0.15	±1.15	±0.020

*Abbreviations: AP, mean ascending aorta pressure during systole; CO, cardiac output; HR, heart rate; SV, stroke volume; SW, stroke work; and TPR, total peripheral resistance.

TABLE II.—Postinfarct Values* of Measured and Calculated Cardiovascular Dynamics† for Individual Dogs with Mean and Standard Deviation Values for all 12 Dogs

Experiment no.	*Weight (kg)*	*AP (mm Hg)*	*CO (l/min)*	*HR (beats/min)*	*SV (ml)*	*SP (watts)*	*SW (joules x 10^{-3})*	*TPR (mm Hg/ml · min)*
171	30	120	1.56	136	11.4	0.43	3.16	0.080
173	24	135	2.26	187	12.0	0.70	3.74	0.059
177	26	133	1.98	150	13.2	0.60	4.00	0.070
178	26	146	2.65	167	15.9	0.89	5.30	0.056
179	32	90	2.90	188	15.5	0.60	3.20	0.031
180	27	86	2.52	144	17.3	0.50	3.48	0.034
182	25	144	1.57	167	9.4	0.52	3.11	0.092
193	22	157	1.70	176	9.7	0.61	3.46	0.092
194	22	118	2.00	116	17.2	0.54	4.65	0.059
195	22	115	2.20	140	15.7	0.58	4.15	0.052
196	20	136	2.50	131	19.1	0.78	5.95	0.054
198	20	137	2.65	150	17.6	0.83	5.55	0.052
Mean	24.7	126.4	2.21	154.3	14.5	0.63	4.15	0.061
SD	± 3.8	± 21.6	±0.45	± 22.8	± 3.3	±0.14	±0.99	±0.02

*Values are for data measured approximately 30 minutes postinfarct.
†Abbreviations as in Table I.

TABLE III.—Statistical Analysis of Hemodynamic Percentage Changes in Anterior Myocardial Infarction* in 12 Dogs

Hemodynamic	*Mean*	*Range*	*Standard deviation*
Ascending aorta pressure	− 6.8	−11.5 → + 2.4	± 7.4
Cardiac output	− 7.0	−12.0 → + 11.9	± 8.1
Heart rate	− 0.4	−11.4 → + 11.1	± 6.6
Stroke volume	− 7.1	−19.8 → + 10.6	±10.2
Stroke power	−10.7	− 4.1 → − 21.5	± 7.1
Stroke work	−10.4	− 0.1 → − 23.2	± 7.8
Total peripheral resistance	+ 5.9	−14.0 → + 22.7	±11.2
Derivative of left ventricular pressure†	− 1.6	−16.5 → + 13.3	±11.6

*Infarct size (percentage of left ventricular myocardium that is infarcted muscle) = 41 ± 8.1%.
†Figures given for derivative of left ventricular pressure represent statistics for changes in maximum positive values of derivative. Note that largest mean changes occurred in stroke power and stroke work, and that smallest ratio of standard deviation to mean values is for stroke power.

monary disease.[7] Right atrial pressure is also poorly correlated with left ventricular end-diastolic pressure (LVEDP).[8] Also, in chronic left ventricular dysfunction, pulmonary artery pressure may not be indicative of LVEDP.[9] However, there is, in general, a high correlation (r = 0.93) between pulmonary wedge pressure and left atrial pressure.[10] It appears, therefore, that the use of right heart pressures to reflect the pressure in the left ventricle is currently being reassessed. Furthermore, the assumption that LVEDP adequately reflects left ventricular end-diastolic volume is not considered as being valid either.[11] A poor correlation (r = 0.06) has been reported between the presence of myocardial infarction and the magnitude of LVEDP.[12] In light of the above findings, the use of left ventricular function curves (plot of stroke work against right atrial pressure) is quite misleading, for right atrial pressure probably does not reflect LVEDP, which in turn is not indicative of left ventricular end-diastolic volume, and consequently fibre length. Finally, animal studies have led to the conclusion that ventricular function curves are not a reliable index of ventricular function.[13]

The variables measured in this study were assessed based on their correlation with respect to three aspects of myocardial infarction: presence, size and site. To the best of our knowledge this type of correlation study has not been investigated previously.

Presence of Infarct

The results shown in Table III suggest that, except for stroke power and work, car-

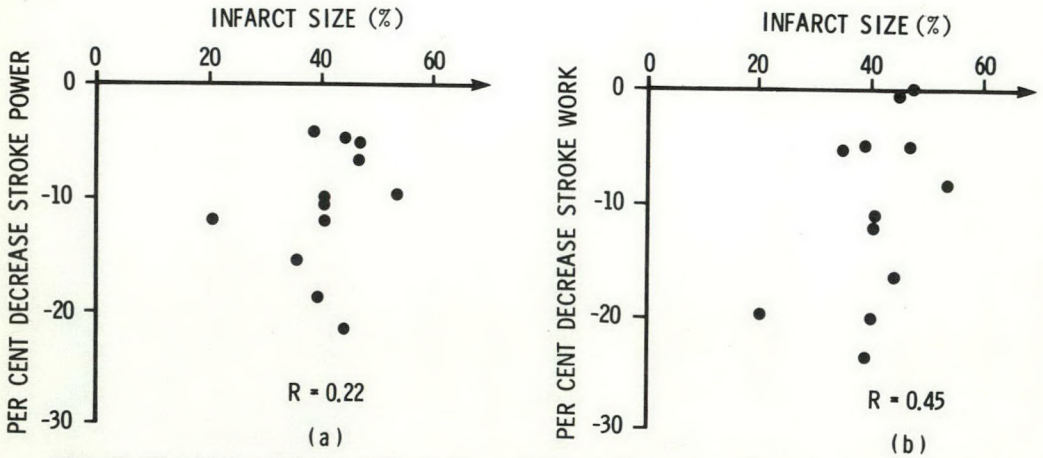

Fig. 2.—Correlation between infarct size and (a) stroke power changes and (b) stroke work changes. Size of infarct is designated by percentage of left ventricular myocardium that has been infarcted.

diovascular hemodynamic changes accompanying infarction are poorly correlated with the presence of the infarct. For all other variables, the changes accompanying the infarct were either positive or negative; the direction of change was unpredictable, which suggests that these variables are not reliable indicators of even the presence of the infarct. This is borne out statistically in that the standard deviations of the changes in such variables as ascending aorta pressure, cardiac output, heart rate, stroke volume, total peripheral resistance and derivative of left ventricular pressure are large relative to the mean change in these variables.

The literature on this topic is sparse, and in some cases the findings are conflicting. In general, however, the changes in the variables reported by others were similar to those we noted, except for stroke power and work. Braunwald[14] and Karliner and Ross[8] both reported a slight decrease in arterial pressure after myocardial infarction. Rushmer[15] stated that cardiac output is unchanged after infarction, whereas Karliner and Ross[8] as well as Freis and colleagues,[16] reported a slight decrease in this variable. The increase in cardiac output accompanying infarction, noted for two of our dogs, is not uncommon.[17] Rushmer[15] reported that heart rate increased slightly on infarction and that stroke volume remained constant. Braunwald[14] also stated that stroke volume remained unchanged but Freis and colleagues[16] found that this variable decreased with infarction. Shillingford and Thomas,[17] and also Karliner and Ross,[8] both reported that total peripheral resistance increased on infarction, a finding that is consistent with our own findings.

With respect to stroke work, we observed a mean decrease of 10.4%, with a standard

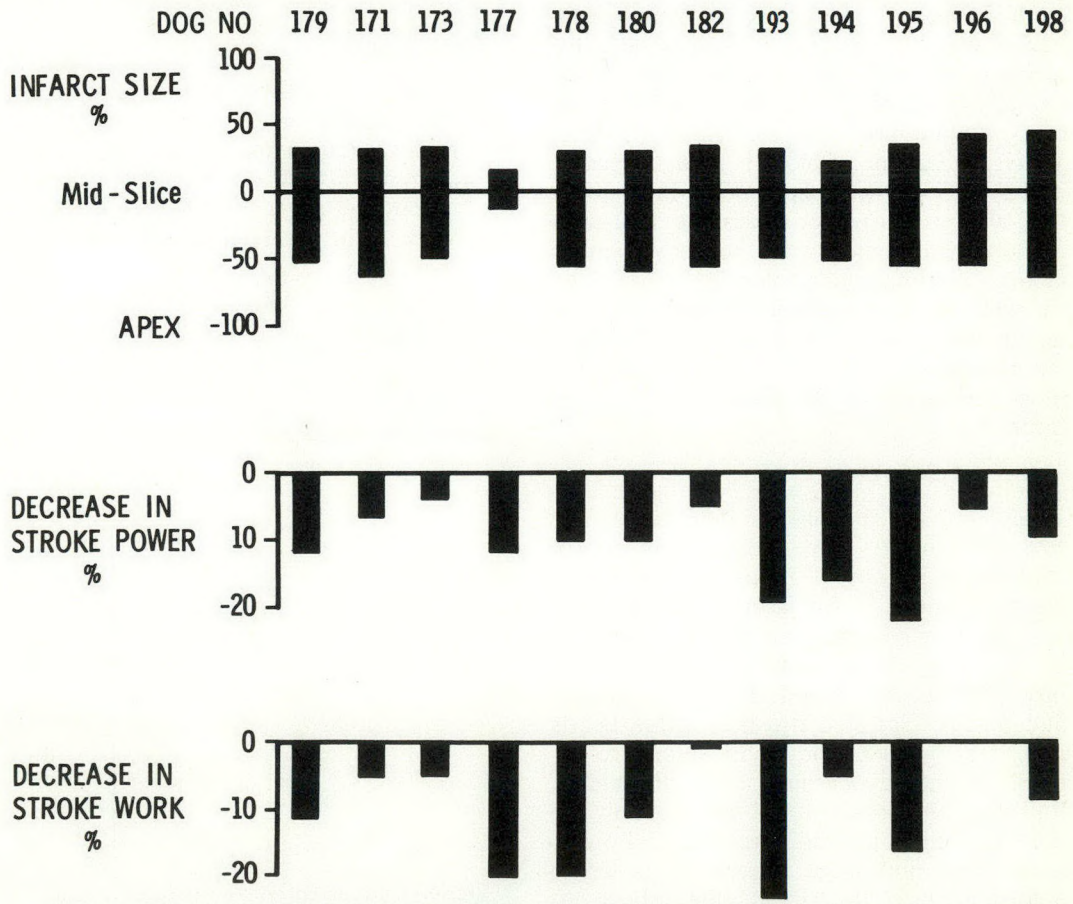

Fig. 3.—Findings in 12 dogs with respect to site of anterior myocardial infarction and corresponding alterations in stroke power and work. (Reference line is mid-slice of each heart.)

deviation of ±7.8%. In this study, stroke work and stroke power were the only variables that consistently decreased in all the experimental animals. Braunwald[14] suggested that stroke work changes should parallel stroke volume changes. Fig. 4 shows stroke volume changes plotted against stroke work changes for the 12 dogs we studied. It does show a rather high correlation ($r = 0.92$) between the two variables, but it does not reveal the fact that, for two dogs, stroke volume increased +3% and +10.6% and stroke work decreased by −4.8% and −0.5%. In other words, stroke volume changes were not consistent with the presence of the infarct, whereas stroke work consistently decreased because of infarction. Hamosh and Cohn[18] found that stroke work decreased moderately with infarction. To the best of our knowledge, stroke power has not been measured and assessed with respect to alteration with myocardial infarction. It may, however, be the most indicative variable, because it incorporates the element of time and is a function of the velocity of contraction.[5] Stroke volume and work do not take into account the rate at which the volume of blood is being removed. The results of these experiments indicate, in fact, that stroke power represents the hemodynamic parameter with the largest mean change accompanying infarction (−10.7%) as well as the smallest deviation in the mean (±7.1%). Of the eight variables studied, stroke power was definitely the most indicative of the presence of the infarct.

Size of Infarct

Most of the methods of determining the size of an infarct have relied on the use of radioactive isotopes[19, 20] or dyes.[21] Griggs and Nakamura,[19] for instance, used radioactive iodine to determine the site of infarct by scanning the myocardium after an infarct had been created. Krug, Rochmont and Korb[21] injected dye into feline hearts in order to assess the blood supply to regions of the myocardium after an infarct. Pairolero and colleagues,[22] are probably the only investigators who have artificially created small and large infarcts in order to determine how the size of the infarct affected energetics. However, the energetics that were measured were LVEDP and cardiac output, neither of which have been established as good indicators of infarction.

Fig. 2 shows the correlations between the size of the infarct and the corresponding changes in stroke power and stroke work. The correlation coefficients of 0.22 and 0.45 suggest that the alterations in energetics associated with myocardial infarction are not closely related to the size of the infarction.

Site of Infarct

Myocardial scanning[23] and scintiphotography[20] have been used to locate the site of infarcts. To our knowledge, correlation studies between infarct site and cardiovascular dynamics have not been carried out. In regard to stroke power and stroke work, it appears from Fig. 3 that there is little correlation between these hemodynamic changes and infarct site.

Conclusion

The results presented in this paper show that the changes in cardiovascular hemodynamics accompanying anterior myocardial infarction of 35 to 45% of the left ventricular myocardium are, except for stroke power and work, poorly correlated with the pres-

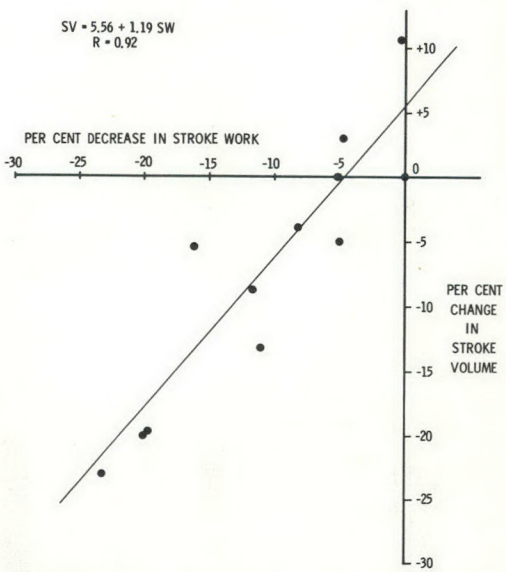

Fig. 4.—Correlation between stroke volume and stroke work changes accompanying myocardial infarction in 12 dogs.

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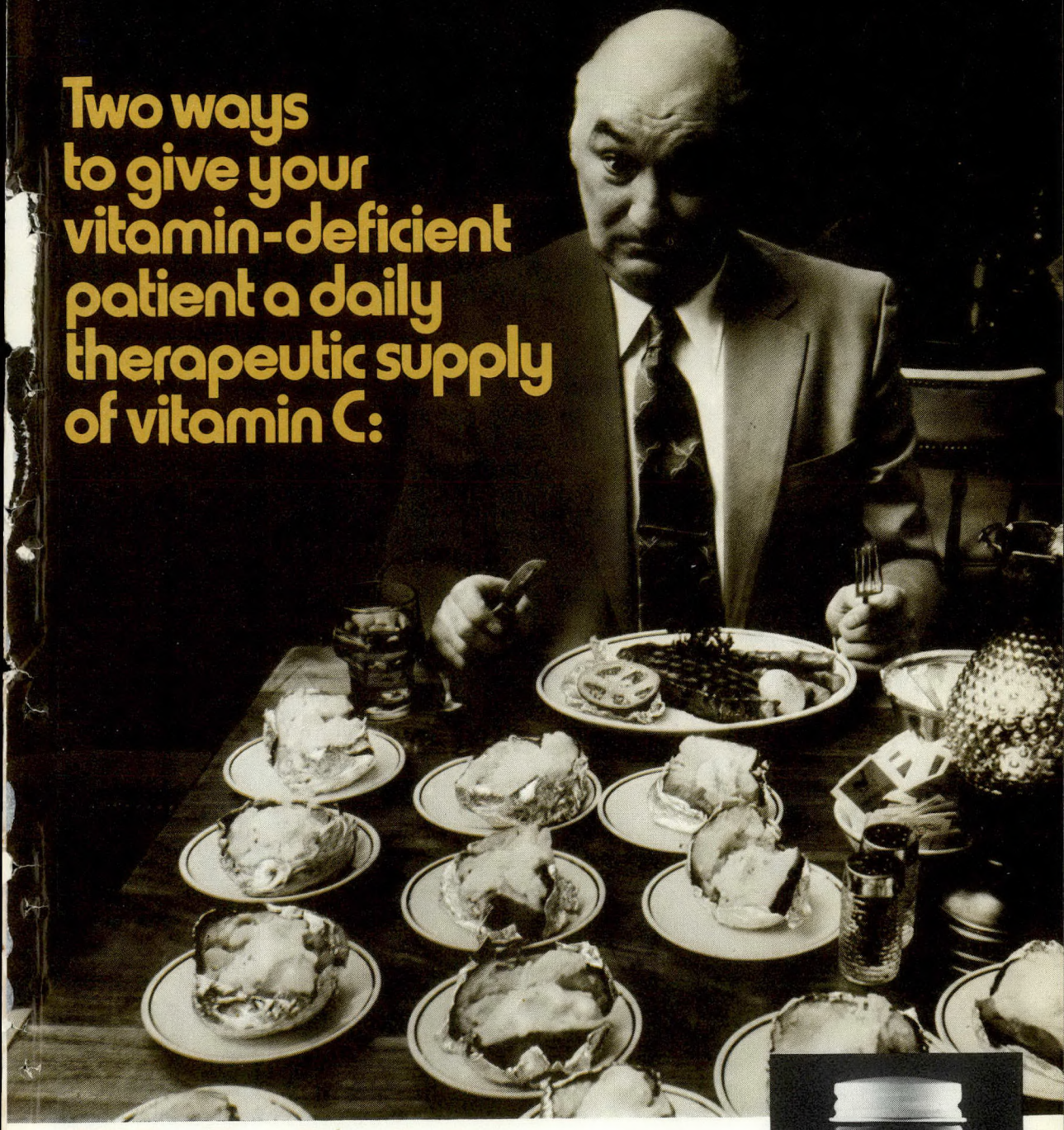

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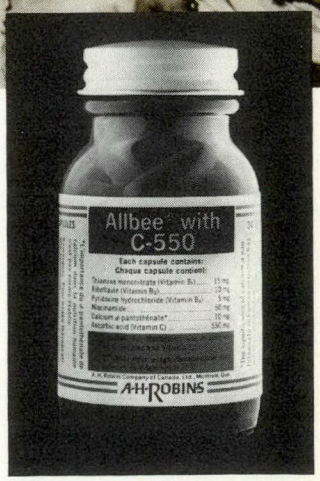

ence, size, and site of infarction. Stroke power is the most accurate indicator of the presence of the infarction, but is not highly correlated with the size or site of the infarction. These results suggest that the most important hemodynamic parameter to monitor in the assessment of cardiac function is stroke power. Reliance on arterial pressure, heart rate, or cardiac output measurements can lead to incorrect conclusions regarding the state of the myocardium.

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SURGERY FOR CORONARY ARTERY DISEASE AND CONGESTIVE HEART FAILURE*

P. BEDARD, MD, FRCS[C], W. J. KEON, MD, FRCS[C], G. TAYLOR, MD and Y. AKYUREKLI, MD, FRCS[C]

Summary: A group of 41 patients presenting primarily with symptoms of congestive heart failure was investigated by coronary arteriography and myocardial revascularization. Of these patients 20 underwent resection of left ventricular aneurysm or left ventricular plication as well as revascularization. Revascularization plus resection of left ventricular aneurysm gives gratifying results, but revascularization in the presence of severe generalized hypokinesis is less satisfactory; however, the improvement in clinical condition in a sufficient number of patients is such that this approach to their management is justified. Accordingly, every patient with coronary artery disease and congestive heart failure should be investigated by angiography. Numerous factors influence the results of revascularization for the relief of congestive heart failure; the most useful as a criterion to aid patient selection is left ventriculography. In this group of 41 patients 66% were helped by myocardial revascularization.

Résumé: Nous avons étudié par artériographie coronarienne et par revascularisation du myocarde un groupe de 41 malades présentant principalement les symptômes d'une insuffisance cardiaque globale. Parmi ces malades, 20 ont eu une résection d'un anévrisme du ventricule gauche ou une plicature du ventricule gauche ainsi qu'une revascularisation. Cette dernière intervention couplée avec la résection de l'anévrisme du ventricule gauche a donné des résultats satisfaisants, mais la revascularisation en présence d'une hypocinésie sévère et généralisée est moins satisfaisante. Il faut cependant admettre que l'amélioration clinique constatée chez un nombre suffisant de patients permet de justifier ce mode de traitement. Il s'ensuit que tout malade présentant une maladie coronarienne et une insuffisance cardiaque devrait être examiné d'abord par angiographie. De nombreux facteurs exercent une influence sur les résultats de la revascularisation pratiquée pour améliorer l'insuffisance cardiaque. Le critère le plus utile pour la sélection du traitement est la ventriculographie gauche. Parmi notre groupe de 41 malades, 66% ont été améliorés par une revascularisation du myocarde.

In cases of congestive heart failure the results of myocardial revascularization may be disappointing. We believe the value of bypass grafting for congestive heart failure is still uncertain, and there is evidence that aortocoronary bypass does increase contractility.[1-3] This paper presents our experience with cardiac revascularization in patients with congestive heart failure.

Method

From February 1970 to April 1973 inclusive, 41 patients with congestive heart failure underwent cardiac revascularization. There were 40 men and 1 woman; their ages ranged from 38 to 66 years (average, 51 years). The diagnosis of congestive heart failure was made only if the criteria of McKee *et al*[4] were satisfied. Excluded from this study were the patients with a left ventricular aneurysm or with an elevated left ventricular end-diastolic pressure (LVEDP) without clinical evidence of congestive heart failure.

Patients were classified clinically according to the New York Heart Association classification; of the 41 patients, 18 patients were graded as class IV, 22 were graded as class III and 1 patient, class II (Table I). Among those in class IV, 7 required left ventricular reconstruction and 11 bypass grafting only; among those in class III, 13 patients required left ventricular reconstruction and 9 did not.

The surgical procedure in all patients was

TABLE I.—Preoperative Classification of 41 Patients with Congestive Heart Failure

Class (NYHA)	*No. of patients*	
	Without LV reconstruction	*With LV reconstruction*
IV (n = 18)	11	7
III (n = 22)	9	13
II (n = 1)	1	0

*From the University of Ottawa cardiac unit, Ottawa Civic Hospital, Ottawa, Ont.

Supported by the Ontario Heart Foundation.

Reprint requests to: Dr. P. Bédard, University of Ottawa Cardiac Unit, Ottawa Civic Hospital, 1053 Carling Ave., Ottawa, Ont. KIY 4E9.

performed under cardiopulmonary bypass with normothermia, hemodilution and a high perfusion flow. A vent was always introduced at the apex of the left ventricle, and anoxic arrest was used in most patients. The operative procedures performed on these 41 patients were as follows: resection or plication of the left ventricle in 20, 17 of whom underwent resection of an aneurysm and 3 of whom underwent plication of the left ventricular wall; revascularization with bypass grafting in 37; internal mammary implants in addition to other procedures in 23, and endarterectomy in 5 patients, among whom a total of eight endarterectomies were performed.

We also analyzed certain factors that might influence the operative results. These factors were *angina; systemic hypertension; cardiomegaly* as measured by cardiothoracic ratio; *LVEDP; cardiac index; left ventricular contraction* as analyzed by a left ventriculogram in the RAO position; *blood flow in graft;* and *reconstruction of left ventricular wall.*

Results

The mortality in this group of patients was 24%; 10 of 41 patients died. Two of the patients died within 3 weeks of operation and eight died between 3 weeks and 29 months later. There were no operating-room deaths.

Of the 20 patients who underwent reconstruction of the left ventricle, the preoperative clinical grading was class IV in 7 patients and class III in 13 patients. The postoperative course of those with class IV disease was as follows: two died, one was reclassified as having class III disease, two patients were reclassified as having class II disease and two patients as having class I disease. Of those with class III disease preoperatively, one died, six were reclassified as having class II disease and six were reclassified as having class I disease. Thus, of these 20 patients, 3 (15%) died and the condition of the remaining 17 (85%) was improved after operation (Fig. 1).

Of the 21 patients in whom revascularization was performed without any reconstruction of the left ventricular wall, 11 were originally graded as having class IV disease, 9 as having class III disease and 1 as having class II disease. Among those with class IV disease, two patients died, two continued to have class IV disease, four were reclassified as having class III disease, and three patients were reclassified as having class II disease. Of those with class III disease, five patients died, none became worse, two were no better, and two were judged to have class II disease. In the one patient whose disease was assessed as class II preoperatively the condition was reclassified as class I postoperatively. As Fig. 2 shows, of these 21 patients, 7 (33%) died postoperatively, 10 (48%) patients manifested improvement, and 4 (19%) noted no improvement. These last four patients when assessed for congestive heart failure did, however, note that their angina was less severe.

With respect to the 10 patients who died,

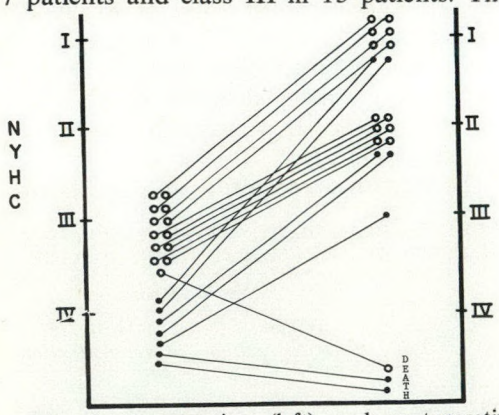

Fig. 1.—Preoperative (left) and postoperative (right) functional classification of patients receiving aortocoronary bypass grafts and left ventricular reconstruction. Preoperative classification: open circle—class III, blocked circle—class IV (New York Heart Association classification).

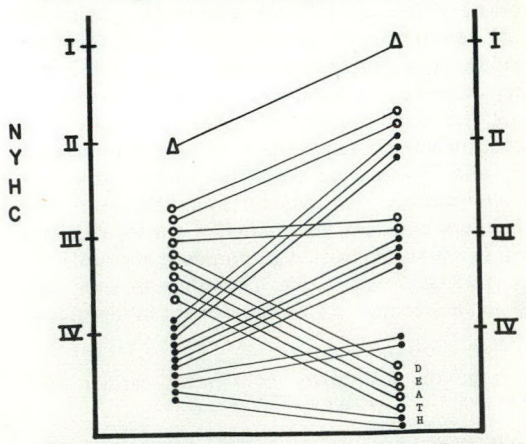

Fig. 2.—Preoperative and postoperative functional classification of patients receiving aortocoronary bypass grafts. Preoperative classification: open triangle—class II, open circle—class III and blocked circle—class IV.

in 1 angiography 8 weeks before death showed that both grafts were patent, and in 2 of the 5 others in whom autopsy was performed the grafts were either completely or severely occluded.

Discussion

Analysis of the various factors that can influence the outcome of surgery is useful in developing criteria for management. Angina was absent in only four patients. One of these patients died and two underwent resection of an aneurysm. Systemic hypertension was noted in three patients; two of them died, 7 and 29 months later, respectively.

Cardiomegaly and LVEDP were considered as factors in patients without a left ventricular aneurysm (Fig. 3). One patient with a normal cardiothoracic ratio and a normal LVEDP died but there were other patients with a high cardiothoracic ratio and elevated LVEDP whose condition improved. In some patients the LVEDP was low but the heart was enlarged; in others the cardiothoracic ratio was normal but LVEDP was elevated. Thus, in our patients, the cardiothoracic ratio and LVEDP were not useful as predictors of the outcome of surgery.

We also considered the cardiac index, the left ventricular contraction and the blood flows in the graft at the time of surgery, but none of these were useful as predictors of outcome. Ejection fractions were not determined in these patients. Bourassa *et al*[5] and Solignac and Bourassa[6] have described a classification of the left ventricular function using an "asynergy index", which has enabled them to predict surgical prognosis, and this may prove to be the appropriate way of selecting patients for surgery.

In our experience, reconstruction of the left ventricular wall has been associated with an 85% improvement and this appears to be the only useful criterion with which to predict a possible outcome of surgery. Reducing the left ventricular size by plication or resection of its noncontractile wall probably allows a more efficient contraction as the wall tension required to generate a given ventricular pressure is diminished, thus decreasing oxygen consumption. Direct myocardial revascularization would also improve oxygenation in hypoxic regions of the myocardium with improvement of the left ventricular performance.[1-3] Favaloro and his colleagues[7] have reported a generally better prognosis after excision of an aneurysm if all three coronary arteries were not involved. Among recent reports, that of Spencer's group[8] indicates that there is an initial mortality of 25% and an overall mortality of 37%. The results were fair or good in 53% of patients. The left ventricle was reconstructed in 45% of these patients; the mortality was 38%. In Mundth's series[8] of 50 patients, 25% underwent reconstruction of the left ventricle; the overall hospital mortality was 15% and some postoperative improvement was noted in 60%. Kouchoukos *et al*[9] resected aneurysms in nine patients who had congestive heart failure and reported an overall mortality of 77%; the condition of neither of the two survivors was improved. Aldridge[10] followed 20 patients with severe left ventricular dysfunction treated medically and found that 65% of them were dead at the end of 5 years, the condition of the survivors not having improved throughout this period. The difficulty in assessing these results stems from the wide variety of patients presenting with congestive heart failure secondary to coronary artery disease. Thus, only a precise and widely accepted set of criteria of left ventricular function will allow one to make a proper assessment of surgery in this group of patients; the most useful criterion is a proper analysis of the left ventriculogram.

Conclusion

Patients with congestive heart failure

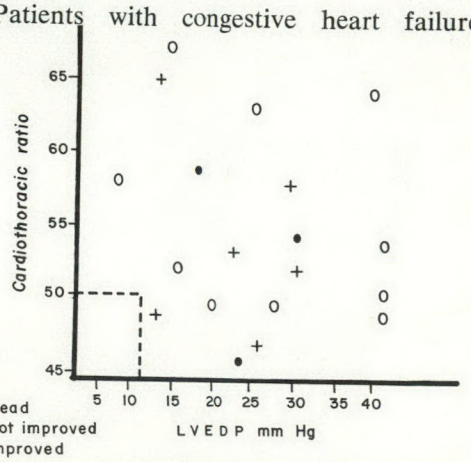

Fig. 3.—Cardiothoracic ratio and left ventricular end-diastolic pressure in patients without ventricular reconstruction.

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should be investigated by angiography. If an aneurysm is present and resectable, or if a large left ventricular cavity can be reduced in size, the condition of these patients can be improved by aneurysmectomy or plication and revascularization. If there is no angiographic evidence of ventricular aneurysm but severe ventricular dysfunction, revascularization led to improvement in some patients. Although results of revascularization in patients with severe ventricular dysfunction are obviously disappointing, we believe that investigation and surgical management of such patients should be pursued until more information becomes available. Currently, surgical treatment offers the only hope of rehabilitating many of these terminal patients to a point where they can be discharged from hospital.

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PROPHYLACTIC ANTIBIOTIC THERAPY IN SURGERY*

LLOYD D. MacLEAN, MD, FRCS[C]

Summary: Prophylactic (preventive) antibiotic therapy initiated preoperatively, with antibiotics administered in moderately high dosage for short periods, is recommended on the basis of experimental and prospective, randomized clinical trials for patients who require surgery that is likely to expose tissue planes to contamination. The value of prophylactic antibiotics in clean operations is not presently supported but must be considered in patients with decreased resistance and in those in whom infection of a prosthesis would have catastrophic results. In these patients topical antibiotics might prove useful and less dangerous.

It is clear that surgical technique remains an important but as yet unmeasured factor in wound infection.

Résumé: L'antibiothérapie préventive entreprise durant la période préopératoire, avec des posologies modérément élevées d'antibiotiques pendant de brèves périodes, nous paraît recommandable, si nous nous basons sur des essais cliniques faits au hasard, à titre d'expérience et de prospective, chez des malades devant subir une opération susceptible d'exposer des plans tissulaires à la contamination. La valeur de l'antibiothérapie prophylactique dans les opérations exemptes de risque de contamination n'est actuellement pas admise, mais doit être envisagée chez les malades dont la résistance est affaiblie et chez ceux où l'infection d'une prothèse pourrait avoir des conséquences désastreuses. Chez ces malades, l'emploi local d'antibiotiques pourrait s'avérer utile et est, de toute façon, moins dangereux.

Il est évident que la technique chirurgicale demeure un facteur très important relatif à la prévention de l'infection des plaies, mais qu'il est malheureusement encore négligé, faute d'être évalué à sa juste mesure.

---

*From the department of surgery, Royal Victoria Hospital and McGill University, Montréal, Qué.

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Supported by a grant from the Medical Research Council of Canada.

Reprint requests to: Dr. L. D. MacLean, Surgeon-in-Chief, Royal Victoria Hospital, 687 Pine Ave. W., Montréal, Qué. H3A 1A1.

THE indiscriminate administration of antibiotics given prophylactically, based originally on the mistaken idea that they might be useful but certainly could do no harm, is no longer acceptable. The emergence of resistant strains, their failure to control surgical infections, their cost, and the clinical masking of infections amenable to surgical therapy are the main reasons for condemning this policy.

Despite these adverse effects, the selective use of antibiotics to prevent infection in surgical practice is an important adjunct to care. The acceptance of this newer concept is based on the experimental demonstration that preoperative treatment is necessary, clinical evidence that the organisms in the wound at the conclusion of the operation cause the infection, and results of several supporting trials that were prospective, double-blind, and randomized. This communication evaluates the experimental evidence supporting prophylactic antibiotic therapy and offers some clinical guides.

CLASSIFICATION OF WOUNDS AND RISK OF INFECTION

A purulent wound is generally agreed to be infected. The classification of wounds defined by the National Research Council and the National Academy of Sciences is most useful in determining patients at risk.[1]

1. *Clean.*—A wound is clean if, during an operation, the gastrointestinal and respiratory tracts were not entered, if no inflammation was encountered and if there was no break in aseptic technique. Hernia repair, thyroidectomy and appendectomy *"en passant"* are included in this category.

2. *Clean-contaminated.*—"Clean" operations during which the gastrointestinal or respiratory tract, or both, are entered but without appreciable spillage produce clean-contaminated wounds.

3. *Contaminated.*—A surgical wound is contaminated if there is either acute inflammation (without pus formation) or gross spillage from a hollow viscus. Fresh traumatic wounds and operations in which there

is a major break in aseptic technique are included in this category.

4. *Dirty.*—In cases of either a purulent operative site or a perforated viscus a wound is said to be dirty. Included in this category are old traumatic wounds.

The risks of infection in these four categories in one large study were as follows: clean wounds, 1.8%; clean-contaminated, 8.9%; contaminated, 21.5%; and dirty, 38.3%.[2]

Evidence Favouring Preoperative Treatment

Epinephrine injected into tissues of experimental animals decreases host resistance to an inoculation of bacteria, as measured by the size of the lesion. The increase in lesion size, reflecting the most severe decrease in host resistance, is greatest when the ischemia produced by adrenalin occurs at the same time as the bacteria are introduced; if the onset of ischemia is delayed 3 hours after bacterial inoculation, the resulting lesion is not different from those of controls.[3] Similar findings have been reported for shock caused by bacterial toxins or the intraperitoneal injection of hypertonic glucose.[4] The skin infections caused by *Staphylococcus aureus, Pseudomonas pyocyaneus* and *Clostridium welchii* became more serious only if the shock period was within 2 to 3 hours of the intradermal injection of these bacteria.

The short decisive period of increased host susceptibility also applies to the bacteria in the lesions. Infections 3 to 5 hours old are not alleviated by intravenous antibiotic therapy in doses that are effective when given earlier.[5] The diameter of the lesion 24 hours after the intradermal injection of *S. aureus* into guinea pigs is directly related to the time of injection of the antibiotics. The most effective time for antibiotic administration preceded the inoculation of bacteria.[6]

These studies permit one to conclude that if prophylactic antibiotic therapy is to be used it should be started before the incision is made.

Indications for Prophylactic Antibiotic Therapy

In considering when prophylactic antibiotic therapy is indicated, it is reasonable to select those operations in which there is definite risk of infection; these are operations producing clean-contaminated, contaminated and dirty wounds. Most infections in these instances are caused by gram-negative organisms and originate from the patient; they differ from infections caused by *S. aureus* which are usually air borne. This question has been carefully studied by Thomsen, Larsen and Jepsen[7] who, by phage-typing and serotyping, traced the source of wound infections associated with *Escherichia coli* and *S. aureus*. They found that with *E. coli* of the same serotype as of the organism causing the wound infection after an abdominal procedure the organisms usually originated in the organ being operated on. In contrast, the staphylococcal infections almost always originated in air samples from the ward rather than from either the patient or the operating theatre environment. For the *E. coli* group of infections, prophylactic measures should be directed against contamination at the time of surgery in predictable surgical problems.

With staphylococcal infections it is probable that there are a multitude of sources and routes of infection and that no simple measure would suffice as a prophylactic precaution. Control of infection with *S. aureus* at other sites in patients, in the operating room air, in the ward air and in hospital personnel are probably all implicated on occasion. Currently, it is not practical to treat all patients at risk with antibiotics that are effective against *S. aureus,* nor is it possible to predict a high-risk group as has been done in the case of gram-negative infections.

A useful adjunct to prophylactic antibiotic therapy is routine intraoperative wound culture. This provides the best indication as to the causative organisms and to the appropriate antibiotic when clinical infection develops. Polk[8] found that a positive culture of material taken from the subcutaneous tissue after the fascia had been closed was the most accurate prognostic indicator of wound sepsis and that the results of culture were useful in selecting the appropriate antibiotic. Polk's study was of a prospective trial. Wound culture during closure was also the most useful of 14 variables examined in a regression analysis by Davidson, Clark and

Smith.[9] These workers computed the relative importance of variables known to be associated with increased risk of wound infection. These variables included, among others, the following:

1. Concentration of bacteria in the wound at the end of the procedure.
2. Age of the patient.
3. Duration of the operation.
4. Contamination during the operation.
5. Patient's hospital environment (i.e. whether the patient was from an open ward or a single room).
6. Occurrence of glove punctures.
7. Nasal carrier state.
8. Operative urgency (i.e., whether or not the procedure was an emergency).
9. Absence of skin towels, use of a drain.

Only the first five factors were judged to be contributory and the positive culture from the subcutaneous layer at the time of closure was by far the most important in determining the ultimate behaviour of the wound. In this study a positive wound culture was more than three times as important as any other single factor.

The value of prophylactic antibiotic therapy is confirmed by the results of several randomized trials. Table I summarizes the findings for patients undergoing operations in the clean-contaminated, contaminated and dirty categories.[10-17]

Washington and colleagues[10] assessed the value of neomycin alone, neomycin with tetracycline, and a placebo in bowel preparation for colon surgery. The study was double-blind and randomized on a total of 196 patients; all were operated on by the same surgeon. A wound infection rate of 43% was reported for the placebo group and of 41% for the neomycin group, in contrast to an infection rate of 4.6% for the neomycin-tetracycline group. No case of pseudomembranous enterocolitis was reported in any of the groups.

The study of Andersen, Korner and Østergaard[11] supports the additional use of topical antibiotics in preparation for colon surgery. They studied the results in 240 patients with cancer who underwent surgery on the colon or rectum. Mechanical preparation was used in all patients, and all but 55 patients with low rectal carcinomas received neomycin sulfate and chlorchinaldole for 3 days before operation. In the treatment group ampicillin powder (1 g) was applied to the subfascial and subcutaneous spaces at the time of wound closure. The control group had a wound infection rate of 18.3%, the ampicillin powder group, 2.5%.

Rickett and Jackson[12] demonstrated the

TABLE I.—PROSPECTIVE, RANDOMIZED TRIALS OF PROPHYLACTIC ANTIBIOTIC THERAPY IN OPERATIONS WITH HIGH RISK OF INFECTION

Author(s)	*Operative site*	*Antibiotic therapy*	*Infection rate (%)*	
			Experimental group	*Control group*
Washington et al[10]*	Colon	Neomycin and tetracycline	4.6	43
Andersen, Korner and Østergaard[11]†	Colon and rectum	Ampicillin (topical)	2.5	18.3
Rickett and Jackson[12]*	Appendix	Ampicillin (topical)	3	24
Bernard and Cole[13]	Gastrointestinal and biliary tracts	Penicillin G, methicillin, chloramphenicol	8	27
Fullen, Hunt and Altemeier[14]	Penetrating wounds of abdomen	Penicillin and tetracycline or chloramphenicol	7	30
Polk and Lopez-Mayor[15]	Gastrointestinal tract	Cephaloridine	6	29
Hughes *et al*[16]*	Colon	Penicillin G	12.5	58
Chetlin and Elliott[17]	Biliary tract	Cephaloridine	4	27

*Double-blind study.
†Triple-blind study.

value of topical ampicillin powder at the time of appendectomy in a double-blind study. In a 5-month period all patients undergoing appendectomy were included except those who reported a sensitivity to penicillin. The study included patients who were being operated on for acute appendicitis as well as those undergoing "cold" appendectomy. The group that received the ampicillin had a wound infection rate of 3% and the controls, 24%.

The retrospective study of Fullen, Hunt and Altemeier[14] concerning 295 patients supports the preoperative administration of antibiotics in patients with penetrating wounds of the abdomen. Antibiotic therapy started before operation was associated with a wound infection rate of 7%, whereas therapy started during or after operation resulted in rates of 33 and 30% respectively.

Polk and Lopez-Mayor[15] obtained convincing results in a randomized trial of 199 patients in whom therapy was started before operation. They noted a definite difference in wound infection rates associated with surgery on the gastrointestinal tract depending on whether or not the patient received antibiotics. The patients in the treatment group received cephaloridine, given parenterally 1 g on call to surgery, 1 g at 5 hours and 1 g at 12 hours thereafter. Planned surgery on the biliary tract was excluded. In the treated group the wound infection rate was 6%, in contrast to a rate of 29% in the controls. Emergence of resistant strains was not detected.

A similar regimen was used prospectively (not double-blind) by Chetlin and Elliott[17] in 84 patients undergoing biliary tract surgery with a high risk of infection. The high-risk category included one or more of the following variables: age over 70 years, acute cholecystitis, obstructive jaundice or common duct stones without jaundice. Invasive infections occurred in only 4% of 47 treated patients but in 27% of similar but untreated controls.

The evidence for prophylactic antibiotics in the categories covered by these studies is convincing. Changes in sensitivities might alter this opinion in the future and this emphasizes the need for continued evaluation of results.

Indications for Prophylactic Therapy Before Clean Operations

There are two situations in which prophylactic antibiotic therapy might be considered for clean surgical procedures: (a) when operations are performed on infection-prone individuals, and (b) when permanent prostheses are inserted.

Evidence to support this approach is not as easily obtained as for the other categories of contamination. Boyd, Burke and Colton[18] noted that, after operation for hip fracture, prophylactic antibiotic therapy was associated with a decrease in wound infection rate among 417 patients. Nafcillin was used randomly and in a double-blind fashion starting before operation. The wound infection rate in controls (glucose group) was 4.8%; in the patients who received nafcillin it was 0.8% ($P < 0.05$). This study supports the prophylactic use of antibiotics in "clean" operations in which the risk of infection was increased because of hematoma formation and the use of anticoagulant therapy.

A study on patients at increased risk that compared the topical use of antibiotics in renal transplantation is of interest. Two groups were studied: patients with primary renal transplantation incisions (group I) and patients who required re-exploration (group II). In patients of both groups the wound was irrigated with 50 000 units of bacitracin and 1 g of neomycin in 200 ml of saline. In group I the wound infection decreased from 5.0 to 2.5% ($P < 0.02$) and in group II, when the patients were receiving immunosuppressive agents, from 28.6% to 4.8% ($P < 0.001$).[19]

Patients in whom foreign materials are implanted commonly receive prophylactic antibiotic therapy, but there is no firm scientific support for this practice. In such patients the causative organism rather than the infection rate may change.

Conclusions

1. The value of antibiotics given prophylactically for short periods (2 to 4 doses) starting before operation when the procedure contemplated is likely to be clean-contaminated, contaminated or dirty is supported by basic research as well as controlled clinical trials.

2. The value of prophylactic antibiotic therapy in patients undergoing clean operations is currently not supported by evidence. However, this form of therapy may prove useful for patients with decreased resistance to infection or for those in whom infection of a prosthesis would have catastrophic consequences. Local irrigation with antibiotics is useful for some of these patients.

3. The preoperative identification, by immunologic testing, of patients who have decreased resistance is likely to become a useful adjunct to infection control in the hospital and in the surgical patient.

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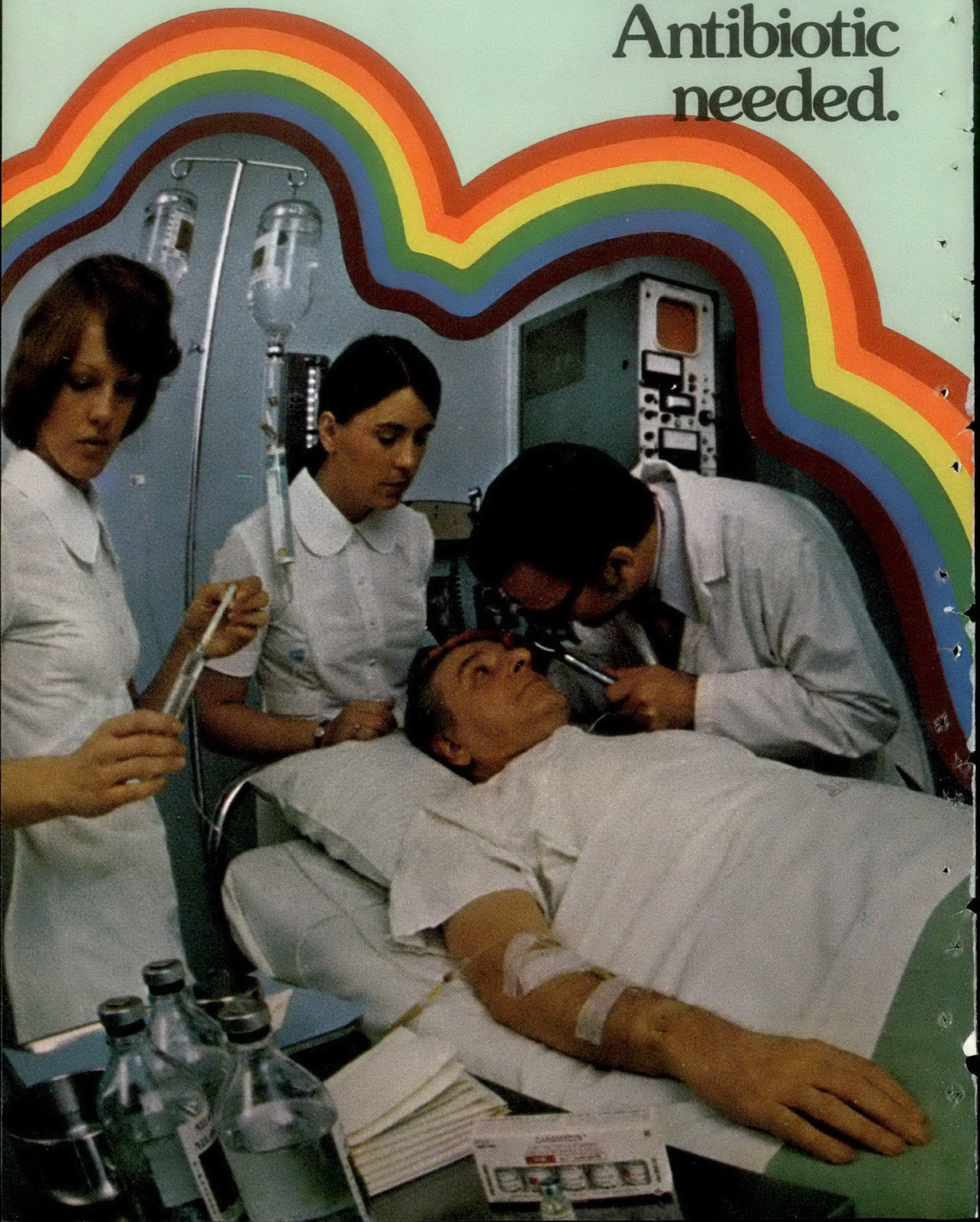

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GLIMPSES OF SURGICAL HISTORY: C FOR CARBOLIC, CHEMOTHERAPY AND ANTIBIOSIS

D. A. E. SHEPHARD

In pre-Listerian days wound infection was the rule; after amputation, 4 of every 10 patients were lucky to survive. In 80 years all this changed, owing largely to the benefits of three classes of antibacterial agents: those represented by CARBOLIC ACID, CHEMOTHERAPEUTIC DRUGS (like 2,4-diaminobenzene-4-sulfonamide [Prontosil]) and PENICILLIN.

A handful of 19th century pioneers and 20th century trailblazers in fields outside surgery made today's sophisticated surgery safe—men like Pasteur, Ehrlich, Domagk and Fleming. Their stories we know in outline but the finer details of their contributions are less well known, but fascinating (and surprising) even so.

Carbolic acid was first used in surgery by Lister in 1865, in dressing a compound fracture. But preceding Lister had been the ancient Egyptians, who used coal tar and pitch to prevent their mummies rotting; Pasteur, who demonstrated the bacterial cause of putrefaction; the Germans, who used carbolic acid to stop putrefaction; and the English, who used carbolic acid to disinfect sewage.

Useful as it was, carbolic acid was caustic. Other chemicals were sought. Ehrlich, who coined the word "chemotherapy", believed tissues had an affinity for dyes and he paved the way for German industrial chemists to develop dye derivatives to cure disease. Domagk was one such man. His boss, Horlein, wanted a drug that would kill streptococci; but he also wanted the drug to be kept secret—and, cannily, patented. Domagk duly synthesized Prontosil. Patented at Christmas 1932, Prontosil did remain unknown—and unavailable—outside Germany for some 3 years; it was the first of many "wonder drugs" to control infection.

The discovery of penicillin is a romantic story. We recognize Fleming as the discoverer, in 1929. But he was not: Gosio (1896), Duchesne (1897), Sturli (1908) and Gratia and Dath (1925) earlier had recognized the antibiotic powers of the Penicillia. *History, though, has favoured the Scotsman.*

It remains necessary to return to Pasteur, who convinced Lister that blood poisoning and gangrene were bacterial manifestations. It was with Pasteur that antimicrobial therapy really began. Besides demonstrating the bacterial nature of putrefaction, he formulated, prophetically, the vital ecologic concept of antibiosis. (Vuillemin actually introduced the word, in 1889.) Two germinal statements of Pasteur, written in 1877, say it all: "La vie empêche la vie" ("Life hinders life") and "Tous ces faits autorisent peut-être les plus grandes espérances au point de vue thérapeutique" ("All these facts justify the greatest hopes for therapeutics").

RENOVASCULAR HYPERTENSION: THE CONTRIBUTION OF SURGERY TO TREATMENT*

JEAN E. MORIN, MD, FRCS[C]

Summary: Surgical treatment for renovascular hypertension resulted in either improvement or cure in 25 of 28 patients. Surgical treatment of hypertension, however, is indicated in only a very small group of patients, and preoperative selection of patients and technical details of the appropriate operative procedure still have to be perfected.

Résumé: Le traitement chirurgical de l'hypertension rénovasculaire nous a permis d'obtenir une amélioration ou une guérison chez 25 malades sur 28. Toutefois, le traitement chirurgical de l'hypertension n'est indiqué que chez un très petit groupe de malades. Par ailleurs, le choix préopératoire des malades et les détails techniques de la méthode opératoire doivent encore être perfectionnés.

*From the division of cardiovascular surgery, McGill University, Montréal, Qué.

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Reprint requests to: Dr. J. E. Morin, Division of Cardiovascular and Thoracic Surgery, McGill University, Royal Victoria Hospital, 687 Pine Ave. W., Montréal, Qué. H3A 1A1.

SURGICALLY correctable hypertension accounts for only 10% of all cases of hypertension, and, among patients with this form of hypertension, the causative mechanism of hypertension can be traced to the renovascular apparatus in only one-half. Great progress has been made in case identification and surgical treatment, but perfection has not yet been attained. In this paper diagnostic features of renovascular hypertension and surgical forms of treatment are described and, in addition, surgical treatment is evaluated in a series of 28 patients with renovascular hypertension.

CLINICAL, LABORATORY AND RADIOGRAPHIC FEATURES, AND SURGICAL TECHNIQUE

The clinical features in the patient with renovascular hypertension differ little from those in the patient with essential hypertension, and it is still difficult for the clinician to decide whether a specific patient should undergo a complete investigation. Family history, recent onset of hypertension, and rapid acceleration of hypertension do not

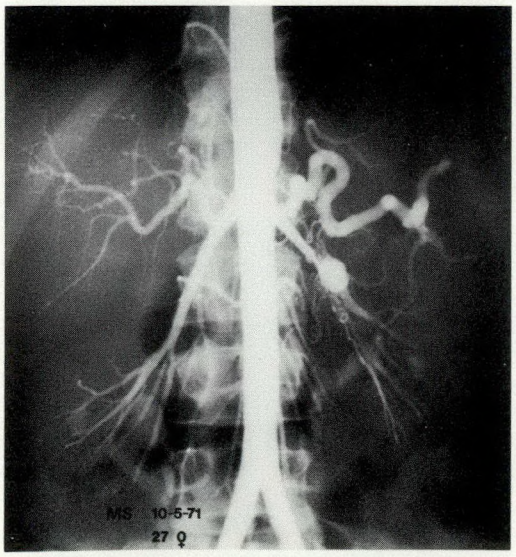

Fig. 1a

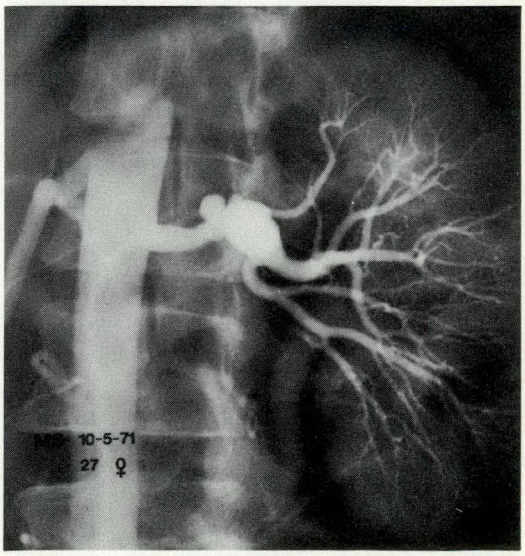

Fig. 1b

Fig. 1.—Renal arteriogram in patient with fibromuscular dysplasia. (a) Initial view. (b) Magnification view.

reliably differentiate these two etiologic groups.[1] Only an abdominal bruit provides a definite clue to a vascular lesion as the basis for the hypertension.

The renal vein renin can be of value in patient selection; its determination is most significant when the patient has been on a low-salt diet, has taken furosemide, and has been ambulatory for 2 hours prior to the determination.

Arteriography is still the most informative investigation. In addition to assessing renal function, it provides an accurate anatomic picture of the lesion (Fig. 1a). Magnification views are most useful in the detailed assessment of the pathologic process and of the planning of precise reconstruction (Fig. 1b).

The surgical procedures to correct renal artery obstructions include endarterectomy with or without patch graft, and bypass graft. Endarterectomy associated with a patch graft is mainly for patients presenting with arteriosclerotic plaques. The pathologic process is such that an appropriate procedure is an endarterectomy completed by an angioplasty with light-weight, knitted Dacron patch; the procedure opens the mouth of the renal artery widely at its take-off from the aorta (Fig. 2). This can usually be best performed through a long transabdominal incision. The bypass graft using the greater saphenous vein is more appropriate for distal or extensive renal artery involvement, as in most cases of fibromuscular dysplasia (Fig. 3). This can be achieved on the left from a transabdominal approach, and on the right from a retroperitoneal approach.

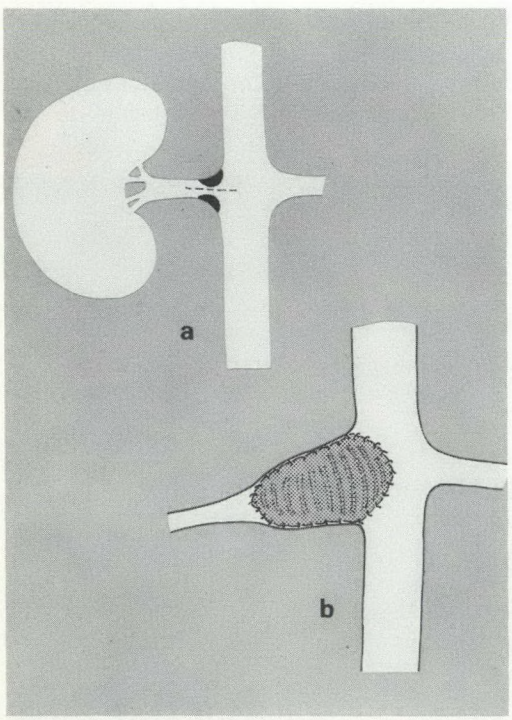

Fig. 2.—Diagrammatic representation of endarterectomy at site of renal artery stenosis (a) and Dacron patch-graft for arteriosclerotic plaques in renal artery (b).

Results of Treatment

A series of 28 patients, seen in the period from 1966 to 1974 inclusive, with severe diastolic hypertension ranging from 90 to 160 mm Hg, uncontrollable by medication, and renal artery lesions on arteriography, were treated surgically and followed. The etiopathogenetic factor was arteriosclerosis in 19 patients (predominantly men) and fibromuscular dysplasia in the other 9 patients (more frequent in women). In the evaluation of the results, the patient is considered cured if the diastolic pressure is below 90 mm Hg without medication, and improved either when the diastolic pressure has decreased by 20 mm Hg or where there is an adequate response to medical therapy. A failure is recorded when there is no change.

Results can be assessed according to etiologic considerations and according to the operative procedure. On the basis of etiologic differentiation, 50% of the arterioscle-

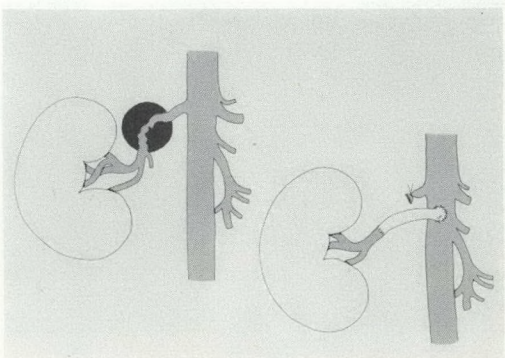

Fig. 3.—Replacement of abnormal renal artery (left) by saphenous vein bypass graft (right) for fibromuscular dysplasia.

TABLE I.—Results of Treatment Based on Etiologic Lesion and on Operative Procedure in 28 Patients

Basis of assessment of result	*Clinical result and no. of patients*		
	Cure	*Improvement*	*Failure*
Etiologic lesion:			
Arteriosclerosis (n = 19)	9	7	3
Fibromuscular dysplasia (n = 9)	7	2	0
Operative procedure:			
Saphenous vein bypass graft (n = 6)	6	0	0
Angioplasty (n = 15)	8	6	1
Dacron graft (n = 2)	0	1	1
Nephrectomy (n = 5)	2	2	1

TABLE II.—Correlation Between Renal Vein Renin Determinations and Clinical Results

Patient	*Renin value*			*Renin ratio R:L*	*Site of lesion/operation**	*Clinical result*	*Correlation†*
	Renal vein						
	R	*L*	*IVC*				
	Determination of renin value as ng/l· min						
1	Nd‡	Nd	—	—	L/BP	Improved	NA
2	Nd	Nd	—	—	R/BP	Failed	NA
3	12.5	20.8	—	1.6	L/N	Cured	+
4	Nd	Nd	—	—	R/P	Cured	NA
5	13.9	20.8	—	1.5	R/E, L/P	Failed	−
6	69.4	34.9	—	1.9	R/P, L/P	Cured	+
7	45.1	34.0	—	1.3	R/P	Cured	−
8	41.6	69.4	—	1.4	L/P	Cured	−
9	13.9	1153.0	—	82.9	L/P	Improved	+
10	69.4	62.0	—	1.3	L/P	Improved	−
11	432.0	139.0	—	3.1	L/P, R/N	Cured	+
12	49.9	95.7	—	1.9	L/P	Improved	+
13	6.6	21.7	—	3.2	L/BP	Cured	+
14	22.9	84.5	—	3.6	L/P	Cured	+
15	24.3	13.9	—	1.7	R/N, L/P	Failed	−
16	164.0	278.0	—	1.6	R/P, L/P	Cured	+
17	21.6	7.1	—	3.0	R/BP	Cured	+
18	13.9	15.5	—	1.1	L/E	Improved	—
19	115.7	52.3	—	2.2	R/BP	Cured	+
20	12.9	0	—	—	R/N	Cured	+
	Determination of renin value as ng/ml · h§						
21	22.0	54.0	Nd	2.4	L/P	Cured	+
22	40.4	30.8	30.9	1.3	R/N	Improved	−
23	4.3	5.3	3.9	1.2	R/BP	Cured	−
24	42.5	17.9	14.3	2.3	R/P	Improved	+
25	29.4	93.3	Nd	3.1	L/N	Improved	+
26	2'0	6.9	1.4	3.4	L/BP	Improved	+
27	5.49	6.41	Nd	1.3	R/BP	Cured	—
28	2.5	1.9	1.3	1.3	R/BP	Cured	−

*BP = bypass graft, P = patch angioplasty, E = endarterectomy, N = nephrectomy.
†Renin value on side of lesion greater by factor of ⩾ 1.5 than value on normal side. + = positive correlation, − = no correlation, NA = not applicable.
‡Nd = not determined.
§As from February 1973.

rotic patients (9/19) were cured, 35% (7/19) were improved and 15% (3/19) were no better; and 75% (7/9) of those with fibromuscular dysplasia were cured and 25% (2/9) were improved (Table I).

When the results were assessed on the basis of the operation performed, the saphenous vein bypass graft, when it could be constructed satisfactorily, yielded the highest cure rate and the endarterectomy plus angioplasty yielded a cure rate of only 50%, being done mainly for arteriosclerosis (Table I).

The renal vein renin values correlated with the expected result (the result determined by postoperative blood pressure measurement) in only 15 out of 25 patients (Table II).

Our total experience is summarized in Fig. 4. We consider 16 patients as cured; they have been followed up from 6 years to a few months. One patient died after 2 years but with a normal blood pressure, and one patient who was cured cannot now be traced, but on the last follow-up visit his blood pressure was normal. In nine patients the condition improved, though one cannot now be traced. Of the three patients whose condition did not improve, two died early and one still has severe hypertension.

Comment

The discovery of the relationship between renal ischemia and hypertension has generated much enthusiasm for surgical treatment of renal hypertension. But if results are sometimes excellent, they are also very often disappointing.[2] The reason for this is the difficulty in identifying patients with reversible vascular lesions. Preoperative investigations are now more precise than they once were, but they still have to be perfected. Finally, an excellent correlation between the preoperative investigation and the result presupposes a perfect surgical repair without morbidity or mortality. This has not yet been achieved. The type of lesion and the location of the renal artery make the surgical repair difficult, and it is only with more experience that the surgical procedures can be improved.

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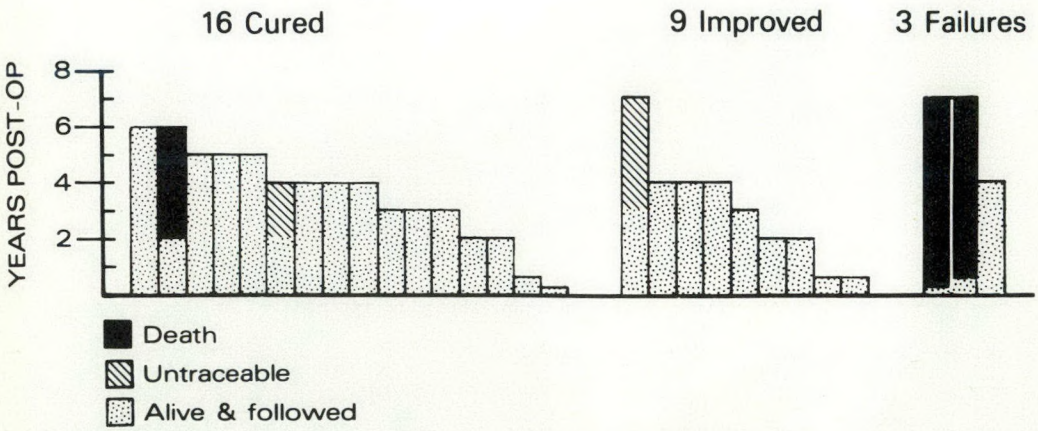

Fig. 4.—Postoperative status of 28 patients with preoperative renovascular hypertension with respect to clinical result and interval since surgery. Each column represents one patient.

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

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This 264-page volume, which has been published annually by The Ontario Cancer Treatment and Research Foundation since 1946, contains brief reports of research projects conducted under its aegis, a series of short papers entitled "Progress in Cancer" and an account of the work of the Foundation for the period 1973-1974. The preface to this volume was contributed by Dr. K. J. R. Wightman, the Foundation's newly appointed medical director.

Two other papers, one on statistics and one on medical records, are of particular interest. The first is the "Statistical Report on Cancer in Ontario, 1973", incorporating the highlights of cancer mortality and morbidity, and data on new cases registered at the regional treatment centres and the Princess Margaret Hospital. These statistics, which have been collected uniformly since 1938, represent a resource of considerable interest and value. The second is "The Ontario Cancer Registry: The Use of Record Linkage in the Measurement of Cancer Incidence and Prevalence, and in the Evaluation of Cancer Care" by Dr. W. R. Bruce, Mr. J. A. Darlington and Drs. E. N. MacKay and A. H. Sellers. The Foundation's data management systems now possess a flexibility and sophistication and an economy of operation that, a decade ago, would have been dismissed as science fiction. Readers concerned with data storage and retrieval will find this brief review of one aspect of the Ontario Cancer Registry's work of much interest.

While the supply lasts, copies are available without charge from the editor of publications, The Ontario Cancer Treatment and Research Foundation, 7 Overlea Blvd., Toronto, Ont. M4H 1A8.

HOST DEFENCE MECHANISMS: EVALUATION AND ROLES OF ACQUIRED DEFECTS AND IMMUNOTHERAPY*

JONATHAN L. MEAKINS, MD, DSc, FRCS[C]

Summary: The development of an infectious process is a result of the interaction of the three determinants of infection: the infecting organism, the local site of infection and systemic host defences. Interaction of the various components is important in an understanding of the development of sepsis. Acquired defects of host defence mechanisms are attributable to a variety of factors and can be both the cause and the result of sepsis. The burn injury illustrates alterations in host defence and the interaction of the determinants of sepsis. Methods of evaluating the components of host defence are available, though sometimes difficult; in the future, evaluation of the effect of one component on another will become clinically feasible, allowing more complete assessment of acquired defects. Immunotherapy is not yet widely available; however, definition of the acquired defects of host defence mechanisms in surgical patients may eventually lead to introduction of effective treatment.

Résumé: L'évolution d'une infection s'effectue suivant l'interaction des trois facteurs qui la déterminent: l'organisme pathogène, le siège local de l'infection et les mécanismes immunitaires de l'hôte. Si on veut comprendre le développement de l'infection, il importe de saisir l'interaction des divers facteurs. Les déficiences immunologiques acquises dans les mécanismes immunitaires sont attribuables à une grande variété de facteurs et peuvent être à la fois la cause et le résultat de l'infection. La lésion par brûlure illustre bien les altérations qui se produisent chez le blessé et l'interaction des déterminants de l'infection. On possède des moyens d'évaluer les composants des mécanismes immunitaires, mais ils sont encore difficiles d'accès. A l'avenir, l'évaluation de l'effet qu'exerce un facteur sur un autre deviendra accessible en clinique, ce qui permettra d'évaluer plus complètement les déficiences acquises. L'immunothérapie n'est pas encore une thérapeutique largement établie, mais une évaluation plus précise des déficiences acquises des mécanismes immunitaires du malade opéré pourra finalement rendre le traitement plus efficace.

WOUND infection, deep sepsis and septicemia continue to be common surgical problems.[1, 2] The development of any one of these septic processes is a result of the interaction of the three determinants of infection: bacteria, environment and host defence mechanisms (HDM). The relative importance of each determinant is schematically represented in Fig. 1; in this instance the normal situation reflects homeostasis, a state of balance resulting in an absence of infection. The bacterial determinant comprises the set of potential pathogens and their virulence factors that might become important in an infection; for example, the bacterial contamination of a compound fracture or pathogenic properties of β-hemolytic streptococcus when in the tissues. The environment comprises the site of infection and local factors that, when changed, allow infection to develop (Table I). The ability

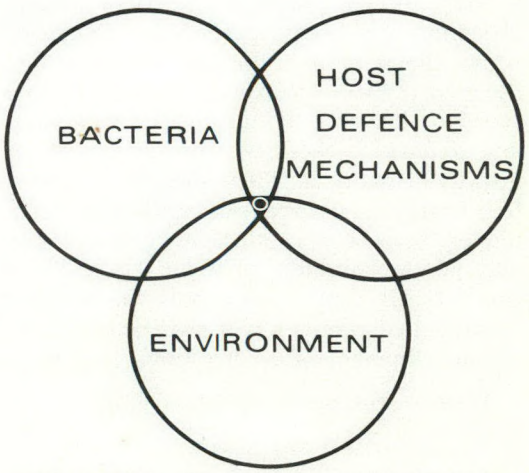

Fig. 1.—Interaction of determinants of infection. Point of intersection of three circles represents zero probability of sepsis and homeostasis—normal state of no infection.

*From the departments of surgery and microbiology, Royal Victoria Hospital, and McGill University, Montréal, Qué.

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Reprint requests to: Dr. J. L. Meakins, Department of Surgery, Royal Victoria Hospital, 687 Pine Ave. W., Montréal, Qué. H3A 1A1.

TABLE I.—NATURE AND FUNCTION OF ENVIRONMENT AND HOST DEFENCE MECHANISMS

Determinant	*Nature of determinant*	*Function of determinant*
Environment (Local factors)	Mechanical barrier	Prevention of lodgement
	Biologic decontamination	
	Mechanical component	
	Chemical component	
	Normal flora	
Host Defence Mechanisms (Systemic factors)	Inflammatory component (vascular, cellular and molecular)	Containment and resolution
	Humoral component	
	Phagocytic component	
	Cellular immunity	
	Complement	

of the potential site to prevent lodgement of organisms and resist infection is a function of effective local defence factors. Local or environmental factors may be destroyed, as with a compound fracture or burn injury, both of which permit the bacteria easier access to the internal milieu. The host defence mechanisms, the third determinant, consist of the systemic response to bacteria at a potential site of infection and this determinant incorporates the immunologic response to infection (Table I).

Enlargement of the area of intersection of the three determinants of sepsis (Fig. 2) is a function of bacterial properties of virulence, a breakdown in the environment or a failure of systemic HDM. Fig. 2 depicts the resultant area representing the probability of infection for a burn injury, after which local factors are obviously altered and there are acquired defects of HDM.

Many of the practical aspects of surgery are aimed at preventing infections. Operating room practice and surgical technique are directed towards the control of numbers and types of bacteria having access to wounds and to making these wounds unsuitable for growth of bacteria. These practices include, for example, aseptic and antiseptic techniques, hemostasis, reduction of dead space, and gentle handling of tissue. It is likely that HDMs that cannot now be suitably manipulated dictate to a significant extent the development of an infectious process.[3]

BODY'S RESPONSE TO INFECTION

Natural History of Sepsis

The natural history of each infection can be conceptualized on an anatomic basis—that is, the body first attempts to localize infection at the original site and then, with failure of localization, to confine the process regionally. When regionalization fails, the blood stream is invaded and septicemia must be controlled with all homeostatic mechanisms.

At the site of injury, the body reacts with the classical inflammatory response to contain invasion of bacteria. The usual result is control and resolution of the potential infection. When infection becomes established, the inflammatory response attempts to contain and localize the process. Suppuration and spontaneous drainage constitute an obviously successful resolution of this response although suppuration is frequently not required for local control.

Failure to localize then leads to cellulitis or some degree of lymphangitis, or both,

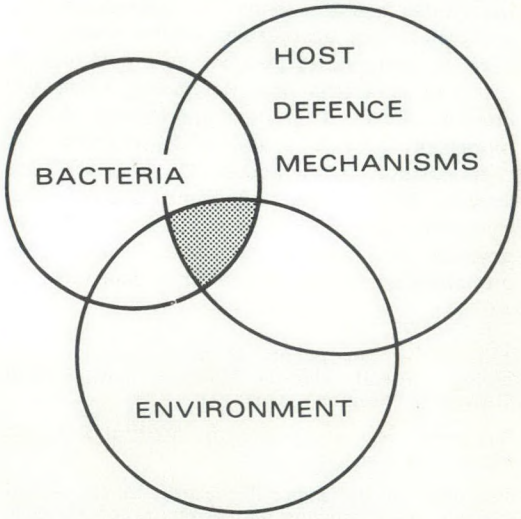

Fig. 2.—Determinants of infection in burn injury. The common area secondary to abnormal environment and host defence mechanisms indicates increase in probability of infection.

and passage of the infecting organism through the lymphatic channels. This results in regional lymphadenopathy, secondary to local inflammation, and reactive edema effectively blocks lymph flow. Suppuration may result with regionalization of the infection. Cutaneous and pulmonary infections are commonly controlled by these mechanisms. Streptococcal lymphangitis and lymphadenitis, mesenteric lymphadenopathy with acute, nonperforated appendicitis, and the Ghon complex in tuberculosis are common examples of the body's attempt to regionalize and contain a septic process. Although this cannot occur in some regions (e.g. the pleural cavity and the brain) the concept is a useful one.

A few infections are not contained by these attempts at localization or regionalization, and systemic invasion results. Similarly, failure of localization may be followed by systemic sepsis, often as the result of specific bacterial properties; infections with *Clostridium welchii* are examples of this. When bacteremia does develop, the responses are many and various, including fever, chills and cardiovascular collapse. The reticuloendothelial system (RES), which attempts to clear the blood stream of bacteria by active phagocytosis, represents the final controlling mechanism against invasive sepsis. These lines of defence are an integral part of homeostasis just as the maintenance of cardiovascular stability is a homeostatic mechanism that prolongs life until the septic focus or process can be controlled.

Environment: Local Factors

Local factors are mechanisms designed to prevent lodgement of infecting organisms (Table I). The skin and various mucous membranes throughout the body provide a mechanical barrier to bacterial invasion. In addition to presenting the purely mechanical barrier, local factors have specialized biologic properties that facilitate control or eradication of bacteria. Biologic decontamination may be mechanical or chemical or a function of the normal flora, which can restrain potential pathogens.

The skin, the body's largest organ, presents a formidable mechanical barrier to the outside world. In addition, biologic decontamination is the result of a number of biologic properties, which remove or control potential pathogens: mechanically, the skin sheds itself so that bacteria are removed; chemically, its fatty acids can be bactericidal; and these fatty acids, together with the normal flora, biologically control the growth of potential pathogens. The tracheobronchial cilia constitute a biologic mechanism to remove foreign materials and bacteria from the depths of the lungs. Tears have an antibacterial effect that helps to protect the eyes chemically and mechanically. The body's normal flora can exert considerable protection against pathogens, most commonly in the mouth and gastrointestinal tract. Oral candidiasis developing after the administration of penicillin lozenges and diarrhea or pseudomembranous ulcerative colitis complicating oral antibiotic therapy indicate the protective value of normal flora. The internal environment is protected from external pathogens by the barriers presented by skin and specialized membranes. When these barriers break down, infection is a potential problem because of failure to prevent the lodgement of bacteria.

The most obvious environmental alteration of the skin is a thermal injury. Sepsis is common and is frequently the cause of death. Although other systemic sequels result from the burn injury, the loss of the skin envelope represents a failure of the initial barrier to infection. Much of the care, in cases of burns after resuscitation, is designed to create, artificially, a protective barrier. Pig skin, artificial skin, and topical therapy are all aimed at excluding microbes. Success of these therapeutic methods is reflected by continued improvements with respect to the morbidity and mortality from thermal injury.

Frequently these anatomic barriers are broken down by iatrogenic means, surgery being the most obvious example. The urinary catheter,[4] the indwelling plastic intravenous cannula[5] and the tracheostomy tube[6] all bypass or interfere with normal anatomic barriers to change the environment and so make it more susceptible to invasive microbes.

Host Defence Components

To be effective, host defence requires the integrated and efficient function of a variety

of component parts (Table I). The failure of any segment of the system can result in sepsis, as is apparent in the congenital immunologic deficiencies that affect single-cell systems and frequently result in persistent sepsis or lethal sepsis, or both.

Initially the inflammatory response acts as the basic delivery system. The classical signs of inflammation—rubor, dolor, tumor and calor—can be explained by examining the vascular, cellular and molecular components of the inflammatory response.[7, 8]

The vascular changes are largely mediated through vasoactive amines, notably histamine, serotonin and the kinins. These substances are coordinated to produce the vascular and endothelial changes that then allow delivery of the fluid and cellular components to the inflammatory response. The precise sequence of these components is not completely understood but the following is a synthesis of the process: The vascular response, initially vasoconstriction, occurs within minutes of the initial lesion and this is followed in 10 to 30 minutes by a persistent vasodilation. The overt cutaneous signs are the triple response of Lewis. Vasodilation is accompanied by changes in the vessel wall and subsequently by blood flow; stasis of blood is associated with increased margination and adherence to the endothelial lining by polymorphonuclear leukocytes (PMNs). Endothelial changes allow diapedesis of the PMN into the inflammatory focus. The altered vessel wall and raised capillary pressure increase vascular permeability and this leads to delivery of plasma proteins—notably immunoglobulins, complement and fibrinogen. The breakdown of certain large protein molecules and the increased fluidity of the tissue ground substance also contribute to the "tumour" associated with inflammation.

The development of the cellular exudate parallels the formation of the fluid exudate; initially, the exudate consists almost exclusively of PMNs.[9] After the first 24 hours, the monocyte tends to replace the neutrophil as the predominant phagocytic cell. The monocyte, when activated, becomes an activated macrophage and, as such, is a more effective phagocyte. However, the macrophage also processes bacterial antigens or other antigens for delivery to the lymphocyte and production of specific antibody. As the inflammatory process develops, the lymphatics enlarge, in part secondary to local swelling, and lymphatic flow increases aiding delivery of antigen to the regional lymph nodes.

For purposes of this discussion, the inflammatory exudate is considered to be directed against microbial invasion—primarily, bacterial infection. The humoral opsonic component is composed of complement and immunoglobulins. The role of complement is multifaceted; in this context it facilitates immune adherence, bacterial cytolysis, PMN chemotaxis and phagocytosis. Immunoglobulins—notably IgG and IgM—are, together with complement, involved in PMN bacterial phagocytosis. Bacterial cytolysis can be effected by complement and immunoglobulin but this has a small part in the control of invasive bacteria. The crucial role of complement is to attract PMNs to the bacteria and then, with IgG, to opsonize them for effective PMN phagocytosis. In the absence of complement or immunoglobulins, phagocytosis is substantially decreased. Fibrinogen facilitates localization of the infection when it is able to form fibrin, as in abscesses, and it also supplies a matrix against which neutrophils can phagocytize the bacteria that are not opsonized. Thus, the humoral and cellular components work together to control bacterial growth.

PMN activity constitutes the initial cellular response to a lesion. PMNs are actively phagocytic when delivered by means of diapedesis to the inflammatory focus. With ingestion, the bacterium is encased in a membrane-lined sac, the phagosome, which becomes a phagolysosome with degranulation of the enzyme-rich contents of PMN lysosomes.[10, 11] In these lysosomes are the many enzymatic and metabolic processes that result in bactericidal action.[12] The PMN, a short-lived cell (half-life in circulation, 6 hours), is constantly being produced by the bone marrow. Of the 2 to 3 billion PMNs in circulation, 50% are marginated on vessel walls or in closed capillary loops, and 200 to 300 billion PMNs are maintained in reserve in the bone marrow,[9] so that large numbers of PMNs can be generated when required. The PMN is the initial bactericidal cell and is essential to the maintenance of

intact host defence.[3] Cyclic variation of neutrophil function has been demonstrated in both normal persons and in burn and transplant patients. This cyclic variation of neutrophil bactericidal function is related to the development of sepsis in both normal and burn patients and to variations in quantitative burn wound cultures.[3, 13] Leukemic patients with profound neutropenia caused by chemotherapy have a very high incidence of septicemia that may not be controlled until either the neutropenia abates or granulocytes are transfused. The inability to contain sepsis associated with a lesion is a critical factor that then permits active microbial invasion.

The second line of phagocytic response is the monocyte.[8, 14] At an area of inflammation the monocyte is activated to become an aggressive phagocytic and bactericidal cell, the macrophage, with a long half-life. Macrophage chemotaxis, active bacterial phagocytosis and intracellular killing require antibody and complement as do PMNs. After its ingestion and digestion, the microbial antigen is processed by the macrophage and transported locally or regionally to lymphocytes for production of specific antibody. The cells that take part in this activity may be bone-marrow (B) lymphocytes or thymus-derived (T) lymphocytes. B cells produce specific antibodies and T cells produce specifically sensitized lymphocytes with a major role in protection against intracellular parasites through the macrophage, which, when activated, becomes the effective microbicidal cell.[15]

The macrophage is an effective "mop-up" cell that is able to ingest and dispose of cellular debris, fibrin and other particulate matter. The PMN is primarily bactericidal and does not have the other extensive functions of the wandering macrophage. There are numerous tissue macrophages, probably also derived from monocytes, that are essential to the microbial host defence. These cells constitute the fixed RES made up of Kupffer cells (liver), littoral cells (spleen), microglial cells (brain), and pulmonary alveolar macrophages. There are macrophages in most other tissues and organ systems, but they are less numerous and are intensely supplemented by circulating cells when required. The fixed RES is primarily a blood filter and is the clearance mechanism for particulate matter as well as any microbes that may have entered the circulation. The Kupffer cells form the largest mass of the RES and are instrumental in control of systemic as well as transient portal vein bacteremia. The alveolar macrophage is important in controlling pulmonary sepsis and clearing any particulate matter that is not removed by the liver. Therefore, the lung may become a target organ in sepsis and other comparable low-flow states. The macrophage also has a role in cellular immunity.

In this discussion, cell-mediated immunity (CMI) will be considered to be limited to intracellular parasites, most notably *Mycobacterium tuberculosis* and *Listeria monocytogenes*,[15] and fungal infections (Table II). CMI is also of importance in viral infections, tumour and transplant immunity, and autoimmune disease. Delayed hypersensitivity is mediated through CMI, and failure to respond appropriately can reflect an alteration in immune response. The antimicrobial action of CMI is mediated through a complex system of recognition and cell activation involving different cells and numerous humoral mediators. In simplified terms, the cell-mediated antimicrobial system is based on recognition of antigen by T lymphocytes and subsequent macrophage attraction and stimulation. If the body has not previously been infected with the specific organism, time is required before sensitized lymphocytes are produced. In this situation the reaction will work somewhat in reverse; that is, the bacterial antigen will be processed by macrophages and delivered to lymphocytes for production of specifically sensitized T cells, which then will be effective at the site of infection.

When the host has previously been infected with a particular microbe, specific T cells are attracted to the focus of infection, where they are more specifically activated to produce lymphokines,[16] a family of soluble humoral mediators, some of which can affect macrophages. The lymphokines of specific interest are migration inhibition factor (MIF) and macrophage activation factor (MAF). MIF attracts macrophages to the infective focus and retains them in the area and MAF converts them into activated cells capable of effective antibacterial function.

The process and mechanism of intracellular killing is similar to those typical of PMNs. Failure of T-cell function or congenital absence of T cells results in failure to mount an effective antimicrobial response against intracellular parasites.[17]

The three compartments of host defence —humoral, phagocytic and CMI—each are most effective against certain organisms or classes of organisms (Table II). The host has a complex defence system; usually two of the three compartments are active against invading microbes though one may be predominant. For example, in the absence of specific antibody, the pneumococcus is not phagocytized by PMNs, but, once present, phagocytosis and intracellular killing proceed rapidly; the key to this defence is the specific antibody although control of the actual infection is a two-compartment effort.

Clinical Aspect of Defects in Host Defence

The defects in host defence of particular interest to the surgeon are those that develop secondary to physiologic status, drug therapy or disease state. The first immune defect reported was agammaglobulinemia.[18] Many other congenital abnormalities of PNM, lymphocyte and thymic function have been identified since, incorporating all aspects of host defence.[19] But although patients with such defects persistently manifest serious septic complications, they do not commonly present with surgical problems.

Acquired defects of host defence (Table III) are different, for many of them are caused by, or related to, surgical disease or secondary to surgical complications.[20] Drugs may have a major role in the alteration of host defence. Acquired defects primarily affect patients receiving cancer chemotherapy, steroids or immunosuppressive agents. Age, sepsis, some antibiotics, radiation, colchicine and phenylbutazone all can depress host resistance.[3, 19-28]

The burn injury presents the best example of wide-ranging alteration of systemic host defence secondary to the basic illness.[3, 21, 22] Within days after a severe burn injury of at least 30%, alterations in neutrophil bactericidal function become apparent. Qualitative and quantitative bacteriologic findings with respect to the burn wound and severe sepsis are related to abnormal neutrophil bactericidal function,[3, 22] and severe sepsis can be the cause as well as the result of abnormal neutrophil function.[28] In addition, there are defects in cellular immunity, reflected by the inability to reject skin grafts and anergic responses to recall antigens and alterations in alternate

TABLE II.—Efficacy of Three Compartments of Host Defence in Countering Various Infectious Organisms (Greatly Simplified)

Component effective against infectious agent		
Humoral	*Cell-mediated*	*Phagocytic*
Bacteria *Pneumococcus* *Streptococcus* *Hemophilus* *Meningococcus* *Pseudomonas*	Bacteria *Mycobacteria* *Listeria* *Brucella* *Salmonella* *Staphylococcus**	Bacteria *Staphylococcus** *Klebsiella* *Aerobacter* *Serratia* *Proteus* Probably most other enteric and anaerobic bacteria
Toxins Diphtheria Tetanus	Fungi *Candida* spp.* *Aspergillus* *Histoplasma* *Mucor*	Fungi *Candida* spp.*
Viruses Poliomyelitis Hepatitis Rubella Others	Viruses Vaccinia Cytomegalic inclusion disease Most others	
	Parasites *Pneumocystis carinii*	

*Many infectious agents are countered by two compartments of host defence; selecting the predominant compartment may not be possible.

pathway to complement activation.[21] Antibody response is adequate, though it is not as striking as in healthy persons. Antibody production is sufficient in response to heptavalent *Pseudomonas* vaccine to provide significant protection against invasive sepsis resulting from *Pseudomonas* spp.[29] The immunologic alterations in the burn injury do not return to normal until the burn wound is completely covered. Although the burn patient is unusual in the extent and severity of injury as well as the broad immunologic changes secondary to that injury, it is becoming apparent that severe sepsis in surgical patients, major operative procedures and nutritional defects can lead to alterations in basic immunologic homeostasis that are a threat to life.

The burn injury also produces a definite alteration in local protective factors; the environment has been clearly changed. Not only has the protective barrier been changed and its biologic properties destroyed but also in its place is a superb culture medium. As Fig. 2 suggests, the environmental and HDM sets are proportionally larger with no change in the bacterial determinant. The resultant common area is significant and reflects the increased probability of sepsis in the burn injury. As the treatment of burns has progressed, much attention has been directed to control of burn wound flora and the burn wound itself. The bacteria in the wound are largely being controlled with use of antimicrobial topical therapy. Modern therapy incorporates a better understanding of, and care for, the burn wound itself, presenting a less attractive environment for sepsis. The remaining obvious objective is in the understanding and role of immunologic mechanisms in the development of infections in burns. Recent work indicates that these are important.[3, 22, 30] The therapeutic goal is to reduce the size of the respective environmental and HDM sets thereby reducing the area of intersection and the probability of sepsis.

Laboratory Evaluation of Host Defence

The concept of the interaction of HDM and microbes as determinants of sepsis is very useful. However, at the practical level, it is important to be able to define the defects that are or may become amenable to therapy. Many of these investigations can be conducted in any general hospital although some are available only in large centres or, indeed, in specialized research laboratories. Table IV outlines the approaches that might be available at these various institutions; they are arranged approximately in the order of a reasonable investigation.

Before a vast array of laboratory examinations is requested, a careful clinical assessment is made to exclude continuing sepsis on the basis of, for example, an overlooked lesion, a foreign body, or undrained abscess. Additionally, a history concerning past in-

TABLE III.—Acquired Defects of Host Defence

	Host defence mechanism			
Defect	*Inflammation*	*Humoral*	*Phagocytic*	*Cell-mediated*
Physiology				
Perfusion	+			
Age	±			+
Malnutrition		+	±(?)	+
Disease-related				
Diabetes			+	
Burns		±	+	+
Cancer		±	±	+
Lymphoproliferative		+	+	+
Sepsis	+		+	+
Trauma		±	±	±
Therapy				
Steroid	+		±	+
Chemotherapeutic		+		+
Immunosuppressive			±	+
Radiation	± (Local)			+

+ = clear defect; ± = relative defect.

fections, susceptibility to sepsis and ease of therapy together with an assessment of a patient's ability to localize infection, to develop lymphadenopathy and to mount an apparent inflammatory response in light of age, nutrition, underlying disease and drug therapy are all essential before one orders thousands of dollars' worth of laboratory studies.

Initial studies comprise a total leukocyte count with differential and a morphologic assessment of PMNs and lymphocytes. The appropriate response to sepsis can be assessed and the question of whether neutropenia or lymphocytopenia might be a problem can be considered. The inflammatory response can be estimated from the clinical evaluation, use of a skin window and determination of humoral factors by means of immunoelectrophoresis or quantitation of the specific immunoglobulins IgG, IgA and IgM. Skin testing with the antigens listed in Table IV, to which 95% of persons will respond with a delayed hypersensitivity reaction, will indicate anergy.[31, 32] Cellular immunity may further be assessed from the patient's ability to reject a skin graft.

Neutrophil bactericidal function, mobility and response to chemotaxis can be reasonably evaluated.[3, 20, 28] Nitroblue-tetrazolium reduction (NBT)[22, 33] can be evaluated qualitatively or quantitatively. Dinitrochlorbenzene (DNCB) sensitization requires some skill and experience in application and assessment and indicates a particular patient's ability to respond to a specific antigen with a cell-mediated response.[24] Values of some components of complement are readily determined, though evaluation of the complete cascade and the alternative pathway are more specialized. Mixed lymphocyte culture and phytohemagglutinin (PHA) stimulation indicate the ability of lymphocytes to respond to appropriate stimuli.

It is possible to evaluate effectively most aspects of the immune response. Areas of difficulties or expense are RES clearance, monocyte function and accurate assessment of monocyte:macrophage:lymphocyte interaction. In microbial infection—whether this is viral, fungal, or bacterial—the host is generally obliged to destroy the parasite to control infection effectively. Evaluation of the effector cell mechanism and the method of activation become important and are not yet available for clinical studies. Thus, ultimately the interaction of humoral factors, phagocytic cells and lymphocytes become an important assessment.

Immunotherapy

At present, immunotherapy is usually considered to be an anticancer form of therapy. However, this form of therapy has been used in bacterial infections for 60 years. Passive immunotherapy was started when Behring[34] successfully introduced diphtheria antitoxin in 1913. Specific antitoxins in other forms of bacterial sepsis have had considerable use, a recent example being human hyperimmune globulin against tetanus. Antisera

TABLE IV.—Laboratory Evaluation of Host Defence Conducted According to Sophistication of Medical Facility

	Laboratory testing according to sophistication of medical facility		
Host defence mechanism	*Community hospital*	*Referral hospital*	*Specialized laboratory*
Inflammation	Skin window		
Humoral	Immunoelectrophoresis	Complement	Alternate pathway
	Immunoglobulin: IgG, IgA, IgM		Antibody response to specific antigens
Phagocytic	Neutrophils, monocytes: count, morphology	PMN: bactericidal function, motility, chemotaxis	Monocytes, macrophages: bactericidal function
	NBT	Quantitative NBT	RES clearance
	Skin window		MIF
Cell-mediated	Lymphocytes: count, morphology	DNCB sensitization	Mixed lymphocyte culture PHA stimulation
	Skin tests: PPD, varidase, mumps, trichophyton, *Candida* spp.	Skin graft rejection	

have also been used, the best known being the antiserum against pneumococcal pneumonia. *Pseudomonas* hyperimmune globulin is a polyvalent hyperimmune serum that has proved effective in the management of invasive sepsis of the burn wound and septicemia resulting from infection with *Pseudomonas* spp.[29] Active humoral immunotherapy with vaccines has been effective in prevention of tetanus and more recently the use of *Pseudomonas* heptavalent vaccine has proved helpful in thermal injuries.[29] These antitoxins, antisera and vaccines are directed against specific bacterial or viral disease. It is apparent that the pathogen must be susceptible to a humoral approach either by neutralization of toxins or opsonization of microbes for phagocytosis. Nonspecific use of gamma globulin is effective in patients with hypogammaglobulinemia or agammaglobulinemia.

Comparable techniques to support phagocyte function are not yet available. Granulocyte transfusions are helpful in the management of severe neutropenia,[35] usually the result of bone marrow suppression. Large volumes of viable cells are required. But because nonspecific stimulation of abnormal neutrophil function has not so far been achieved it is not yet possible to help patients with PMNs that are normal in number although not functioning adequately. In some cases of burns, enteric hyperalimentation has alleviated severe abnormalities of PMN function.[30] The specific factors are not yet clear. Nutrition can be considered a form of immunotherapy, albeit nonspecific. In animals, the RES can be stimulated with a variety of nonspecific agents or colloidal suspensions; however, such measures (e.g. endotoxin) are not suitable for human use.

The critical role attributed to CMI in the control of neoplasia has stimulated a great deal of research in this field, much of which will provide insight into problems of surgical sepsis. The initial steps were taken in attempts to control disease in children with congenital defects of CMI; the approach revolved around cellular reconstitution through transplantation of thymic tissue, bone marrow or fetal hematopoietic tissue. Lymphocytotherapy has also been used in these situations. There are many difficulties with these forms of therapy, not least of which is obtaining material for transplantation; however, more serious is the graft-versus-host reaction, which is common and can be life-threatening. These modalities are primarily applied to the treatment of congenital abnormalities or to the management of a patient after bone marrow ablation secondary to drugs or radiation. Nevertheless, it is possible that identification of specific acquired defects of CMI will make reconstitution or cellular support possible for a finite period.

Nonspecific stimulants of CMI demonstrate some interesting results in management of both neoplasia and infection. BCG vaccine and levamisole hydrochloride are at present undergoing large-scale trials in Canada and the United States as adjunctive therapy in cases of melanoma, sarcoma, cancer of the lung and gastrointestinal tract. As yet there seems to be no application of these agents to infection. However, transfer factor,[36] a soluble lymphokine that can be produced *in vitro,* has been useful in the treatment of chronic mucocutaneous candidiasis and, more recently, of leprosy.[37] These are not surgical illnesses; however, it is becoming increasingly apparent that acquired defects in CMI in surgical patients develop under situations of protracted serious illness and sustained sepsis. Law, Dudrick and Abdou,[24] have recently demonstrated that prolonged hypoalimentation leading to protein calorie malnutrition can produce defects in CMI that can be corrected with hyperalimentation. The specific abnormalities that were corrected were the ability to produce antibody response to DNCB, recovery from an anergic or relatively anergic state and a relative improvement in lymphocyte response to PHA. It is to be hoped that the time when general support of the various components of host defence can be accomplished is not too far away.

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RESULTS OF MINOR FOOT AMPUTATIONS FOR ISCHEMIA OF THE LOWER EXTREMITY IN DIABETICS AND NONDIABETICS*

GORDON A. HUNTER, MB, FRCS(Eng), FRCS[C]

Summary: Results of 208 minor amputations were analyzed in 179 patients who had no foot pulses. Wound healing was assessed at 3 months in relation to diabetes and previous vascular surgery. The results suggest that simple removal of the toe or toes is not advisable unless the blood supply to the foot can be improved by vascular reconstruction or sympathectomy, or both. Transmetatarsal amputation should be considered more often as a conservative amputation for gangrene of the toes. The absence of a palpable posterior tibial pulse is a contraindication to the Syme's amputation.

Résumé: Nous analysons les résultats de 208 amputations mineures pratiquées chez 179 malades qui n'avaient pas de pouls aux artères pédieuses. Au bout de 3 mois, nous avons évalué la cicatrisation de la plaie, en tenant compte de la présence de diabète et d'interventions vasculaires antérieures. Il appert de ces résultats que la simple ablation d'un orteil ou de plusieurs orteils n'est pas recommandée à moins que la circulation dans le pied puisse être améliorée par reconstruction vasculaire ou par sympathectomie, ou par les deux méthodes. Une amputation transmétatarsienne devrait être envisagée plus souvent comme mesure conservatoire pour la gangrène des orteils. L'absence d'un pouls tibial postérieur palpable est une contre-indication formelle à l'amputation de Syme.

GANGRENE of one or more toes is a late presenting feature of patients with peripheral vascular disease. In view of the high mortality rate of thigh amputations,[1] and the fact that elderly patients find it difficult to master the use of a prosthesis, recent reports[2, 3] have stressed the value of below-knee amputations.

There is little information in the recent literature about the results of minor amputations of the foot (toe or toes, transmetatarsal and Syme's)[4-19] in patients with peripheral vascular disease with or without diabetes. Table I summarizes the results recorded in the literature. In addition, Burgess (personal communication, 1973) estimated that in less than 5% of patients with gangrene of the toes due to arteriosclerosis will healing occur after simple toe removal only. Kelly (personal communication, 1973) put the success rate following minor amputation of toes at between 40 and 50%. Also of interest is the text by Gillis,[20] who states that the Toronto school believed Syme's amputation to be an excellent operation, based on the work of Dale[11] and Harris.[21] Dale, however, suggested that he often achieved success in the patient who already had palpable pulses in the foot. Harris[21] stressed the importance of avoiding division of the posterior tibial artery for fear that the flap would slough.

These conflicting reports stimulated a retrospective review of the results of removal of toes and Syme's amputations in peripheral vascular disease from the Toronto teaching hospitals during a 10-year period, 1964 to 1974. It became possible to assess the results of transmetatarsal amputation and to compare them with the results from the available literature.

CRITERIA FOR SELECTION AND DETAILS OF OPERATIVE PROCEDURES

My criteria for selection in this review were as follows:

1. Peripheral vascular disease, indicated by the lack of palpable foot pulses (dorsalis pedis and posterior tibial arteries). Patients with Buerger's disease were excluded because of the confusion about the true nature of this disease.
2. Necrosis or gangrene of one or more toes.
3. Classification of operation as removal of toe or toes, or as transmetatarsal or Syme's amputation.

In addition, the patient may or may not have been diabetic, and note was made as to whether the patient had had recent vascular surgery or sympathectomy, or both, within the month preceding the minor operation.

With respect to the operative results, delay in wound healing implied continued

*From the division of orthopedic surgery, department of surgery, St. Michael's Hospital, University of Toronto, Toronto, Ont.

Reprint requests to: Dr. G. A. Hunter, Division of Orthopedic Surgery, St. Michael's Hospital, 30 Bond St., Toronto, Ont. M5B 1W8.

failure of the wound to heal 3 months after the initial operation. If subsequent revision was necessary 1 or 2 years later—in my experience this is rare—the initial operation was still considered a success.

Sufficient information was available on 208 minor amputations in 179 patients. Five patients had bilateral, minor foot amputations. The operations are enumerated in Table II.

Wound healing was reported as a success or failure 3 months after the initial operation.

Data relating to wound healing at 3 months are presented in Tables II and III. Table III gives the success rate in terms of wound healing for each level of amputation.

Healing in Relation to Diabetes

Long-standing diabetes is commonly associated with a general disorder of small blood vessels, seen as an abnormal thickening of the basement membrane of the capillaries throughout the body.[22]

In the assessment of the "diabetic foot" (Fig. 1) these small-vessel changes have

TABLE I.—SUMMARY OF RESULTS OF MINOR AMPUTATIONS OF THE FOOT RECORDED IN THE LITERATURE

Author(s)	*No. of operations*	*No. (and %) of wounds healed*	*Comment*
	Amputation of Toe(s)		
Kelly and Janes[9]	49	19 (39)	Diabetics and nondiabetics; all had arteriosclerosis
Schlitt and Serlin[10]	21	15 (71)	Diabetics and nondiabetics; all had peripheral vascular disease
Baddeley and Fulford[13]	74	30 (41)	All were diabetics with arteriosclerosis
Bradham and Smoak[14]	15	8 (53)	Diabetics and nondiabetics; most had no foot pulses
Warren and Kihn[15]	10	4 (40)	Diabetics and nondiabetics; details of foot pulses not given
Hunter (present series)	128	42 (33)	Diabetics and nondiabetics; no foot pulses
	Transmetatarsal Amputation		
McKittrick, McKittrick and Risley[4]	145	94 (65)	No mention of state of foot pulses
Warren *et al*[5]	43	27 (63)	—
Pedersen and Day[7]	33	25 (76)	Majority were diabetics; all had peripheral vascular disease
Carney and Goldowsky[8]	10	2 (20)	—
Schlitt and Serlin[10]	9	3 (33)	Diabetics and nondiabetics; all had peripheral vascular disease
Wheelock[12]	336	213 (63)	All were diabetics; healed at 2 years; no mention of foot pulses
Baddeley and Fulford[13]	4	2 (50)	—
Bradham and Smoak[14]	12	4 (33)	Diabetics and nondiabetics; most had no foot pulses
Warren and Kihn[15]	32	16 (50)	Diabetics and nondiabetics; details of foot pulses not given
Schwindt, Lulloff and Rogers[18]	88	55 (63)	Diabetics and nondiabetics; some had foot pulses
Hunter (present series)	26	12 (46)	Diabetics and nondiabetics; no foot pulses
	Syme's Amputation		
Warren *et al*[6]	6	5 (83)	Included 3 diabetics; nonc had foot pulses
Schlitt and Serlin[10]	1	0 (0)	—
Dale[11]	13	5 (38)	Other good results had foot pulses, or surgery was performed for old trauma
Baddeley and Fulford[13]	7	5 (71)	—
Rosenman[16]	13	9 (69)	Included 6 diabetics; no foot pulses
Sarmiento[17]	38	19 (50)	Majority were diabetics; all had peripheral vascular disease
Hunter (present series)	54	15 (28)	Diabetics and nondiabetics; no foot pulses

probably been emphasized too much. In diabetic patients requiring an amputation, loss of palpable foot pulses is common, and histologic studies[23, 24] indicate that the arterial lesion in the limb amputated for arteriosclerosis obliterans without diabetes is not pathologically different from the arterial lesion in the limb amputated for arteriosclerosis obliterans with associated diabetes.

The results of this study (Table III) suggest that diabetics with ischemic feet (i.e. an absence of foot pulses) should not be treated any differently from nondiabetics, when the level of amputation is being considered.

Healing in Relation to Previous Vascular Surgery

This study also suggests that the results of removal of one or more toes were enhanced if vascular reconstruction with or without sympathectomy had been performed during the preceding month (Table II). This improvement in results, however, did not affect patients who underwent amputation at the transmetatarsal level or Syme's amputation.

On physiologic grounds, sympathectomy may be expected to improve the skin circulation for the first 48 hours, but there is no evidence to suggest that it improves muscle blood flow.[25]

Each patient therefore should be assessed for possible vascular reconstruction before minor amputation is performed.

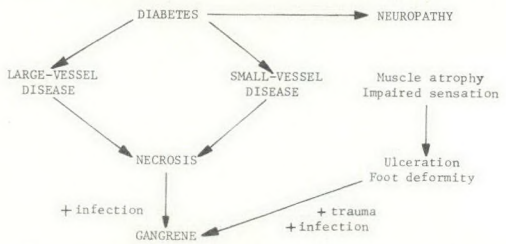

Fig. 1.—Interrelationship of diabetes and ischemia in gangrene of toe.

TABLE II.—WOUND HEALING IN RELATION TO LEVEL OF AMPUTATION

Level of amputation	*No. of operations*	*No. of wounds (and %) healed at 3 mo*
Toe(s)	128	42 (33)
Transmetatarsal	26	12 (46)
Ankle (Syme's)	54	15 (28)

CONCLUSIONS

This survey justifies the following statements with respect to assessment of the level for minor amputations in patients with ischemic feet whose toes are necrotic or gangrenous:

1. Simple removal of the toe or toes is not recommended unless vascular surgery is successful in improving the circulation to the foot before amputation.

2. Transmetatarsal amputation should be more seriously considered as a suitable conservative procedure. Contraindications to this procedure include gangrene of the dorsal or plantar aspects of the foot and severe rest pain in the foot.[4]

3. There is little place for Syme's amputation in a pulseless foot, an observation confirmed by Shelswell[26] and Sarmiento.[17]

My thanks are due to the medical records departments of the teaching hospitals in Toronto. I am indebted to the department of medical arts at St. Michael's Hospital for the illustration.

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TABLE III.—WOUND HEALING IN RELATION TO PRESENCE AND ABSENCE OF DIABETES AND TO RECENT VASCULAR SURGERY

Level of amputation	*No. of operations*	*No. (and %) of wounds healed at 3 mo*	*No. (and %) of patients with healed wounds*		
			Presence or absence of diabetes		*Recent vascular surgery and/or sympathectomy**
			Diabetic	*Nondiabetic*	
Toe(s)	128	42 (33)	13 (31)	29 (69)	27 (64)
Transmetatarsal	26	12 (46)	7 (58)	5 (42)	3 (25)
Ankle (Syme's)	54	15 (28)	6 (40)	9 (60)	2 (13)

*One month before operation.

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SQUAMOUS CELL CARCINOMAS OF THE SKIN OF THE PINNA*

NORMAN J. SHIFFMAN, MD

Summary: Among 52 patients with squamous cell carcinoma of the skin of the pinna seen consecutively between 1952 and 1973, a single course of treatment failed to control the disease in 10 (19%). This failure rate is higher than that usually reported for squamous cell carcinomas of the skin in general (2 to 6%), and appears to be in conflict with the belief that squamous cell carcinomas of the skin of the pinna rarely metastasize. It appears that other factors than neglect are responsible for this discrepancy. In this series it was not possible to judge the relative efficacy of one mode of treatment over another.

Résumé: Parmi les 52 malades atteints d'épithéliome de la peau du pavillon auriculaire que nous avons vus consécutivement de 1952 à 1973, une seule séance thérapeutique n'a pas permis de guérir la maladie chez 10 malades (soit 19% du total). Ce pourcentage d'échecs est plus élevé que celui qu'on a signalé dans les cas d'épithéliome de la peau en général (2 à 6%) et il semble être en désaccord avec la croyance que la tumeur du pavillon auriculaire n'est que rarement l'objet du métastases. D'autres facteurs que la négligence jouent un rôle dans cette divergence. Dans notre groupe de malades, nous n'avons pu juger l'efficacité relative d'un traitement sur un autre.

AMONG white persons living in temperate climatic zones, squamous cell carcinoma of the skin accounts for approximately 20% of all skin cancers. Although the malignant potential of such cancers is somewhat greater than that of basal cell carcinoma, they are generally treated successfully by electrodesiccation and curettage, surgery and radiotherapy.[1] Their malignant potential is indicated in three studies: Williamson and Jackson[2] reported 108 cases of squamous cell carcinoma of the skin, of which 6 (5.5%) showed evidence of metastases; Lund[3] found that 4 of 780 (0.5%) such lesions metastasized; and Epstein and colleagues[4] reported a series of 7000 lesions, of which 2% manifested evidence of metastases at the time of diagnosis.

The incidence of metastases from squamous cell carcinomas of the skin of the pinna appears to be much higher than the incidence reported in these studies.[5] The purpose of this article is to determine the incidence of recurrence or metastases, or both, from squamous cell carcinomas of the pinna and to determine whether this incidence is related to the initial treatment of these lesions.

PATIENTS AND METHODS

The material for this study is derived from the records of 52 patients with squamous cell carcinoma of the skin of the pinna seen consecutively between 1952 and 1973 inclusive, at the Ottawa Civic Hospital division, Ottawa clinic, Ontario Cancer Foundation. The skin tumour clinic at the Ottawa Civic Hospital is a general referral and multidisciplinary clinic, the members of which include a radiotherapist, a plastic surgeon, a dermatologist and a pathologist. The diagnosis in each patient was made by biopsy, and each patient was managed and followed under the direction of the clinic. The majority of patients referred to this clinic are of Irish, Scottish or French descent and live in the Ottawa valley; a large number live in rural areas. There were 50 men and 2 women; their mean age was 73 years (range, 28 to 96 years).

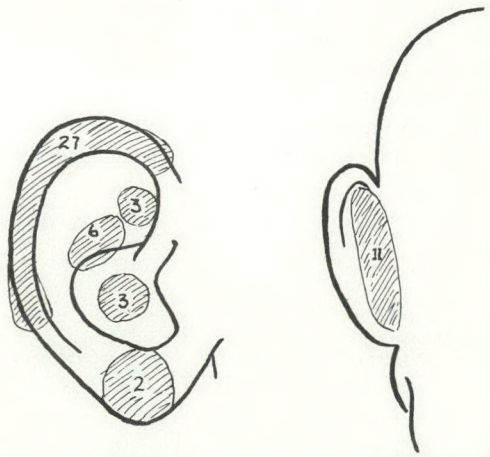

Fig. 1.—Distribution of squamous cell carcinoma of pinna in 52 patients.

*From the Civic Hospital division, Ottawa clinic, Ontario Cancer Foundation, Ottawa, Ont.

Reprint requests to: Dr. N. J. Shiffman, Suite 508, 1081 Carling Ave., Ottawa, Ont. K1Y 4G2.

Results

Distribution and Pathologic Features

The site of the lesion was the left pinna in 30 patients and the right in 22. Of the 52 lesions, the most common site of occurrence was on the helix (27 lesions); the medial aspect of the pinna (helix not included) was the site of 11, the antihelix of 6, the triangular fossa of 3, the concha of 3 and the lobule was the site of 2 lesions (Fig. 1). The greatest diameter of the lesion was less than 2 cm in 31 instances, 2 to 4 cm in 15, greater than 4 cm in 2 and not recorded in 4. With respect to duration, 22 lesions had been present for less than 6 months at the time of diagnosis, 7 for between 6 months and 1 year, 10 for between 1 and 3 years, and 10 lesions had been noted for longer than 3 years; in the other 3 cases the duration of the lesion was not known.

Invasion of the cartilage at the time of diagnosis had occurred in 11 lesions. At this time none showed any evidence of skin, lymph-node or distant metastases.

Treatment and Outcome

The initial therapy was surgical excision in 31 patients, radiotherapy in 2, surgery and radiotherapy in 4, and electrodesiccation and curettage or surgery and curettage in 15. The mode of treatment with respect to size of lesion is indicated in Table I. The period of follow-up was less than 1 year in 15 patients, from 1 to 3 years in 11 and for more than 3 years in 26.

In 10 patients, all men, the initial treatment failed to control the disease. Details of the lesions, the treatment and the outcome are summarized in Table II. Five of the patients were initially treated surgically, four had been treated by surgery and curettage or electrodesiccation and curettage, and one had been treated with radiotherapy. In three of the patients, there was definite evidence of destruction of cartilage at the time of initial treatment. In 3 of these 10 patients there was local recurrence; in 1, lymph-node metastases; in 1, skin metastases; in 2, local recurrence and lymph-node metastases; in 1, local recurrence, lymph-node and distant metastases; in 1, local recurrence and distant metastases; and in the remaining 1, lymph-node and distant metastases. The site of 5 of the 10 lesions was the helix and of the other 5, the medial aspect of the ear. With respect to greatest diameter of the lesion at the time of diagnosis, two measured less than 2 cm, seven had been between 2 and 4 cm and one had measured more than 4 cm. Five of the lesions had been present for less than 1 year at the time of diagnosis and three had been present for more than 3 years; the duration of the other two lesions before diagnosis was not known.

Of the 10 patients in whom the initial treatment failed to control the disease, 4 died as a direct result of their neoplasm, 4 died of unrelated causes with no evidence of neoplastic disease after a second treatment, and 1 died of unrelated causes but had evidence of local recurrence after having refused a second treatment; the remaining patient was lost to follow-up after having received a second course of treatment.

Discussion

Since the publication of the report by Broders in 1971,[6] many authors[7-17] have agreed that squamous cell carcinomas of the skin of the pinna have a worse prognosis than squamous cell carcinomas elsewhere on

TABLE I.—Mode of Initial Therapy with Respect to Size of Lesion

Greatest diameter (cm)	*Initial therapy*				
	Surgery	*Radiotherapy*	*Surgery and radiotherapy*	*Electrodesiccation or surgery with curettage*	*Total*
2	18 (1)*	0	1	12 (1)	31 (2)
2 — 4	9 (2)	1 (1)	2	3 (3)	15 (6)
4	2 (2)	0	0	0	2 (2)
Not recorded	2	1	1	0	4
Total	31	2	4	15	52

*Numbers in parentheses refer to cases of failure to control disease.

TABLE II.—DETAILS OF 10 CASES OF FAILURE OF CONTROL OF DISEASE

Case	Status post-treatment	Age, Sex (yr)	Initial lesion: Size (cm)	Initial lesion: Location	Initial lesion: Duration before treatment	Initial lesion: Mode of treatment	Time Init Trmt to Recur	Comment
1	Local recurrence	88, M	3	Medial surface	4 mo	Electrodesiccation, curettage	2	Ear excised; died of heart failure 3½ yr later
2	Local recurrence	89, M	4	Medial surface	Unknown	Surgical excision	2	Refused further treatment; died of heart failure 2 mo later
3	Local recurrence	96, M	1.8	Helix	10 yr	Surgical excision	8	Widely excised; died of pneumonia 7 mo later
4	Skin metastases to adjacent scalp	84, M	2.3	Helix	Unknown	Surgical excision	18	Retreated with superficial x-ray; lost to follow-up
5	Lymph-node metastases	76, M	4.5	Medial surface	5 mo	Surgical excision	9	Radical neck dissection; died of pneumonia 9 mo later with no evidence of recurrence
6	Local recurrence, lymph-node metastases	96, M	1	Medial surface	10 yr	Surgery, curettage	7	Wedge excision and lymph-node biopsy; died of heart failure 1 mo later
7	Local recurrence, lymph-node metastases	81, M	2.5	Helix	6 mo	Radiotherapy	12	Refused further treatment; died 1 mo later of carcinomatosis
8	Local recurrence, lymph-node and distant metastases	88, M	2.5	Medial surface	3 mo	Electrodesiccation, curettage	6	Explosively malignant despite therapy; died 1 yr later of carcinomatosis
9	Local recurrence, distant metastases	65, M	3	Helix	6 mo	Electr odesiccation, curettage	6	Metastasized to brain; died 3 yr later of carcinomatosis
10	Lymph-node and distant metastases	72, M	3	Helix	10 yr	Surgical excision	9	Widespread metastases; died 2 yr later of carcinomatosis

the body surface. A notable contradictory opinion is that of Ash, Beck and Wilkes,[18] who observed that these tumours rarely metastasize. However, review of the literature discloses many problems. Authors of all of the reports, save three, have grouped squamous and basal cell carcinomas together, even though it is well known that they behave differently. Also, most of these authors considered all cancers of the external ear together, regardless of whether they originated in the external canal or on the skin of the pinna. For the purposes of this discussion, only those reports that made it possible to ascertain, with some certainty, which lesions were actually squamous cell carcinomas arising on the skin of the pinna will be considered.

Mohs[10] described 107 cancers of the pinna, of which 52 were squamous cell carcinomas. All of these were treated by chemosurgery. Of 31 patients who were followed for between 6 months and 3 years, 23 (74.2%) were cured. However, 10 patients died of their cancer within 6 months of diagnosis and 23 (44.2%) died as a result of their cancer within 5 years.

Huriez, Lebeurre and Leperre[5] reviewed 75 cases of squamous cell carcinoma of the skin of the pinna, of which 71 were treated. Of the 62 patients for whom there was adequate follow-up, 50 (80.6%) were cured and 12 (19.4%) had recurrence; 8 (12.9%) died of their cancer.

Blake and Wilson[19] reported a series of 81 squamous cell carcinomas of the skin of the pinna. Of the 71 lesions treated surgically, 15 recurred, and of 8 lesions treated with radiotherapy there was evidence of recurrence in 6. The authors noted an overall recurrence rate of approximately 25%, and eight patients died as a result of their malignancy.[19]

The difference in prognosis between squamous cell carcinomas of the skin of the pinna and squamous cell carcinomas on other parts of the skin can be explained in three possible ways: (a) through neglect both by patients, who do not seek medical attention, and by physicians, who do not treat these lesions adequately, the prognosis is worsened; (b) squamous cell carcinomas arising from the skin of the pinna are biologically different from those occurring on the skin elsewhere; and (c) the unique anatomy of the pinna, with its lack of adipose tissue or its lymphatic drainage, or both, lends itself to the early dissemination or inadequate treatment of neoplastic lesions, or to both of these eventualities.

At one time—20 to 30 years ago—most authors accepted the first hypothesis and certainly at that time physicians saw larger lesions (diameter, > 4 cm), some of which had cervical or generalized metastases, or both, at the time of diagnosis. However, in the present series, such was not the case. Of the 52 cases, in only 2 was the lesion more than 4 cm greatest diameter at the time of diagnosis. In fact, 31 of 52 (59.6%) lesions were less than 2 cm in diameter, and there was no evidence of lymph-node or distant metastases when treatment was started.

Even so, there were 10 cases (19.2%) in which the disease was not controlled. In five cases, the lesion had been present for less than 1 year at the time of initial treatment. Of particular interest is case 8 (Table II); treatment, which consisted of electrodesiccation and curettage, was initiated only 3 months after the lesion had been first observed, yet the lesion recurred and metastasized widely within 6 months of treatment. It appears that other factors in addition to neglect must have brought about this poor result.

The mode of initial treatment seemed to have little bearing on the results of treatment in the present series. The data do not allow one to draw conclusions as to the relative efficacy of various forms of treatment. Of the four patients who died as a direct result of their disease, two had initially been treated with electrodesiccation and curettage, one had been treated surgically and one had been treated with radiotherapy. Probably because of their advanced age, many of the patients, including five in whom the disease was not controlled, died of unrelated causes.

A brief comment should be made concerning the paucity of women in this series. Presumably the explanation is the protection that longer hair in women affords the pinna from the effect of actinic rays. Perhaps, with longer hair having become more fashionable in men, this cancer will become less common.

Thanks are due to the office staff of the Ottawa Civic Hospital division, Ottawa clinic, Ontario Cancer Foundation, for their efforts, and to Dr. R. Jackson, without whose enthusiasm and guidance this study would not have been possible.

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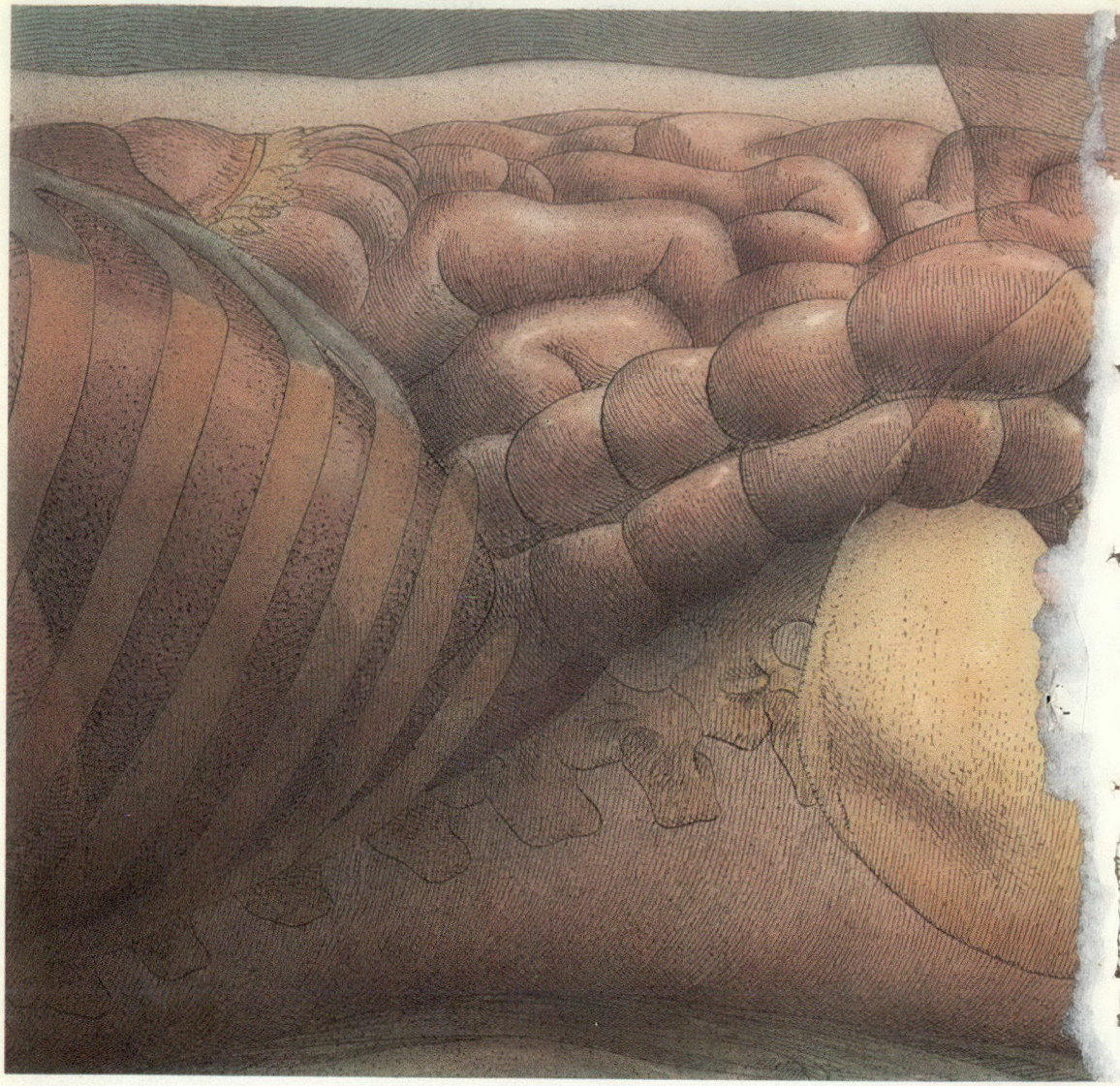
PERITONEAL LAVAGE IN DIAGNOSIS OF ACUTE ABDOMEN

The diagnosis of the acute abdomen may be difficult in the presence of severe, multiple injuries or poor patient cooperation. Examination of the peritoneal fluid is then useful. Paracentesis does not always yield fluid, but peritoneal lavage does.

C. Evans and his colleagues (Br J Surg *62: 119, 1975) used peritoneal lavage in 47 selected adult patients. Routine investigations had been unhelpful. The technique was as follows: Diazepam (10 mg) was injected intravenously and lidocaine (2%) was infiltrated into the abdominal wall. A dialysis catheter was introduced into the peritoneal cavity (usually below the umbilicus, in the midline) and 1 l of saline or other fluid was run in over 5 to 10 minutes; after a further 10 minutes it was drained. Aliquots were tested for bacteriologic and biochemical abnormalities. Fluid was normal if it was sterile and contained less than 0.1 x* 10^{12} *erythrocytes per litre and less than 100 Somogyi units of amylase per decilitre. Peritoneal lavage confirmed the clinical diagnosis in 34 of the 47 patients; in 11 it was of positive value, correcting an erroneous diagnosis, and in 2 the results were misleading. Lavage can only be used for determining the presence or absence of intraperitoneal bleeding or inflammation, not the cause itself.*

Peritoneal lavage was used for diagnostic purposes in a large series of patients with multiple trauma by W. Gill and colleagues (Br J Surg *62: 121, 1975). Bloodstained fluid was an indication for laparotomy; 299 of 671 patients examined were in this category. In 89% of the 299, surgically significant lesions were found and in 3% the results of laparotomy were negative. Considering the whole series of 671 patients, false-positive results were reported in 0.11% and false-negative results in 0.03%. These authors rely on peritoneal lavage in the initial evaluation of the abdomen in cases of blunt trauma and have had no cause for regret.*



an emerging problem

"Bacteroides species are often overlooked as a cause of serious infection both by clinicians and microbiologists. They are most commonly associated with intra-abdominal and pelvic sepsis following gastrointestinal surgery."

Tracy, O., et al. (29 Jan.'72).
Brit. med. J., p. 280.

"Our experience with this series of seriously ill patients provides clinical confirmation to complement recent in vitro evidence that clindamycin is the antibiotic of choice for use in bacteroides infections. Not only was the response in 17 of the 18 patients favourable, but in several it was dramatic."

Haldane, E.V. and van Rooyen, C.E. (1972).
C.M.A.A., p. 1177.

DIAGNOSIS OF TORSION OF TESTICLE BY ULTRASOUND

Because delayed or missed diagnosis of torsion of the testicle may result in necrosis, accurate diagnosis is important. The diagnosis may be obvious but, especially when epididymitis or torsion of the appendix testis is suspect, it may be difficult. A diagnostic technique based on ultrasound may then be useful.

On the basis that the distinguishing feature of torsion of the testicle is loss of blood flow, B. J. Levy (J Urol *113: 63, 1975) used the Doppler ultrasonic stethoscope to evaluate blood flow and thus diagnostic accuracy. With this instrument the intensity of the sound is proportional to the blood flow. The technique is this: The testicle is auscultated systematically, starting behind the testicle directly over the testicular artery as it enters the testicle. The normal side is the patient's own control. The Doppler stethoscope was used in seven patients in whom testicular torsion could not be excluded. In each of the three patients with torsion subsequently proven surgically, the ultrasonic stethoscope gave a correct preoperative diagnosis. In the two who had proven epididymitis blood flow was greater on the affected than on the healthy side, and in the two patients with proven torsion of the appendix testis blood flow was similar on both sides.*

A surface ultrasonic probe connected to either a rate meter or an earphone was used by J. F. Pedersen, H. H. Holm and T. Hald (J Urol *113: 66, 1975). These authors used the Doppler principle in 4 adults and 1 newborn with suspected torsion of the testicle, 10 adults with unilateral epididymitis and 30 control patients without intrascrotal disease. In those with acute torsion no sounds emanated from the affected testicle; in those with epididymitis the sounds were increased on the affected side; and in the controls the sounds were equal on both sides.*

The diagnostic technique is simple and accurate. It might be useful in other clinical disorders as well, such as arterial embolism and thrombosis, and venous thrombosis.

HISTORY OF MEDICINE

INFLUENCE OF THE EDINBURGH MEDICAL SCHOOL ON THE EARLY DEVELOPMENT OF McGILL UNIVERSITY*

MAURICE EWING, FRACS†

IT would be surprising if an Edinburgh medical graduate, walking up to the entrance of the Royal Victoria Hospital, Montréal, for the first time, were not immediately reminded of home. Here is the Royal Infirmary, Edinburgh, all over again—the same proportions, the crow-step gables and the same grey enduring stone. Even the turrets are so similar from without that they must surely conceal within the domestic plumbing so well known to all who have explored the intimate recesses of the buildings of Lauriston Place. Needless to say, none of the long, open wards of Florence Nightingale's day still serve their original purpose; a discreet glimpse through the ground floor windows of the east wing, sadly reveals, instead of the familiar orderly row of iron bedsteads with red blankets and well-worn sheets, tucked in with military precision, only dreary stacks of hospital records. The top floor of what used to be the old medical wing has, however, been cleverly converted into a warren of laboratories, which serve the department of surgery; and here (and this is a familiar story) work is done of an excellence that matches, in no way, the cramped and shabby environment.

Even if the resemblance between the Royal Victoria Hospital and the Royal Infirmary is fortuitous, it is no accident that the Edinburgh medical school has had an important influence, not only in the establishment of medical teaching at McGill University but also in shaping the development of the entire University during the first 25 years of its existence.

* * *

The story of the early years of McGill University is fascinating, and it is not surprising that this period should have been assiduously examined and faithfully recorded by many historians and archivists, both professional and amateur. In this respect, no one was more diligent and more productive than Maude Abbott. She was for many years curator of the Pathological Museum at McGill, where she prepared an exhaustive dossier of cardiac anomalies—a contribution that not only established her personal reputation in the field of cardiology but also provided a valuable starting point for those who later became committed to the surgical correction of congenital heart disease. Her industry and enthusiasm in recording the early days of the teaching of medicine in Montréal have assured her of an important place among the medical historians of North America.

When I arrived in Montréal, early in 1974, to spend part of my sabbatical at McGill University, my host, Dr. Lloyd MacLean, being aware of my antecedents, not surprisingly mentioned the close links joining the University of Edinburgh with McGill University. In view of my plan to spend the second leg of my journey in Edinburgh, it seemed proper that I should explore this interesting historical association.

EARLY 19TH CENTURY AND DEVELOPMENT OF MEDICINE IN MONTRÉAL

At the beginning of the 19th century, the right to practise medicine in Lower Canada (now the province of Québec) depended on the granting of a licence issued by the governor, on the recommendation of a district board of examiners (of which there was one in Montréal) composed of a group of doctors of known integrity. Provision of an adequate number of well-qualified doctors to meet the needs of a rapidly expanding community was obviously a matter of some concern. It was, however, inevitable that, as the province grew in size and in importance, possession of a

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*Presented to the faculty of medicine, University of Edinburgh, Edinburgh, Scotland, December 1974.

†James Stewart professor, University of Melbourne, Melbourne, Australia.

Reprint requests to: Dr. M. Ewing, Department of Surgery, University of Melbourne, Royal Melbourne Hospital, Melbourne, Victoria 3050, Australia.

university degree should become a prerequisite for licensure. For this reason, most of the doctors who were admitted to the register were migrants, in possession of a degree from one of the British or, less often, continental, medical schools. Although a young Canadian who wished to shape a career in medicine could complete part of his apprenticeship in his own country, he was at some stage required to go overseas in order to obtain a university degree. This must have been both a demanding and an expensive undertaking. The crossing of the Atlantic, even in summer, could be hazardous. None the less many of these young men found their way to Europe and more particularly to Edinburgh, which appeared to have an almost unlimited ability to cater to the needs of the large numbers of students who came not only from other parts of Scotland and from the rest of the United Kingdom, but also from the Caribbean, from India and from North America.

During the war years, between 1812 and 1814, the numbers of migrants diminished, but the numbers arriving in Canada increased sharply thereafter, when there was a fresh exodus of emigrants from the old country. Needless to say, the move across the Atlantic was not easy, certainly for those with few material assets, and this was true of most. Often, having arrived in Montréal at the start of the Canadian winter and physically exhausted by the privations of the journey, they found themselves at the mercy of a predominantly French society at a time when outdoor work was out of the question, and when there was little or no suitable indoor employment. The newcomers suffered cruelly from inanition and disease. The only hospitals available were those run by the Roman Catholic Church and, in the face of spiralling numbers, it was evident that l'Hôtel-Dieu, which was the first hospital to be established in Montréal, was unable to give room to all those presenting. The problem was most acute for the English-speaking, predominantly Protestant community. When, at last, the privations of the newcomers were recognized, it was this group that set up, in 1816, the Female Benevolent Society "for the distribution of charity and the establishment of a school where the children of the poor could be taught that the fear of the Lord is the beginning of wisdom". As part of a program of charity, the society rented a "house or refuge" in the suburb of Recollet, just to the south of the old city. As a result of the exertions of the deputy commissioner general, members of the society obtained some condemned barracks clothing and with such slender resources they were able to accommodate four patients in the care of Dr. T. P. Blackwood, a retired army surgeon, who gave his services gratuitously.

The scheme, set up as a pilot project, was judged to be an immediate success. Plans for a more realistic expansion of the hospital services were then prepared and put before the government of Lower Canada and the people. In 1819 a new house was rented, this time within the city itself (on Craig Street); its greatly expanded facilities allowed the accommodation of 24 patients in three wards. This house was named the Montreal General Hospital and such was its success that the building of the central block of a new hospital was completed only a year later. This was the genesis of a great teaching hospital with an impressive record in scholarship and in patient care.

The first medical officers of the Montreal General Hospital were a group of five and their names—Robertson, Caldwell, Stephenson, Holmes and Loedel—are written large in the annals of McGill University.

When these men had first begun to recruit interest in the establishment of a new hospital they already had in mind the urgent need to make provision for the training of medical students. During their long association with the Montreal General Hospital and with McGill University, the members of this group never set this purpose aside, although they ran into serious opposition on that account. In fact, when the new hospital building had only just been completed, they made the bold decision to set up what they proposed to call the Montreal Medical Institution; and with this in mind they petitioned the Governor General, the Earl of Dalhousie. They pointed out the inadequacy of medical skill in Lower Canada, the demands made by students for an opportunity to study medicine and the existence of good facilities for clinical teaching at the new hospital. At the same time, they petitioned the Governor General to remodel the board of examiners of the district of Montréal so

that it would consist of the medical officers of the proposed new Montreal Medical Insitution. This was an astute move which was certain to give them authority in realizing their educational ambitions.

Dalhousie promptly accepted both of these requests. The institution became active without delay, opened rooms in St. James Street and advertised, in the daily press, a comprehensive course of lectures, which they immediately implemented. A library was added in 1824. Although the number of students attending in the early years was not large and although there was no hint of financial reward, it is clear that all of them continued to honour their declared purpose so assiduously that the original momentum of the enterprise was sustained and its ultimate success ensured.

James McGill

One of the leading citizens of Montréal of this era, James McGill died in 1813; the provisions of his will had an important influence on the progress of post-secondary education in that city.

James McGill had been born on Oct. 6, 1745 in Glasgow, Scotland, where his father plied his trade as a blacksmith. Old McGill must have had some ambition for scholarship; he entered the University of Glasgow at the age of 12 but left soon after, not surprisingly without a degree. Believing that he could discover for his family a life of greater opportunity in North America, he came with his two sons and eventually settled in Montréal. Being a Scot by birth and a Jacobite by inclination (evidently the sympathy of the family was with Prince Charles and at least one member fought at Culloden), he found himself on good terms with the French businessmen and through this association James, his son, became a fur trader.

Having served an apprenticeship in the rigours of trapping on foot and by canoe, young James graduated to a more secure and more comfortable existence as a middleman exporting the pelts overseas. He became a citizen of consequence and a member of the executive council of the province, and, during the alarms of 1812, was appointed colonel in charge of the city militia, and responsible for the defence of Montréal against the Americans. He came to own a house of distinction at the end of Place Jacques Cartier in the old city, a historic home that unhappily no longer stands. But more important was his acquisition, in 1798, of a parcel of land of about 46 acres on the north side of the city. It was partly cultivated and its upper boundary came close to the lower slopes of Mont Royal. A small stream that crossed the east boundary just north of what is now the main east entrance to McGill University was joined by a second and then described a wide curve through the property. Little wonder that McGill called the property Burnside, a name that is still commemorated on the sign of an adjoining city street. It was already a place of some historical importance, for it marked the site of an Indian settlement where Jacques Cartier, the discoverer of the St. Lawrence, first parleyed with the Hochelaga Indians.

McGill was buried in a city cemetery, but later his remains were brought to the university and reinterred, appropriately, in the middle of the campus.

Origins of McGill University

In his will, McGill had provided for the establishment of a university or college for the advance of learning in Lower Canada. The value of the land (on which there was also a house or cottage) was £5000, but to this McGill had added another £10 000 in cash. Among the clauses in his will was that requiring one college to be named and perpetually be known and distinguished by the appellation "McGill College".

Also he directed wisely—as it soon became evident—that the purpose of his benefaction should be achieved within 10 years of his death (i.e. by 1823); it would otherwise revert, *in toto,* to his heir in law or to his successors. The estate, meantime, was to be made over to the "Royal Institution for the Advancement of Learning". Although the creation of this body had been contemplated by those in government in 1801, there was more than a suggestion that this was a noncommittal notice of intent aimed mainly at placating public opinion. Action in relation to its implementation was precipitated by the need to safeguard the McGill benefaction and it was, at long last, constituted in 1819.

Another 2 years were spent in seeking the royal charter from King George III.

This was finally granted in 1821 by King George IV. Time was running out for the trustees and it was apparent that prompt action would be necessary if the conditions of the benefaction were to be honoured.

McGill had (again very wisely) required the appointment of a competent number of professors and teachers to render such an establishment effective and beneficial for the purpose indicated. Sadly, the institution had no money, but, in a hurried move to save the day, a series of nominal appointments was made, of which one of the first was that of a professor of medicine. He was Thomas Fargues, a Canadian and, appropriately, a graduate of the University of Edinburgh, having submitted in 1811, for the degree of MD, a thesis on chorea. He did not not even live in Montréal, but in the city of Québec. Here he enjoyed, in his profession, a position of some consequence and one suspects that the propriety of his shadow appointment to the chair of medicine at McGill must have caused him some embarrassment. It is also highly likely that the trustees recognized the weakness of their case at a time when they still had a legal battle on their hands, and that they were anxious to establish their claim on a more secure basis.

McGill University and the Medical School

In casting around for ways of gaining legal and academic respectability, the trustees of the Royal Institution for the Advancement of Learning were immediately attracted by the claims of the Montreal Medical Institution, which had been going ahead quietly with its declared purpose. There was no question of the soundness of the credentials of the group, for the University of Edinburgh had already agreed to accept, as condition for the admission of a candidate to the degree of medicine, a class ticket from the institution, although, to be sure, the rate of exchange was in favour of the University of Edinburgh on a two to one basis. With this in mind, the members of the Montreal Medical Institution were invited to the first meeting of what was to become the Burnside University of McGill College. It was held in Burnside Cottage in June 1829, when the important decision was made to "engraft" the Montreal Medical Institution on to the university as its medical faculty. Perhaps the trustees were urged on by the medical profession and by their friends, and no doubt their action was in some degree conditioned by the urgency of the situation. It is, however, unthinkable that the final judgment was not made on the basis of acknowledged academic excellence. It must therefore have been a source of immense satisfaction for the administrators of the new university that, on the day of the inauguration, the University of Edinburgh promptly amended the prevailing rate of exchange and agreed to accept, for its degree requirements, a class ticket from McGill as being of precisely the same value as one from its own medical school.

Only one chair was created at the university, that in medicine; appointed to it was William Robertson, a distinguished and respected senior member of the profession.

Loedel stood down from the faculty soon thereafter, but the other four—Robertson, Caldwell, Stephenson and Holmes—continued loyally and effectively to direct medical education, both in the Montreal General Hospital and in the university. They did

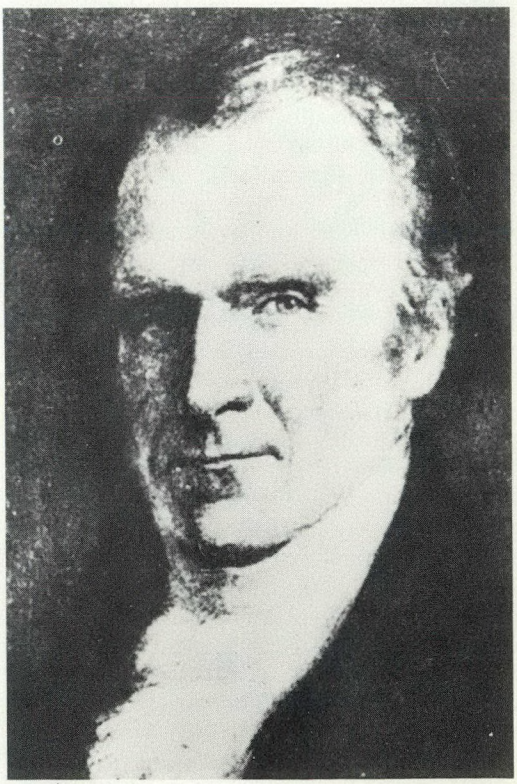

Fig. 1.—William Robertson.

more than that, for they can properly claim not only to have established a medical school but also to have initiated and sustained McGill in the first 25 years of its history, during which time medicine was its one and only faculty. Further, they appear to have achieved this noble purpose without any hint of domestic dissension and without any hint of professional or of community conflict.

William Robertson (Fig. 1)

Robertson, in terms of experience, was the senior member of the group. He was born in Kindrochet, Perthshire, Scotland in 1784 of a well-known highland family. Of his education he is reported to have said that he "went to school young, under the tuition of a country dominie and got on as well as highland laddies usually do". At the age of 13 he became an ensign of a highland regiment, but he still graduated in medicine at the University of Edinburgh before he was 21. He joined the army as an assistant surgeon. He served in the war of 1812 and was present at the battle of Queenston Heights and also at the storming of Fort Niagara. In 1815, at the age of 29, he resigned from the army on half pay and settled in Montréal, where he became one of its leading practitioners.

Fig. 2.—William Caldwell.

William Caldwell (Fig. 2)

William Caldwell, like Robertson, began his medical career in the army. He, too, was a Scot, born in Ayrshire in 1782. He studied medicine in Edinburgh between 1801 and 1803, but for some reason, which is obscure, he received his degree by attestation from Marischal College in Aberdeen. He arrived in Montréal in 1819. Although he contributed to the care of the sick in the city of Montréal, his contribution to the development of the Montreal General Hospital and of the McGill University medical school is best remembered by an exciting duel at Windmill Point on l'Ile Perrot on the morning of Sunday, Apr. 11, 1819. The original petition to the government of Lower Canada seeking the development of a new hospital had been blocked by O'Sullivan, an Irish-born attorney at law, who challenged it on the ground that the situation could be solved more promptly, more effectively and more economically by simply enlarging l'Hôtel-Dieu. This seemed to most moderates to be a reasonable suggestion. Unfortunately, he went on to contrast the service of the nuns of that institution with the "mercenary hirelings" who would presumably be appointed to the staff of the proposed new hospital. This was a thoughtless remark that immediately upset the promoters of the new hospital, prominent among whom were the doctors.

The dispute was debated in the press and matters went from bad to worse; many harsh words were spoken on both sides. Then O'Sullivan's personal courage was called into question with the inevitable consequence. The pistol duel was fought with exceptional tenacity that seems to have been no surprise to those who knew the temperament of the two contestants. It was only after the discharge of five exchanges that honour was deemed to have been done. By now, Caldwell was wounded in the arm and "the bone much shattered", and O'Sullivan was wounded in the chest; and when we recall that they were were firing 1-oz bullets, it is surprising that they both survived.

After the duel, the original petition to the

government lapsed, but the development of the hospital was already assured by enthusiastic public support. Caldwell had fought his duel in defence of an important principle in medical education, and when his antagonist blocked the proposal for the creation of a new hospital, he challenged it most vigorously on the score that its promoters planned to make it a place for the "perfection of medical science", an objective that implied, as a prime consideration, the admission of medical students. O'Sullivan is reported (in the Hansard of that day) to have said in debate that a hospital contributed to that perfection, because no doubt it afforded the best opportunities to make experiments—and one of the consequences of the perfection of medical science would be to render the hospital totally insufficient for the public wants. Since then, many others have resisted the legitimate development of teaching hospitals using precisely the same argument; namely, the role of a hospital in the training of young doctors cannot be reconciled with its primary function in patient care. Happily, this view did not prevail, and it must have been for Caldwell a matter of immense satisfaction that the teaching of students was, from the very beginning, a primary aim of the Montreal General Hospital. Its purpose was quite clearly defined: it was "for the care of the sick and the advancement of medical knowledge through teaching and research".

O'Sullivan became chief justice of the court of the Queen's Bench in Montréal. Caldwell became one of the staff members of the faculty of medicine. He died of gangrene of the lung in the winter of 1832/33, only a few months before the medical school capped its first graduate, William Logie, a man evidently of Scottish descent.

John Stephenson (Fig. 3)

Stephenson was a born leader. It was he who prepared the proposal for the creation of the Montreal Medical Institution. He became its first secretary and it was appropriate that he delivered the first lectures on anatomy and physiology in October 1822. Later, his administrative skill was acknowledged when he was made the first registrar of the university. He was born in 1794 in St. Paul's Street, Montréal, the narrow busy street that still runs east and west along the length of the old city. His parents, from a Scottish family, were among the first English-speaking settlers in Lower Canada. Although he was never a Catholic, he received much of his early education from the priests of the Collège de Montréal; later he accepted appointment as a physician to the order of St. Sulpice. He was then apprenticed on payment of a fee of £50 to Robertson, the first professor of medicine, who gave him an excellent report when he went on to study in Edinburgh and later in Paris.

In Paris he worked assiduously for 6 months under the direction of Dr. Roux, one of the leading surgeons of his time. It was when Stephenson was just about to return to Edinburgh to receive his degree that Roux, in an unsolicited consultation (it seems that it was the first time Stephenson had spoken to his teacher), discovered that his young pupil had a median cleft in his soft palate. Stephenson, beset with grave feeding difficulties in infancy, had been left with a gross speech defect, which, on the basis of a rather casual examination by the family doctor early in life, had been ascribed

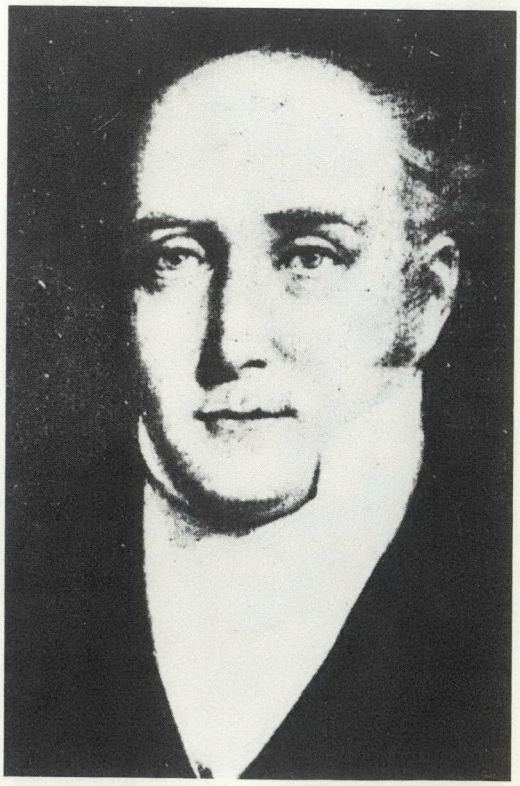

Fig. 3.—John Stephenson.

to infection; there was more than a suggestion that it was syphilitic in origin, as his brother was similarly affected. Stephenson was anxious to explore the possibility of operative repair of the deficiency and Roux was equally receptive to the idea. Stephenson's return to Edinburgh was deferred and the operation was carried out a few days later. It was completed in 1 hour and without anesthesia. It was conducted in some secrecy for it was the first time that Roux had attempted the operation and he was somewhat fearful of the outcome. However, it was a great success and Stephenson was able to give a personal account of it to the members of the Royal Institution of Paris on the 13th postoperative day, before leaving the next day for the long trip back to Scotland. Not surprisingly when, in 1820, the name of Jonnes Stephenson appeared in the list of successful candidates for the degree of MD in Edinburgh, the title of his thesis was "De Velosynthesis". (The fascinating story of this important landmark in the evolution of the operation for cleft palate has been delightfully told by Wallace.[1, 2]) Stephenson returned to Montréal where he built up a large surgical practice. He was a man of great scholarship and he was much influenced by recollection of the kind of educational experience he had enjoyed when he studied in Europe. His nephew was to say later:

"He was very much aware of the absence of that literary and artistic culture and society which had become almost necessary to him and the absolute dearth then existing of educational establishments for the English speaking portion of the community, that he resolved to do, what in him lay, to serve those for his countrymen and devoted himself for the first year of his return, to procure them that advantage."

Fig. 4.—Andrew Holmes.

Andrew Holmes (Fig. 4)

Holmes, the fourth member of the group, was undoubtedly the best scholar of them all. In the list of graduates in medicine of the University of Edinburgh for the degree of MD the entry reads as follows: "Holmes, Andreas F. Americanus de Tetano". His middle name was Fernando and this no doubt records the accident of his birth in Cadiz in 1797. His parents had been taken there as prisoners, when captured by a French frigate while sailing to Canada on a British ship. Four years elapsed before the family was allowed to continue its journey to North America, settling first in Québec and later in Montréal. Here he received, at the school of Dr. Alexander Skakel, the formal training in the classics that was then a prerequisite for a career in medicine.

Dr. Alexander Skakel had been born in Fochabers in Banffshire in 1776, graduating as an MA in Aberdeen in 1797. He started the Montreal Classical and Mathematical School, which came to enjoy a notable reputation. Perhaps his career is relevant to the development of McGill University. He emigrated from Scotland with John Strachan, a Presbyterian who later joined the Anglican Church and became the bishop of Toronto. Both Strachan and Skakel became close personal friends of McGill and are believed to have played an important part in encouraging him to leave his estate for the establishment of a university. Skakel later became the first chairman of the Montreal General Hospital. His scholarship was acknowledge by the bestowal of an honorary LL B of the University of Aberdeen, and his success as a dominie was evident from

the size of his estate (£15 000), all of which he willed to the Montreal General Hospital.

But to return to Andrew Holmes. At the age of 14 he was articled to Dr. David Arnoldi, perhaps the most prominent man in his profession in Lower Canada. It was apparent, however, that Holmes had ambitions to progress further in his profession and he went overseas to join Stephenson, with whom he then studied in Edinburgh, in Dublin and in Paris.

While in Edinburgh, he made a notable collection of the local flora and because of his interest, not only in botany, but also in gemmology and geology, he was, in 1818, made a member of the Edinburgh Physical Society. In July 1819, on the eve of his departure, he was afforded the rare privilege of being elevated to extraordinary membership in the society.

On his return from overseas, Holmes made moves to incorporate the Natural History Society in Montréal and made a comprehensive collection of 500 plants illustrating the flora of Montréal. Between 1822 and 1838 he collected about 4000 geological specimens, all of which he made over to the Redpath Museum at McGill University Among them was what he believed to be a new mineral, a brittle mica consisting largely of magnesia, which he had discovered in Amity in New York state. This was submitted to Professor Thompson in Glasgow who suggested that it should be called holmesite. Later, however, it became evident that Holmes had been beaten to the post by a Swiss geologist who had reported his discovery only a few weeks earlier. Although dispersed widely in the Redpath Museum, Holmes' collection still forms a valuable reference to the geological configuration of the city of Montréal, because access to most of Montréal's geological structure is now denied by building development.

He taught chemistry in the university until 1843 when, on the death of Robertson, he was appointed to the chair in medicine. Although Holmes became the first dean of the faculty in 1854 and although he played a prominent part in the development of the Lying-in Hospital, he never seems to have become involved in the rough and tumble of medical politics, but continued rather to foster his scholastic pursuits.

Holmes made several modest contributions to the medical literature of his time. Early in his career he reported a case of vagitus uterinus.[3] He lived through the agonies of the cholera epidemic that struck Montréal in 1833 and literally decimated its population of 30 000; on June 19 of that year there were no fewer than 149 burials. Later, he answered a series of questions directed to him by a Dr. Patel of Philadelphia and the correspondence between the two was published in the form of a paper in the *British American Journal*. This incorporated, in Holmes' contribution, an excellent account of the clinical appearance of a patient with cholera. He had tried the intravenous use of salt and water in six patients, five of whom died. One, who survived for 8 days, died from "an oppressed brain". Of bloodletting, he had nothing good to say; it was evident that he had, under these circumstances, the greatest of difficulty in recovering any blood at all.

Holmes was, in every sense, a great scholar. MacCallum, who was a student at McGill in 1847 and who was later to occupy the chair of obstetrics and gynecology, saw him as a person with a quiet voice and little animation. He was, however, impressed by his vigorous and lucid style of which his valedictory address to the students at convocation in 1854 is a good example:

"There are two errors to be avoided: an overweening preoccupation that we are very wise, which leads to dogmatism and quackery; and want of self reliance, which leads to inefficiency. In our approaches to one or other of these errors, a great deal will depend on temperament; both of them, however, lead to one result, a system of routine—the one asserting the supremacy of its knowledge, will not condescend to alter; the other, fearful of untried consequences, prefers the beaten track. Routine is not the part of a scientific physician whose decisions and directions should always have a basis of reason."

This was the good advice he gave to his students on another occasion (a message that he passed on almost 125 years ago):

"If I have succeeded in impressing you with the propriety of not lagging behind any advance which your profession is continually making, I shall point out to you one easy means by which you may always know what is going on in the world of medicine. It is to

take *one or more* of the periodicals which are now so numerous and so low priced that no-one is justified in remaining in ignorance with so easy a method of acquiring information. Many of you no doubt will fix your residences in country parts where you may have little opportunity of communion with other practitioners and you will therefore be very likely to become 'rusty' in regard even to the knowledge which you now have and much more in regard to that which is being developed every day. The best way of preventing this is to take a periodical whose pages contain a condensation of the mass of new matter which is monthly and weekly poured upon the profession. The practice of reading such work may have another benefit; it may stir you up to communicate the results of your own experience and many valuable facts and observations may thus be saved and rendered useful; and hereby you will be fulfilling, in some measure, the duty which I passed upon you namely, that of becoming a credit to the University."

It is appropriate that the Holmes medal, which was cast in his honour in 1864, is now given each year to the student who gains most marks in all subjects of the curriculum.

Holmes died suddenly at his desk while preparing papers for a faculty meeting. The obituary notice in the local medical journal curiously included, in addition to the customary eulogies, the full autopsy report. Although decomposition had already set in, we are told that all of the members of the faculty of medicine faithfully attended the autopsy, no doubt as a somewhat macabre expression of interest and sympathy—yet a gesture that today would require an unreasonable degree of academic solidarity.

This, then, was the band of relatively young men who staffed the new Montreal General Hospital, who recognized the need to make provision, in it, for the instruction of students of medicine, who formally established the Montreal Medical Institution, who were engrafted on to McGill University as the faculty of medicine and by whose efforts McGill University can properly claim to have been initiated and sustained in the first quarter century of its existence. It is a wonderful story of the birth of a tremendous enterprise from a small beginning. Robertson and Caldwell knew of the opportunities presenting in the old world, and Stephenson and Holmes recognized clearly, from their own personal experience, the difficulties with which young Canadians were confronted in shaping a career in medicine. But from the way the four set out to achieve their purpose, it is evident that they were primarily urged on by the high rating that they all gave to education and to scholarship. It would be satisfying to believe that their sense of values was determined, at least in part, by their period of stay in Edinburgh. It is certainly true that they kept reverting to their common experience and that they must have valued highly, the system of instruction that prevailed in the Royal Infirmary of Edinburgh. From the very beginning students were to be admitted freely to the wards for teaching and for study and there they "followed the methods of Edinburgh, making clinical instruction at the bedside an integral part of hospital routine and an essential feature of the curriculum".

They were also influenced a good deal in their early decisions by the lessons of history, because in paragraph 5 of the original petition for the creation of a new hospital, they noted:

"v. They are further encouraged to attempt the founding of a medical seminary when they reflect that the Medical School of Edinburgh, the basis of which they would adopt for their present institution, now justifiably considered the first in Europe, is of comparatively recent formation, it being little more than one hundred years since medical lectures were first delivered in that city and the early history of the Royal Infirmary of Edinburgh is not dissimilar from that of the Montreal General Hospital."

It is certainly true that, from the time of the opening of the Royal Infirmary of Edinburgh in 1741 or thereabouts, students enjoyed the privilege of attending patients in the hospital; and it was the urgings of the extramural school, the acknowledged shortcomings of the systematic instruction within the university, and the existence of a hospital designed to cater for the needs of medical education that finally provoked the university to accept the responsibility for the formal direction of the clinical subjects in the curriculum.

A Continuing Relationship

As an index of the continuing interest of

McGill University in the University of Edinburgh, the former adopted, in 1842, the *Sponsio Academica*. This was introduced in 1803 by the University of Edinburgh as the declaration of faith and purpose of the students graduating in medicine and represented a modified version of the Hippocratic oath.

The role of the University of Edinburgh in the development of McGill University should be for Edinburgh a source of satisfaction. It was fitting that this association should be commemorated by a plaque that was conveyed to Montréal by Professor Donald, dean of the faculty, some years ago. It now occupies a position of honour in the foyer outside the office of the dean on the sixth floor of the magnificent new McIntyre building which houses a considerable part of the faculty of medicine. On it is inscribed:

"This tablet has been erected by the University of Edinburgh as a symbol of the bond between that historic centre of learning and McGill University, and in memory of the founders of McGill University William Caldwell, A. F. Holmes, William Robertson, John Stephenson, all of whom received their training at the University of Edinburgh."

I would also like to believe that this old and close association continues to mean something to the McGill medical school, as, for example, in meeting the challenge thrown out by Archibald Hall, another Edinburgh graduate, when, in his introductory lecture to the class of students in midwifery in 1869, he said:

"in subsequent years, when we are gathered to our fathers, our young men may point to this city, as we do now to Edinburgh and pronounce it, as well from its edifices as from its educational establishments, the modern Athens of Canada".

The author gratefully acknowledges the help of Dr. E. H. Bensley, department of history of medicine, McGill University; the staff of the Osler library at McGill University; and Miss Wardill, librarian at the Royal College of Surgeons of Edinburgh.

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BOOK REVIEWS

ACUTE FLUID REPLACEMENT IN THE THERAPY OF SHOCK. Edited by Theodore I. Malinin, Robert Zeppa, William R. Drucker and Arthur B. Callahan. 307 pp. Illust. Stratton Intercontinental Medical Book Corp., New York; Longman Canada Limited, Toronto, 1974. $27.00.

This multiauthored text (38 papers) presents the proceedings of a conference sponsored by the office of naval research and the department of surgery, University of Miami. Most of the presentations, which were originally given in June 1973, are excellent but a few are irrelevant. Varied and frequently opposing arguments appear throughout the text, especially on appropriate regimens for volume replacement and dangers to pulmonary function.

Despite these limitations, the volume is an excellent summary of the state of the art with particular reference to blood, blood products and other volume replacements that are now or will in the future be useful in the therapy of hypovolemia.

The clinical implications of severe blood loss are discussed in a particularly interesting section. Surprisingly few controlled clinical studies are available to support therapeutic regimens but overall the text is practical and will be useful to clinician and researcher alike. In a calm and organized summary the editors imply that several routes to successful therapy are possible, that good patient care need not be a research project, and that the framework exists for understanding the physiologic derangements of shock particularly those due to hypovolemia. Firm and useful recommendations on therapy are made without controversy. Obvious areas for clinical investigation are highlighted.

L. D. MacLean

Department of Surgery,
Royal Victoria Hospital,
Montréal, Qué.

ADVANCES IN SURGERY. Volume 8. Edited by R. M. Zollinger. 333 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1974. $24.50.

The format of volume 8 of this annual review, which originated in 1967, is unchanged. Recognized authorities in various fields have contributed well-written chapters emphasizing recent advances in surgery.

Nine diverse clinical and physiologic challenges of specific or widespread surgical interest have been reviewed. Five chapters present current concepts of problems encountered in all surgical specialties. The first of these discusses newer approaches to nutritional problems, starting with a presentation of techniques and methods of alimentation (both gastrointestinal and parenteral) and outlining the advantages and complications of each. Common nutritional problems in surgical patients and the various surgical procedures that alter nutrition are considered. The chapter on the effect of halogenated anesthetics on liver metabolism and immune response is particularly well illustrated. Another section deals well with the general principles of radioimmunoassay, specific assays and their clinical relevance. A chapter on daily problems in the intensive care unit is well organized and presented. Practical physiology and also specific problems are clearly outlined. Finally, a review of the diagnosis and treatment of wound failure details the process of wound repair and considers failure to heal and its surgical complications.

Chapters of more limited interest include an expert overview of the role of surgery in duodenal ulcer and comparison of the overall results of standard surgical procedures and their complications. Highly selective vagotomy is considered in detail. Indications for hepatic resection, techniques and postoperative care are reviewed. Pediatric surgery is represented by a chapter on the treatment of biliary atresia. Finally, there is a detailed current assessment of the management of malignant melanoma.

This book has been well edited. Each chapter is well organized and illustrated, with lengthy bibliographies. It is highly recommended reading for all surgical practitioners and students.

K. D. Bury

Department of Surgery,
The Wellesley Hospital,
Toronto, Ont.

BONNEY'S GYNAECOLOGICAL SURGERY. 8th ed. John Hawkins and John Stallworthy. 868 pp. Illust. Baillière Tindall, London, 1974. £11.00. $26.50 (approx.).

Generations of gynecologists are indebted to this classic work on the surgery of their specialty. Its authority and wisdom arise from the tremendous personal experience of the late Victor Bonney, his meticulous observation of the details of operative procedures, and his objective appraisal of his results. It provides a fund of practical advice for every untoward situation and complication. The illustrations (the work of the author himself) demonstrate clearly every step of the operation described.

Some might question the advisability of attempts to keep up to date established texts that have served their purpose in the past. In the present instance any doubts in this regard are groundless. Since the fifth edition the book has been edited by a succession of Bonney's

former associates who have been successful in incorporating current advances in the art without sacrificing the flavour and outlook of the original. The student will find, therefore, ample descriptions of modern methods of investigating and treating stress incontinence, and the techniques of tubal anastomosis and construction of the artificial vagina. Presentation of results from various centres in the United Kingdom indicate changing trends in practice—for example, the popularity of vaginal hysterectomy combined with vaginal repair instead of the former reliance on the Manchester operation to correct relaxation of the vagina and pelvic floor. As one would expect, apologies are offered for including the description of subtotal hysterectomy, and an account of extraperitoneal cesarean section is deliberately omitted.

This book is a superb testimony to the achievements and influence of a master of its subject and of his disciples.

A. W. ANDISON

Ottawa, Ont.

THE CARE OF THE RHEUMATOID HAND. 3rd ed. Adrian E. Flatt. 296 pp. Illust. The C. V. Mosby Company, St. Louis, 1974. $26.00.

There are now six editions of Flatt's two books on the hand. These have become familiar to orthopedists. I refer to three editions of "The Care of Minor Hand Injuries" and now a third edition of "The Care of the Rheumatoid Hand". I did not intentionally link these books together but they all commence with a rather lengthy discussion on anatomy, with many of the now familiar models describing Flatt's own concept of skeletal anatomy and "kinesiology". Like motherhood this is not to be challenged—yet, do many of us *study* it? I imagine surgeons hurry through to the "techniques". As Flatt (like John Masters and Arthur Hailey) seems intent on producing books every year or so it is not surprising that much of this section is copied from edition to edition.

A previous reviewer described Flatt's style as "ponderous prose". This is unjust. This book comprises the very best of English style and open, well-illustrated American medical printing.

In the general section on rheumatology for surgeons there are some interesting individual viewpoints including a play on words, which concludes that rheumatoid skin heals normally whereas the evidence indicates that it may heal badly if the patient has been on protracted cortisone therapy. The section on splinting is worth close study. It should be noted that dynamic splints alone will not prevent deformity for long. (Rheumatologists in particular should be compelled to read this book before being granted their Fellowship.)

Sections on the surgical management of all the common deformities of the wrist, hand and fingers follow. These are exhaustive, detailed accounts of the various techniques for rheumatoid disease in the hand and are intended for the relatively few (in Canada) who have interested themselves in this subject. I was a little surprised to see continued praise for excisional arthroplasty of the elbow. Some of the newer prostheses are giving better results, certainly more stability.

The continuity of the text suffers from interposition of sections on natural history and end-results described in tables of degrees that will have appeal to only a few individuals.

Much space is given to the role of prosthetic replacement of metacarpophalangeal joints versus excisional arthroplasty. The conclusions are still unclear and most hand surgeons would prefer prosthetic replacement with a Silastic insert. Flatt's own metal prostheses are illustrated but are apparently unobtainable and his technique for these joints is not described. I was surprised to see no reference to one of the principal advantages in the use of metacarpophalangeal prostheses — cosmesis. Patients are often delighted by the alignment of fingers although some movement seems to be lost.

Sections on small-joint procedures are discussed fully and are beyond any real criticism.

This volume is probably already in the possession of every hand surgeon. It should be read by all rheumatologists and surgical examination candidates as well. It represents an authoritative review of a subspecialty. The book demonstrates all that is best in a monograph, and the views of others are well presented.

I shall value my copy, refer to it and await its successor.

A. M. WILEY

Department of Surgery,
Toronto Western Hospital,
Toronto, Ont.

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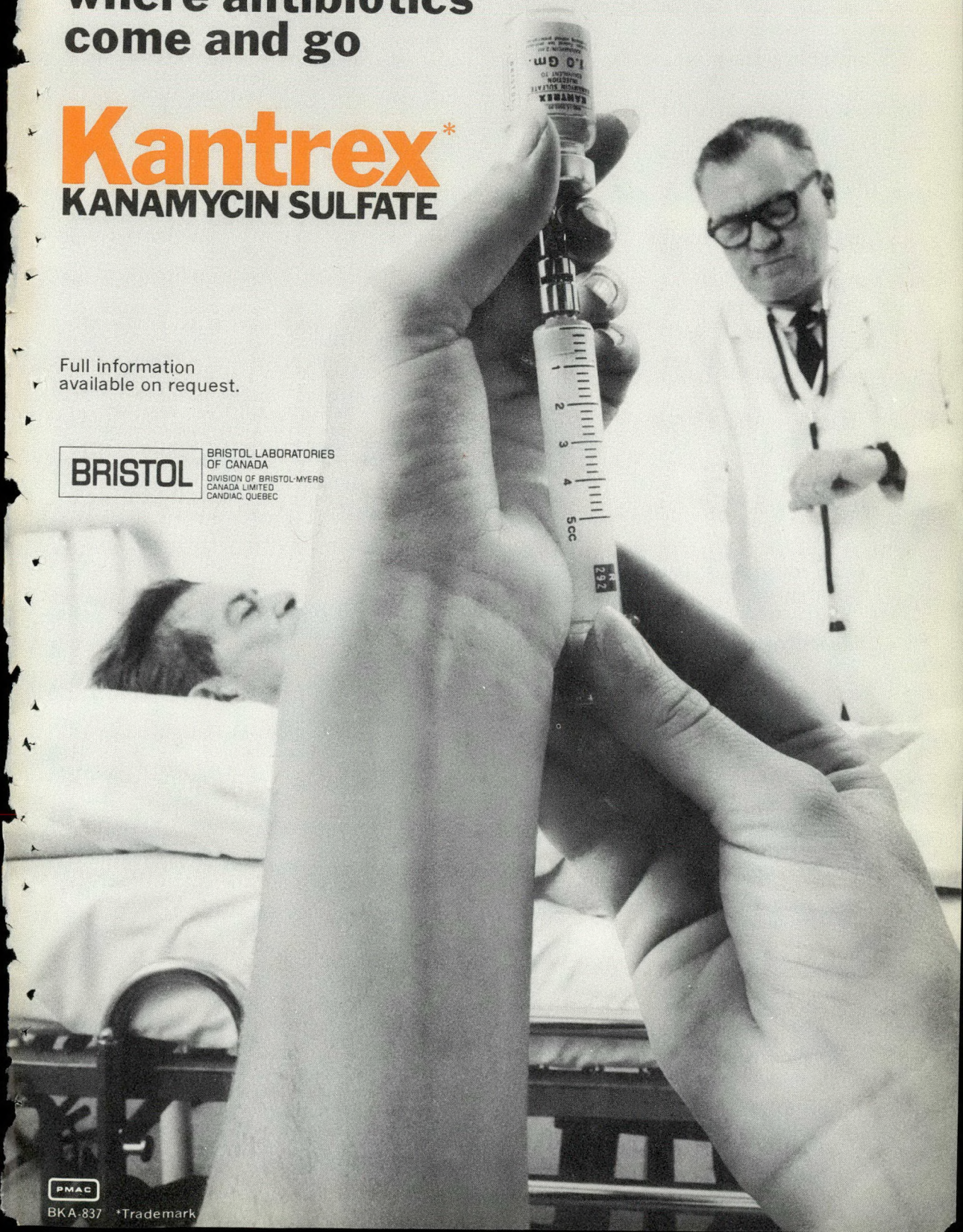

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Vascularization and Tissue Differentiation. F. A. Kiss. 167 pp. Illust. Akadémiai Kiadó, Budapest, 1975. $9.50. Paperbound.

NOTICES

INTERNATIONAL WORKSHOP ON ATHEROSCLEROSIS

An international workshop-conference on atherosclerosis, sponsored by the Ontario Heart Foundation, the Canadian Heart Foundation, the University of Western Ontario and the European Atherosclerosis Group, will be held at the University of Western Ontario from September 1-3, 1975. The registration fee is $50.00. For further information write to: Miss Evelyn McGloin, Director Professional Education, Ontario Heart Foundation, 310 Davenport Rd., Toronto, Ont. M5R 3K2.

INTERNATIONAL SYMPOSIUM ON PEDIATRIC OTORHINOLARYNGOLOGY

The Children's Mercy Hospital of Kansas City, in cooperation with the University of Missouri-Kansas City School of Medicine and the Southwest Pediatric Society, will hold an international symposium on pediatric otorhinolaryngology from September 11-13, 1975. Members of the guest faculty are from Europe, the United States, Canada and Mexico. The registration fee is $150.00 for physicians, $50.00 for residents. For further information write to: Dr. B. Jazbi, Chief of Otorhinolaryngology, The Children's Mercy Hospital, 24th at Gillham Rd., Kansas City, Missouri 64108.